FROM THE EDITOR

It is with great sadness that we inform our readers that the Fall 2013 issue of "Digest of Psychiatry and Neurology" was the final issue after 81 years of continuous publication.

When the Digest began, it filled a unique need. We are proud of the global reach and the impact our publication has had; at one time, the Digest mailing list included 25,000 subscribers, with its readership extending not only throughout the United States and Canada but also to Europe, India, Australia, New Zealand, South America and many other regions of the world. Over the years we have heard frequently from readers in third-world countries for whom the Digest was the primary source of continuing medical education. We gave it away for free whenever asked.

In the years since its inception, however, with the advent of new publishing technologies, a myriad of competing newsletters appeared. As our subscriptions steadily declined, we had to reconsider the Digest's role and transitioned to an exclusively electronic quarterly publication in 2001. While we shortened the length of each issue, we hoped to provide greater value by focusing each on a single theme. As in the past, each review consisted of a concise synopsis, absent any editorializing and drawn from the leading English language journals. By publishing on the Institute of Living/Hartford Hospital website, we aimed to maintain two additional traditional values: global outreach and free access.

In the years since 2001, the Digest has been joined by a myriad of electronic publications focusing on behavioral health. The plethora of online resources is such that the number of “hits” to the online Digest has declined steadily and has now reached the point where further publication is unwarranted.

We remain proud of the role we have played in psychiatric education over these many years but also cognizant of the dramatic changes in the availability of information and the way professionals learn. And so, with regret and gratitude, we say goodbye to our remaining readers, wishing you well in your efforts at continuing medical education.

As you will note, our last electronic edition focuses on suicide. This is in keeping with The Institute of Living’s Suicide Prevention Initiative, a major programmatic focus on suicide assessment and prevention that combines new research initiatives, clinical programming and advocacy efforts. This focus is in keeping with our growing concern about the increasing global threat which suicide presents.

One final word of thanks is in order, to Ms. Elizabeth Fishe, M.L.S., who has assisted with the Digest since 1979 and has been our Associate Editor since 1999. We would not have been able to maintain publication without her and we are very grateful for all her efforts.

Harold I. Schwartz, M.D.
Psychiatrist-in-Chief and
Archived Issues: 2013: WINTER | SPRING | SUMMER | FALL
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Harold I. Schwartz, M.D.
Psychiatrist-in-Chief and
Vice President, Behavioral Health
The Institute of Living/Hartford Hospital
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PSYCHIATRIC IN-PATIENT CARE AND SUICIDE IN ENGLAND, 1997 TO 2008: A LONGITUDINAL STUDY
EXPLORING THE IMPACT OF SUICIDE ON CLINICIANS: A MULTIDISCIPLINARY RETREAT MODEL

Sara Figueroa, MD (Univ. of Michigan, Dept. of Psychiatry, 4250 Plymouth Rd., Ann Arbor, MI 48105; e-mail: gsrd@med.umich.edu); and Gregory W. Dalack, MD

J PSYCHIATR PRACT, 19:72-7, January 2013

While the suicide of a patient is a tragic and traumatic event for the patient’s family, friends, and community, the therapists who treat these patients are also strongly affected and may experience a wide variety of emotional responses and concerns, including shock, disbelief, sadness, anger, guilt, blame, and questioning their ability and competence to treat patients in the future. The authors developed an every-other-year, scheduled retreat model for clinicians and trainees in order to explore emotional and professional reactions that may arise after a patient’s suicide. Psychiatry ambulatory clinical staff, residents, and faculty participated in a half-day retreat, which consisted of an opening panel discussion, in which panel members related their experiences of patient suicide; break-out groups; and a final panel discussion. Unlinked pre- and post-retreat surveys were sent electronically to all potential participants.

The pre-retreat survey was completed by 103 clinicians; 20% were trainees or fellows, and 47% of the respondents reported that they had experienced one or more patient suicides. Text responses to the pre-retreat survey reflected the wish to obtain a better understanding of the impact of patient suicide on caregivers, to cope with the event both personally and professionally, and to gain a clearer understanding of what supports were available within the department. The post-retreat survey was completed by 45 clinicians. Comments after the retreat reflected an increased awareness of both the short- and long-term effects experienced by clinicians after a patient suicide. Nearly all of the respondents (98%) felt that the retreat had met its learning objective, with 93% of these clinicians indicating that they would be able to apply the information gained to their professional practices. In all, 87% of those who completed the post-retreat survey reported that they would be willing to participate in a post-patient suicide, grief/loss support group with their colleagues in the future.

The authors conclude that an all-department ambulatory retreat model has value in providing clinicians with support and information in a structured, educational setting in order to help reduce the sense of stigma and provide an increased awareness of the magnitude of the impact on clinicians who experience the death of a patient by suicide. (18 References) EAF
CHRONIC PAIN AND THE INTERPERSONAL THEORY OF SUICIDE

Keith G. Wilson (Ottawa Hospital Rehabilitation Centre, 505 Smyth Road, Ottawa, ON, K1H 8M2, Canada; e-mail: kewilson@toh.on.ca); John Kowal; Peter R. Henderson; Lachlan A. McWilliams; and Katherine Péloquin

REHABIL PSYCHOL, 58:111-5, February 2013

People with chronic pain have elevated rates of suicidal ideation, but few studies of this population have tested specific predictions about suicide risk factors that are derived from theory. The interpersonal theory of suicide attempts to integrate various psychological and social risk factors for suicidal behavior into a general conceptual framework. It proposes that two factors (thwarted belongingness and perceived burdensomeness) contribute to the psychological context that leads to the desire to commit suicide. The present authors tested this hypothesis in a clinical sample of patients suffering from chronic pain.

A total of 303 patients (114 men, 189 women; mean age, 47.4 years) enrolled in a chronic pain rehabilitation program completed measures of pain severity, duration, and disability; cognitive-affective measures of depression and catastrophizing; and interpersonal measures of relationship distress and self-perceived burden to others. The latter measures were included as indices of the belongingness and burdensomeness constructs. The participants also rated two items pertaining to suicidal ideation. The patients had been experiencing chronic pain for an average of seven years. In all, 124 individuals (40.9%) reported some degree of suicidal ideation. Those participants with longer histories of chronic pain reported more suicidal ideation. Multiple regression analysis revealed that both distress in interpersonal relations and self-perceived burden to others were significant predictors of suicidal ideation, even after statistical adjustments were made for demographic characteristics, pain severity and duration, functional limitations, catastrophizing, and depression.

According to the authors, the current findings suggest that the interpersonal theory is relevant to the understanding of elevated rates of suicidal ideation among people with chronic pain, and it may have broader applicability to other populations with chronic illnesses or disabilities. The present results extend the understanding of suicidal ideation beyond the assessment of pain and depression and highlight the importance of social interactions. Suicidal ideation may be most likely to arise among who suffer from longstanding pain and who are depressed, especially if they feel alienated from valued social groups and believe they have become a burden to others. (24 References)
THE ASSOCIATION BETWEEN ADULT ATTACHMENT STYLE, MENTAL DISORDERS, AND SUICIDALITY
Findings From a Population-Based Study

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J NERV MENT DIS, 201:579-86, July 2013

It is well established that individuals who experience a great degree of difficulty with interpersonal relationships are at higher risk for developing mental disorders and suicidal behaviors. Attachment theory provides a framework for classifying a person’s relational style and categorically assessing how his/her interpersonal approaches relate to mental health outcome. While attachment style is linked to numerous physical and psychological phenomena, there is very little research examining its relationship to suicide ideation and attempt in adults. In the present study, the authors investigated the relationship between adult attachment styles, mental disorders, and suicidal behavior.

The researchers used data from the National Comorbidity Survey Replication. The data were collected between 2001 and 2003 in the 48 adjacent states of the United States. The nationally representative sample was composed of 5,692 participants (2,382 men and 3,310 women; mean age, 45 years). Most of the respondents were married/cohabiting and were of non-Latino white descent. Multiple regression analyses were conducted to study the correlations (if any) between attachment styles, mental disorders, and suicidality. After the authors adjusted for confounding variables, they found that insecure attachment styles were associated with more reporting of suicidal ideation, suicide attempt, and all mental disorder categories analyzed. Secure attachment styles were associated with a decreased likelihood of reporting suicidal ideation, suicide attempt, and any anxiety disorder.

According to the authors, the current findings are the first to demonstrate that an insecure adult attachment style increases the likelihood of having mood, anxiety, impulse control, substance use, or eating disorders. Those individuals with a secure attachment style are less likely to report suicidality and the presence of any anxiety disorder. Future research should be directed toward clarifying the mechanisms of these relationships and investigating the utility of integrating attachment-based assessments and interventions in psychiatric and physical care. (72 References)
Suicide results from interactions between biological, developmental, and social factors. Gene expression changes have been reported in the brains of suicide completers. More recently, differences in promoter DNA methylation between suicide completers and comparison subjects in specific genes have been associated with these changes in gene expression patterns, thereby implicating DNA methylation alterations as plausible components of the pathophysiology of suicide. The present authors used a genome-wide approach to investigate the extent of DNA methylation alterations in the brains of suicide completers.

Promoter DNA methylation was profiled through the use of methylated DNA immune-precipitation (MeDIP) followed by micro-array hybridization in hippocampal tissue from 62 men (46 suicide completers and 16 comparison subjects). The correlation between promoter methylation and expression was examined by comparing the MeDIP data with gene expression profiles generated through mRNA micro-array. Methylation differences between groups were validated on neuronal and non-neuronal DNA fractions isolated by fluorescence-assisted cell sorting. The researchers identified 366 promoters that were differentially methylated in suicide completers relative to comparison subjects (273 hypermethylated and 93 hypomethylated). Overall, promoter methylation differences were inversely correlated with gene expression differences. Functional annotation analyses revealed an enrichment of differential methylation in the promoters of genes involved, among other functions, in cognitive processes. Validation was performed on the top genes from this category, and these differences were found to occur mainly in the neuronal cell fraction.

According to the authors, the current data suggest broad reprogramming of promoter DNA methylation patterns in the hippocampus of suicide completers. This may help explain the gene expression alterations associated with suicide and possibly the behavioral changes that are associated with increasing the risk of suicide. (60 References)
COGNITIVE ABILITY IN EARLY ADULTHOOD IS ASSOCIATED WITH LATER SUICIDE AND SUICIDE ATTEMPT: THE ROLE OF RISK FACTORS OVER THE LIFE COURSE

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P. Allebeck; B. Melin; D. Gunnell; and T. Hemmingsson
PSYCHOL MED, 43:49-60, January 2013

Cognitive ability/intelligence quotient (IQ) in young people previously has been associated with subsequent attempted and completed suicide, although little is known about the mechanisms underlying these associations. In the present longitudinal study, the authors assessed the roles of various risk factors over the life course in an attempt to explain the observed relationships.

This investigation was based on detailed health, psychometric, and socioeconomic data collected on 49,321 young Swedish men (age range, 18-20 years) who were conscripted for military service in 1969 and 1970. Of all men conscripted in 1969 and 1970, 98% were born between 1949 and 1951; the remaining 2% were born before 1949. Linkage to national registers yielded information on suicide and hospital admissions for suicide attempts up to the age of 57 years. For the full follow-up period, information on all the variables included in the final analyses were available for 44,560 men (90.3%). The results showed that lower IQ was associated with increased risks of both suicides and suicide attempts over the 36 years of follow-up. These associations followed a dose-response pattern. They were attenuated by approximately 45% in models controlling for social background, mental illness, aspects of personality and behavior, adult socioeconomic position, and family formation. Psychiatric diagnosis; maladjustment and aspects of personality in young adulthood; and social circumstances in later adulthood all contributed to attenuating the associations found. On the basis of one-unit decreases in IQ test performance on a nine-point scale, the hazard ratios between ages 35 and 57 years were as follows: for suicide, 1.19 [95% confidence interval (CI) 1.13-1.25]; fully adjusted, 1.10 (95% CI 1.04-1.18). For suicide attempt, the hazard ratios were 1.25 (95% CI 1.20-1.31); fully adjusted, 1.14 (95% CI 1.09-1.20).

In the present study, the authors conclude, cognitive ability in young adulthood was found to be associated with subsequent attempted and completed suicide. While the associations were attenuated, they remained statistically significant in models that controlled for a wide range of possible confounding and mediating factors. (50 References)
SUICIDE RISK ASSESSMENT RECEIVED PRIOR TO SUICIDE DEATH
BY VETERANS HEALTH ADMINISTRATION PATIENTS
WITH A HISTORY OF DEPRESSION

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J CLIN PSYCHIATRY, 74:226-32, March 2013

Visits with patients who have current or recent depressive disorders provide an opportunity for clinicians to assess their risk for suicidal behavior and to implement interventions to enhance safety. However, some studies have found that only a minority of patients who commit suicide are assessed for suicidal ideation at the time of their final visit, and among those who are assessed, most deny suicidal ideation. In the present investigation, the authors examined the quality of suicide risk assessment provided to veterans who had a history of depression and who committed suicide.

The researchers conducted a case-control study of suicide risk assessment information recorded in 488 medical charts of veterans previously diagnosed with major depression, depression not otherwise specified, dysthymia, or other less common ICD-9-CM depression codes. Patients who committed suicide from April 1999 through September 2004 and comparison patients were matched in terms of age, sex, entry year, and region (244 pairs). The results showed that 74% of patients with a history of depression received a documented assessment of suicidal ideation within the past year, and 59% received more than one assessment. However, 70% of those who committed suicide did not have a documented assessment for suicidal ideation at their final Veterans Health Administration (VHA) visit, even if that visit occurred within 0 through 7 days prior to suicide. Most patients who committed suicide denied having suicidal thoughts when assessed, even when assessed 0 through 7 days prior to death. Suicidal ideation was assessed more frequently during final outpatient visits with mental health providers (60%) than during final outpatient visits with primary care providers (13%) or other non-mental health providers (10%).

The current data showed that most VHA patients with a history of depression received some suicide risk assessment within the past year, but suicide risk assessments were infrequently administered at the final visit of patients who eventually committed suicide. Among patients who did receive assessments, denial of suicidal ideation appeared to be of limited value. The authors conclude that practice changes are needed to improve suicide risk assessment in patients with histories of depression, including the development of assessment and prevention strategies that are less dependent on the presence or disclosure of suicidal ideation at scheduled medical visits. (22 References)
RISK FACTORS ASSOCIATED WITH SUICIDE IN CURRENT AND FORMER US MILITARY PERSONNEL

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JAMA, 310:496-506, August 7, 2013

Beginning in 2005, the incidence of suicide deaths in the US military started to increase sharply. In the current prospective investigation, the authors examined and quantified factors associated with suicide risk in a large population of active, Reserve, and National Guard members across all branches of the military during and following service.

The participants were drawn from the Millenium Cohort Study (N=151,560), with accrual and assessment of participants occurring in 2001, 2004, and 2007. Cohort participants were requested to complete a survey approximately every three years regarding mental, behavioral, and functional health, regardless of current military status. Questionnaire data were linked with the National Death Index and the Department of Defense Medical Mortality Registry through December 31, 2008. In all, 646 participants died between 2001 and 2008. Of the decedents, 83 were the result of suicide, during a total of 707,493 person-years of observation, yielding a crude rate of 11.73 (95% CI, 9.21-14.26) suicides per 100,000 person-years or an age- and sex-adjusted rate of 9.60 (95% CI, 7.10-12.10) suicides per 100,000 person years. In Cox models adjusted for age and sex, factors significantly associated with increased risk of suicide included male sex, depression, manic-depressive disorder, heavy or binge drinking, and alcohol-related problems. None of the deployment-related factors (combat experience, cumulative days deployed, or number of deployments) were associated with increased suicide risk in any of the models. In multivariate Cox models, individuals with increased risk for suicide were men (hazard ratio [HR], 2.14; 95% CI 1.17-3.92; P=.01; attributable risk [AR], 3.5 cases/10,000 persons), and those with depression (HR, 1.96; 95% CI 1.05-3.64; P=.03; AR, 6.9/10,000 persons), manic-depressive disorder (HR, 4.35; 95% CI 1.56-12.09; P=.005; AR, 35.6/10,000 persons), or alcohol-related problems (HR, 2.56; 95% CI 1.56-4.18; P<.001; AR, 7.7/10,000 persons).

In the present study, mental health concerns, but not military-specific variables, were found to be independently associated with the risk of suicide among current and former US military personnel. (38 References)
PARENTAL SCHIZOPHRENIA AND INCREASED OFFSPRING SUICIDE RISK: EXPLORING THE CAUSAL HYPOTHESIS USING COUSIN COMPARISONS

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PSYCHOL MED, 43:581-90, March 2013

The offspring of parents hospitalized for psychiatric disorders are at increased risk of death from unnatural causes. However, very little is known about the suicide risk among offspring of parents hospitalized for schizophrenia and the possible mechanisms behind such an association. In the present study, the authors attempted to evaluate that risk and to explore whether suicide risk among offspring of schizophrenic patients is more pronounced during specific periods of life; to determine whether the risk differs according to the gender of the parent with schizophrenia; and to investigate the influence of suggested mediating risk factors underlying the association between parental schizophrenia and suicidal behavior of offspring.

The researchers applied a nested case-control design that was based on linkage of Swedish population-based registers. Among 12-to-30-year-old offspring, they identified 68,318 offspring with suicidal behavior (attempted and completed suicide) and their parents. Five healthy control-parent pairs were matched to each suicidal case-parent pair, and conditional logistic regression was used to obtain odds ratios (ORs). To disentangle familial confounding from causal environmental mechanisms, the authors compared the population-based suicide risk with the risk found within full cousins and half cousins differentially exposed to parental schizophrenia. The results showed that the offspring of parents with schizophrenia had a significantly increased risk of suicide after the following variables were accounted for: socioeconomic status, parental suicidal behavior, and offspring mental illness [OR 1.68, 95% confidence interval (CI) 1.53-1.85]. Suicide risks in offspring of schizophrenic mothers and fathers were similar in magnitude, as were risks across different developmental periods. Offspring suicide risk remained essentially unchanged across genetically different relationships; offspring of siblings discordant for schizophrenia had equivalent risk increases within full cousins (OR 1.96, 95% CI 1.66-2.31) and half cousins (OR 1.69, 95% CI 1.17-2.44).

Parental schizophrenia was associated with an increased risk of offspring suicidal behavior that persisted into adulthood and was independent of the gender of the schizophrenia parent. The increased risk appears to be partly due to environmental mechanisms. (37 References)
SEX DIFFERENCES IN SUICIDES AMONG CHILDREN AND YOUTH:
THE POTENTIAL IMPACT OF HELP-SEEKING BEHAVIOUR

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CAN J PSYCHIATRY, 58:274-82, May 2013

Suicide is the second leading cause of death among Canadians between the ages of 15 and 24 years. Suicide rates in childhood and adolescence are often higher in boys than in girls. In the current retrospective study, the authors examined sex differences in health service use among children and young people who had died by suicide.

The study population was composed of children and youth (age range, 10 to 25 years) who had been living in Ontario and who had committed suicide between April 1, 2003, and December 31, 2007. Coroner records were individually linked to outpatient physician visit, emergency department (ED) presentation, and inpatient stay administrative health care records for 724 individuals (532 boys and 192 girls); only 77 (10.6%) were between the ages of 10 and 15 years. Boys and girls were compared with regard to types of health services used, number of contacts made, and last contact made. The most common type of health service used by both boys and girls, respectively, was outpatient physician contact (72% versus 81.8%), followed by ED presentation (47.5% versus 58.3%), and inpatient stay (16.4% versus 34.4%). Girls were more likely than boys to use each type of health service and to have a greater number of outpatient physician and ED contacts (but not inpatient stays). In general, boys were more likely than girls to have no health service contact (21.1% versus 14.1%). Among those who used outpatient physician services, boys were more likely than girls to use these services only. Among ED users, boys were more likely than girls to have ED and outpatient physician contact only, but less likely to have ED, outpatient physician, and inpatient contact.

According to the authors, about 80% of subjects had contact with the health care system in the year before their death, typically with an outpatient physician and/or the ED. However, not all of these individuals were seen for mental health reasons. Girls had more outpatient physician and ED contacts than boys, and these occurred closer in time to their death. Girls were also more likely than boys to have contact in more than one setting. Boys and girls did not differ in their use of an outpatient psychiatrist, some ED presentations, and in the nature and number of inpatient stays. (46 References)
Psychiatric inpatients are at greatly increased risk of suicide compared with the general population. In many countries, a reduction in the number of inpatient beds as well as a shift toward community services may have affected this high risk, but few studies have specifically investigated temporal trends. In the current prospective investigation, the authors explored suicide in psychiatric inpatients over a 12-year period. More specifically, they studied longer-term trends in the rate of inpatient suicide; examined these trends according to age, gender, method, ethnicity, and diagnosis; and evaluated the extent to which inpatient suicide risk may have been transferred to other settings and services.

The study group was composed of all patients admitted to National Health Service inpatient psychiatric care in England between 1997 and 2008. National Confidential Inquiry and Hospital Episode Statistics data were used to determine suicide rates. Over the study period, there were 1,942 psychiatric inpatient suicides. Between the first two years of the study (1997, 1998) and the last two years (2007, 2008), the rate of inpatient suicide fell by nearly one third (from 2.45 to 1.68 per 100,000 bed days). This fall in rate was seen in both males and females and across ethnicities and diagnoses. It was most marked for patients between the ages of 15 and 44 years. In terms of method, there were statistically significant linear falls in deaths by hanging (30.7%), drug poisoning (48.5%), carbon monoxide poisoning (59.6%), drowning (51.2%), and jumping (28.4%). The fall in deaths by hanging was particularly pronounced for those deaths that occurred on the ward; the mean rate of hanging on the ward fell from 0.60 (in 1997 and 1998) to 0.24 (in 2007 and 2008), a 58.9% reduction, with a highly significant linear trend. Although the number of deaths by suicide in the immediate post-discharge period fell, the rate of post-discharge suicide (with discharge as a denominator) may have increased by as much as 19%. The number of suicide deaths in those under the care of crisis resolution/home treatment teams has increased to approximately 160 annually.

The authors conclude that the rate of suicide among psychiatric inpatients in England has fallen considerably. Possible explanations include falling general population rates, changes in the at-risk population, or improved inpatient safety; however, a transfer of risk cannot be ruled out. (39 References)
Abstracts and Reviews of Selected Literature in Psychiatry, Neurology, and their Allied Fields

Editor
Harold I. Schwartz, M.D.

Associate Editor
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Obsessive-compulsive disorder (OCD) is a common neuropsychiatric condition that consists of repeated, distressing ego-dystonic thoughts (obsessions) and behaviors (compulsions). OCD has a complex etiology that involves both genetic and environmental factors; however, the genetic causes of OCD are largely unknown, despite the identification of several promising candidate genes and linkage regions. The aim of the present investigation was to search for genomic regions that potentially harbor OCD susceptibility genes.

The authors conducted genetic linkage studies of the type of OCD thought to have the strongest genetic etiology (i.e., childhood-onset OCD) in 33 Caucasian families with two or more childhood-onset OCD-affected individuals from the United States (245 individuals with genotype data). The families ranged in size from four individuals in two generations to 58 individuals in four generations. Using a selected panel of single nucleotide repeat polymorphisms from the Illumina 610-Quad Bead Chip, the researchers performed parametric and nonparametric genome-wide linkage analyses with Morgan and Merlin in these families. The initial analyses were followed by fine-mapping analyses in genomic regions with initial heterogeneity logarithm of odds (HLOD) scores of ≥2.0. The authors identified five areas of interest (HLOD score ≥2) on chromosomes 1p36, 2p14, 5q13, 6p25, and 10p13. The strongest result was on chromosome 1p36.33-p36.32 (HLOD=3.77, suggestive evidence for linkage after fine mapping). The majority of the linkage signal on 1p36 came from the largest family; however, 16 other families also contributed to the LOD score and had haplotypes that co-segregated with either the narrow or the broad OCD phenotype, suggesting that the finding was not specific to a single family.

According to the authors, the current data represent the strongest linkage finding for OCD in a primary analysis to date and suggest that chromosome 1p36, as well as several other genomic regions, may harbor susceptibility loci for OCD. Multiple brain-expressed genes lie under the primary linkage peak (approximately four megabases in size). (60 References)
ASSOCIATION BETWEEN THE NMDA GLUTAMATE RECEPTOR
GRIN2B GENE AND OBSESSIVE-COMPULSIVE DISORDER

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J PSYCHIATRY NEUROSCI, 37:273-81, July 2012

An emerging body of evidence from neuroimaging, genetic, and clinical trials and from animal models provides support for the hypothesis that dysregulation of glutamate neurotransmission may contribute to the pathophysiology of obsessive-compulsive disorder (OCD). The aim of the present investigation was to determine whether variants in the GRIN2B gene, the gene that encodes the NR2 subunit of the N-methyl-D-aspartate glutamate receptor, may contribute to genetic susceptibility to OCD or to different OCD subphenotypes.

Between 2003 and 2008, the authors carried out a case-control association study in which they genotyped 10 tag single-nucleotide polymorphisms (SNPs) in the 3’ untranslated region (3’ UTR) of GRIN2B. They performed SNP association and haplotype analysis while taking into consideration the OCD diagnosis and different OCD subphenotypes (early-onset OCD, comorbid tic disorders, and OCD clinical symptom dimensions). The sample was composed of 225 patients with OCD (116 men, 109 women; mean age, 34 years) and 279 healthy blood donors (161 men, 118 women; mean age, 40 years) who served as controls but who were not psychiatrically screened. No significant differences between the patients with OCD and the control subjects were found with regard to the distribution of alleles or genotypes. However, when OCD subphenotypes were analyzed, the researchers found that the rs1805476 SNP in the male patients and a 4-SNP haplotype (rs1805476, rs1805501, and rs1805477) in the whole patient group were significantly associated with the presence of contamination obsessions and cleaning compulsions.

According to the authors, the current results converge with other recent findings suggesting that glutamatergic variants may possibly contribute to the genetic vulnerability to OCD or at least to certain OCD manifestations. The researchers conclude that the dissection of OCD into more homogeneous subphenotypes may constitute a useful tool in disentangling the complex genetic basis of OCD. (63 References)
OBSESSIVE-COMPULSIVE-SPECTRUM SYMPTOMS IN PATIENTS WITH FOCAL DYSTONIA, HEMIFACIAL SPASM, AND HEALTHY SUBJECTS

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J NEUROPSYCHIATRY CLIN NEUROSCI, 24:81-6, Winter 2012

Focusing on psychopathological domains of obsessive-compulsive disorder (OCD) and associated psychopathology, the authors of the present study investigated OCD in the following three groups of individuals, all of whom were matched for age and gender: 19 patients (one man, 18 women) with focal dystonia (FD), 18 patients (two men, 16 women) with hemifacial spasm (HFS), and 23 healthy controls (three men, 20 women). The mean age of the total sample was 60 years.

All subjects were administered a variety of assessment instruments, including the Structured Clinical Interview for DSM-IV Axis I Disorders, Patient Version; the Hospital Anxiety and Depression Scale; the Symptom Checklist-90-Revised; and the Structured Clinical Interview for Obsessive-Compulsive Spectrum Self-Report, Lifetime Version (SCI-OBS-SR). In those patients who received a diagnosis of OCD, the severity of symptoms was rated with the Yale-Brown Obsessive-Compulsive Scale. There were significantly higher rates of personal and family psychiatric histories in both patient groups than in the control group. The prevalence of OCD was found to be significantly higher in both the FD patients (26%, 5/19) and the HFS patients (28%, 5/18) than in the healthy controls (0%, 0/23). Among the patients with OCD, only three were newly diagnosed; all the others had received a diagnosis of OCD in young adulthood. On the SCI-OBS-SR, there were significant between-group differences in the thematic content of obsessive symptoms, with the HFS patients showing higher scores than the FD patients and the healthy controls in terms of “contamination” and “aggressiveness.”

According to the authors, the current findings suggest that patients with focal dystonia and hemifacial spasm are characterized by OCD or subsyndromal OCD, usually mild in severity, and the occurrence of which is probably driven by the interaction between the underlying brain condition and a “fertile ground” (past psychiatric history). (23 References)
PHYSICAL COMPLICATIONS OF SEVERE, CHRONIC OBSESSIVE-COMPULSIVE DISORDER: A COMPARISON WITH GENERAL PSYCHIATRIC INPATIENTS

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GEN HOSP PSYCHIATRY, 34:618-25, November-December 2012

Individuals with psychiatric illnesses are at increased risk for physical health problems. Despite the fact that there is a considerable body of research examining physical illness in those with other psychiatric conditions, there is little research focusing on the physical health of patients with obsessive-compulsive disorder (OCD), a chronic mental disorder that is associated with reduced quality of life and significant functional impairment. The authors of the present study investigated the prevalence of medical complications in a cohort of inpatients with severe, treatment-refractory OCD and compared it with the prevalence found in a group of patients admitted to a general psychiatric ward.

The OCD cohort was composed of 104 individuals who were successively admitted to an inpatient unit specifically designed to treat persons with a diagnosis of severe, chronic, disabling OCD. Information on gender, age, weight, and height were recorded, along with the results of blood tests for urea, liver function, electrolytes, and cholesterol. Type and dose of medication being given were also examined. All data obtained on the OCD patients were compared with information gathered from the case records of 101 patients successively admitted to an acute psychiatric unit (control subjects). The OCD patients were generally younger than the control subjects and were receiving lower doses of antipsychotic medication. However, compared with the general psychiatric patients, the OCD patients were more likely to have raised blood lipid and creatinine levels. Most of the OCD patients demonstrated significant self-neglect, including having problems with hygiene and food/fluid intake. Half of the OCD cohort had difficulties with urinary and/or fecal incontinence, which were related to slowness in traveling to the toilet because of compulsive rituals or avoidance of toilet areas due to fear of contamination.

According to the authors, the current data suggest that patients with severe OCD are likely to have serious physical health problems. This study emphasizes the need to insure that physical illness is not overlooked in psychiatric patients, particularly those individuals whose illness is of such severity that it influences their self-care. (26 References)
FIVE-YEAR COURSE OF OBSESSIVE-COMPULSIVE DISORDER: PREDICTORS OF REMISSION AND RELAPSE

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J CLIN PSYCHIATRY, 74:233-9, March 2013

Obsessive-compulsive disorder (OCD) is a common and frequently disabling psychiatric illness. Despite advances in the short-term treatment of this disorder, many OCD sufferers remain significantly impaired. Little is known about the long-term course of the illness, and there is no body of research aimed at examining symptom categories or subtypes as predictors of long-term clinical course in adults with primary OCD. In the present investigation, 213 adults who met DSM-IV diagnostic criteria for OCD were recruited from several mental health treatment sites between July 2001 and February 2006 as part of the Brown Longitudinal Obsessive-Compulsive Study, a prospective, naturalistic study of treatment-seeking adults with primary OCD. OCD symptoms were assessed annually over a five-year follow-up period by means of the Longitudinal Interval Follow-Up Evaluation.

Over the course of five-years, 39% (N=83) of the participants experienced either a partial (22.1%) or a full (16.9%) remission. Two OCD symptom dimensions were found to influence remission. Participants whose primary obsessions revolved around overresponsibility for harm were nearly twice as likely to experience remission as those who endorsed other obsessions as primary. In addition, only two of the 21 individuals with primary hoarding achieved remission. Other predictors of increased remission were less severe OCD and shorter duration of illness. In all, 59% (49/83) of those who achieved full or partial remission subsequently relapsed. Participants with comorbid obsessive-compulsive personality disorder were more than twice as likely to relapse. Those who achieved partial remission were more likely to relapse than those who fully remitted (70% versus 45%).

According to the authors, the contributions of OCD symptom categories and comorbid obsessive-compulsive personality disorder are critically important to advancing the understanding of the prognosis and, ultimately, the successful treatment of OCD. (55 References)
ERROR-RELATED NEGATIVITY AND TIC HISTORY IN PEDIATRIC OBSESSIVE-COMPULSIVE DISORDER

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 51:902-10, September 2012

Obsessive-compulsive disorder (OCD) is a heterogeneous condition, with lifetime prevalence estimates ranging from 1% to 3%. The National Comorbidity Survey Replication (Kessler et al., 2005) found a median age at onset of 19 years in OCD, with 21% of cases beginning by age 10. Approximately 10% to 40% of OCD subjects diagnosed in childhood or adolescence have a lifetime history of chronic tic disorders. The error-related negativity (ERN) is a negative deflection in the event-related potential after an incorrect response, which is often increased in patients with OCD. Nevertheless, the relationship between ERN and comorbid tic disorders has not been examined in those with OCD. In the present study, the authors compared ERN amplitudes in patients with tic-related OCD, patients with non-tic-related OCD, and healthy controls.

The ERN, correct response negativity, and error number were measured during an Eriksen flanker task to assess performance monitoring in 44 youths and with a lifetime diagnosis of OCD and 44 matched healthy controls ranging in age from 10 to 19 years. Of those with OCD, nine had a lifetime history of tics. Compared with the healthy controls, the patients with OCD exhibited a significantly larger ERN amplitude. ERN amplitude was significantly larger in patients with non-tic-related OCD than in patients with tic-related OCD or controls. ERN amplitude was significantly negatively correlated with age in healthy controls but not in patients with OCD. Instead, in patients with non-tic-related OCD, ERN amplitude was significantly positively correlated with age at onset of OCD symptoms. In OCD patients, ERN amplitude was not related to OCD symptom severity, current diagnostic status, or treatment effects.

According to the authors, the results of the current investigation provide further evidence of increased error-related brain activity in pediatric OCD. In addition, the difference in ERN between patients with tic-related OCD and those with non-tic-related OCD provides preliminary evidence for a neurobiological difference between these two OCD subtypes. The present data indicate that the ERN is a trait-like measurement that may serve as a biomarker for non-tic-related OCD. (54 References)
FAMILY FACTORS PREDICT TREATMENT OUTCOME FOR PEDIATRIC OBSESSIVE-COMPULSIVE DISORDER

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J CONSULT CLIN PSYCHOL, 80:255-63, April 2012

Exposure-based cognitive behavior therapy (CBT) is well-documented as an effective and relatively robust intervention for pediatric obsessive-compulsive disorder (OCD). Its advantages over serotonin reuptake inhibitors in terms of safety and response durability make it the current first-line treatment for pediatric OCD. Despite its encouraging success rate, however, large numbers of young people with OCD either fail to respond to CBT or exhibit only a partial response. Efforts to improve treatment outcome increasingly have focused on family factors that may influence the course of illness and/or the ultimate clinical outcome. In the present study, the authors evaluated family conflict, parental blame, and poor family cohesion as possible predictors of treatment outcome in youths receiving family-focused CBT (FCBT) for OCD.

The study sample was composed of 49 youths (59% male; mean age, 12.43 years) who were randomly assigned to receive FCBT as part of a larger clinical trial. The youths and their families were assessed by an independent evaluator (IE) pre- and post-FCBT by means of a standardized battery of measures that evaluated family functioning and OCD severity. Family conflict and cohesion were measured via parent self-report on the Family Environment Scale, and parental blame was measured through use of parent self-report on the Parental Attitudes and Behaviors Scale. Symptom severity was rated by IEs using the Children’s Yale-Brown Obsessive Compulsive Scale. Compared with families who endorsed higher levels of dysfunction prior to treatment, families with lower levels of parental blame and family conflict and higher levels of family cohesion at baseline were more likely to have a child who responded to FCBT, even after adjustments were made for baseline symptom severity. When the data were analyzed with both categorical and continuous outcome measures, the results showed that higher levels of family dysfunction and difficulties in more domains of family functioning were associated with lower rates of treatment response. When the researchers controlled for baseline symptom severity, they found that changes in family cohesion predicted response to FCBT.

According to the authors, the present findings provide preliminary evidence for links between higher levels of family dysfunction and lower rates of treatment response in youths receiving FCBT for OCD. The current data highlight conflict, blame, and cohesion as potential targets of future treatments for pediatric OCD.

(49 References)
INTERNET-BASED COGNITIVE BEHAVIOUR THERAPY FOR OBSESSIVE-COMPULSIVE DISORDER: A RANDOMIZED CONTROLLED TRIAL

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PSYCHOL MED, 42:2193-2203, October 2012

Obsessive-compulsive disorder (OCD) is a prevalent and disabling condition that often follows a chronic course when left untreated. While evidence shows that cognitive behavior therapy (CBT) often results in a reduction of OCD symptoms, few patients actually receive this form of therapy. Internet-based CBT (ICBT) with therapist support has the potential to be more accessible. In the present randomized controlled trial, the authors evaluated the efficacy of ICBT for the treatment of OCD.

The study sample was composed of 101 adults with a primary diagnosis of OCD (according to DSM-IV-TR criteria). The subjects were randomly assigned either to 10 weeks of ICBT (17 men, 33 women; age range, 19 to 62 years; mean age, 33 years) or to an attention control condition, which consisted of online supportive therapy (17 men, 34 women; age range, 18 to 67 years; mean age, 35 years). The primary outcome measure was the clinician-administered Yale-Brown Obsessive Compulsive Scale (YBOCS). All outcome measures were assessed at baseline, post-treatment, and four months after treatment completion. Both ICBT and the attention control condition led to significant improvements in OCD symptoms, but ICBT resulted in greater improvements than the control condition on the YBOCS, with a significant between-group effect size at post-treatment. The proportion of participants showing clinically significant improvement was 60% in the ICBT group and 6% in the control group. The results were sustained at follow-up, with 54% of the ICBT group achieving clinically significant improvement at this time.

According to the authors, the current findings indicate that ICBT is superior to a control condition in terms of improving OCD symptoms, depressive symptoms, and general functioning. ICBT achieved large effect sizes and a large number of treatment responders, yet the time to treat a patient was approximately one fourth of the time required for regular face-to-face CBT. ICBT appears to offer various combinations and opportunities for strengthening treatment adherence and acceptability in patients suffering from OCD, the researchers conclude. (47 References)
GRANISETRON ADJUNCT TO FLUVOXAMINE FOR MODERATE TO SEVERE OBSESSIVE-COMPULSIVE DISORDER
A Randomized, Double-Blind, Placebo-Controlled Trial

Neda Askari; Mahdieh Moin; Mohammad Sanati; Masih Tajdini; Seyed-Mohammad-Reza Hosseini; Amirhossein Modabbernia; Babak Najand; Samrand Salimi; Mina Tabrizi; Mandana Ashrafi; Reza Hajiaghaee; and Shahin Akhondzadeh (Psychiatric Research Center, Roozbeh Psychiatric Hospital, Tehran University of Medical Sciences, South Kargar Street, Tehran 13337, Iran; e-mail: s.akhond@neda.net)

CNS DRUGS, 26:883-92, October 1, 2012

Despite the fact that obsessive-compulsive disorder (OCD) is routinely treated with serotonin reuptake inhibitors, these drugs generally reduce the severity of symptoms by only 20% to 30%. While studies have found ondansetron, a serotonin 5-HT3 receptor antagonist, to be beneficial in the treatment of OCD, the efficacy of other 5-HT3 receptor antagonists remains unclear. Granisetron does not alter cytochrome P450 activity and may have a lower risk of drug interactions, a longer duration of action, and a better tolerability profile than other 5HT3 receptor antagonists. Between November 2011 and March 2012, the authors conducted a randomized, double-blind, placebo-controlled, parallel-group trial to assess the efficacy and tolerability of granisetron when used to augment fluvoxamine in the treatment of patients with moderate to severe OCD.

The participants were between the ages of 18 and 60 years, met DSM-IV-TR diagnostic criteria for OCD, and had a Yale-Brown Obsessive Compulsive Scale (Y-BOCS) score of at least 21. They were randomly assigned to receive granisetron (1 mg) or placebo every 12 hours in addition to fluvoxamine for a period of eight weeks. Patients were assessed with the Y-BOCS at baseline and at the second, fourth, sixth, and eighth weeks. Outcome measures included changes in Y-BOCS total score, obsession subscale, and compulsion subscale, as well as frequencies of partial response, complete response, and remission. Of 42 randomized patients, 39 completed the study (19 in the granisetron group, 20 in the placebo group). Significant time X treatment interactions were seen for Y-BOCS total scores and for obsession and compulsion subscales. By week 8, all patients in the granisetron group and seven in the placebo group met criteria for partial response. At the end of the study, complete response was achieved by all patients in the granisetron group and by seven patients in the placebo group. By week 8, 18 patients (90%) in the granisetron group and seven patients (35%) in the placebo group were considered to have achieved remission.

The authors conclude that granisetron is an efficacious and well-tolerated augmentation therapy for the short-term treatment of patients with moderate to severe OCD. (49 References)
EFFECTS OF KETAMINE IN TREATMENT-REFRACTORY OBSESSIVE-COMPULSIVE DISORDER

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BIOL PSYCHIATRY, 72:964-70, December 1, 2012

Roughly one third of patients with obsessive-compulsive disorder (OCD) fail to experience significant clinical benefit from first-line interventions such as cognitive behavior therapy or pharmacotherapy with selective serotonin reuptake inhibitors. Failure and/or delay of symptom relief with first-line treatments may lead to substantial morbidity and decreased quality of life in OCD patients. Converging lines of evidence from neuroimaging, genetic, and pharmacological studies support the importance of glutamate abnormalities in the pathogenesis of OCD. Ketamine is a moderately potent noncompetitive antagonist of the N-methyl-D-aspartate receptor, a major type of glutamate receptor in the brain. The authors conducted an open-label trial of ketamine for treatment-refractory OCD in order to evaluate its possible efficacy and to determine the time-course of any anti-obsessional effects.

Ketamine (.5 mg/kg IV over 40 minutes) was administered to 10 subjects (six males, four females) with treatment-refractory OCD. The average age at ketamine infusion was 41.7 years (range, 18 to 64 years). The duration of symptoms before ketamine infusion was 24.6 years (range, four to 54 years). Response was defined as >35% improvement in OCD symptoms and >50% improvement in depressive symptoms from baseline at any time between one and three days after ketamine infusion. The ketamine procedure was well tolerated and completed by all the participants. There was a significant acute but transient improvement in OCD symptoms that occurred one to three hours after ketamine infusion and that largely dissipated by the next day. None of the 10 subjects experienced a defined response in OCD symptoms in the first three days after receiving ketamine. However, four of the seven patients with comorbid depression experienced an antidepressant response to ketamine in the first three days after infusion. Compared with baseline values, both OCD and depressive symptoms exhibited a statistically significant improvement in the first three days after infusion, but the OCD response was <12%. The percent reduction in depressive symptoms in the first three days after ketamine infusion was significantly greater than the reduction in OCD symptoms.

According to the authors, the current data indicate that a single dose of ketamine does not have the same sustained/persistent, potent effect on OCD symptoms as it does on depression. (44 References)
DIGEST of NEUROLOGY and PSYCHIATRY

Abstracts and Reviews of Selected Literature in Psychiatry, Neurology, and their Allied Fields

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COUNTRY- AND INDIVIDUAL-LEVEL SOCIOECONOMIC DETERMINANTS OF DEPRESSION: MULTILEVEL CROSS-NATIONAL COMPARISON

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While depression is a leading cause of morbidity and disability worldwide, the prevalence and correlates of depression vary across countries. It has been hypothesized that contextual factors such as country-level income or income inequalities may contribute to these differences. In the present multilevel study, the authors examined interview data of 187,496 individuals from 53 countries participating in the World Health Organization World Health Surveys. They attempted to: (1) estimate variations in the prevalence of depression across countries; (2) quantify the relative importance of contextual- and individual-level factors in this variation; and (3) study the relationship between depression and specific contextual (income inequalities and absolute income) and individual (spending, assets, education, and occupation) socioeconomic characteristics.

The data showed that the prevalence of depression varied substantially across countries, ranging from 0.4% to 15.7%. Individual-level factors were responsible for 86.5% of this variance, but there was also reasonable variation at the country level (13.5%), with the latter appearing to increase with decreasing economic development of countries. Neither gross national income nor country-level income inequality were found to be associated with depression. At the individual level, having fewer material assets, having a lower level of education, being female, being divorced or widowed, and economic inactivity were associated with increased odds of developing depression. Adjusted analysis indicated that unlike material assets, greater household spending was associated with an increased risk of depression. In women, the prevalence of depression increased with rising gross national income, whereas this remained constant in men.

In the present study, the authors conclude, the variance of depression prevalence attributable to country-level factors seemed to increase with decreasing economic development of countries. However, country-level income inequality or gross national income explained little of this variation, and individual-level factors appeared more important than contextual factors as determinants of depression. The divergent relationship of assets and spending with depression serves to emphasize that different socioeconomic measures are not interchangeable in their associations with depression. (46 References)
CLUSTERING OF DEPRESSION AND INFLAMMATION IN ADOLESCENTS PREVIOUSLY EXPOSED TO CHILDHOOD ADVERSITY

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BIOL PSYCHIATRY, 72:34-40, July 1, 2012

Depression is a common psychiatric disorder with significant personal, social, and economic consequences for the patients themselves and for society in general. In addition, depression increases the morbidity and mortality risks from chronic diseases associated with aging, including autoimmune, metabolic, and cardiovascular conditions. There is growing interest in the hypothesis that inflammation contributes to the pathogenesis of depression and underlies depressed patients’ vulnerability to comorbid medical conditions. However, research on depression and inflammation has yielded conflicting results, thereby fostering speculation that these conditions are related only in certain subgroups, such as patients exposed to childhood adversity. The present authors analyzed data from a six-wave study of adolescents, all of whom were healthy at baseline but who were at high risk for an episode of depression because of family history or cognitive vulnerability.

The sample was composed of 147 female adolescents (age range, 15 to 19 years) who were assessed every six months for 2.5 years. The subjects underwent diagnostic interviews and venipuncture for measurement of the following two inflammatory biomarkers: C-reactive protein (CRP) and interleukin-6 (IL-6). Childhood adversity was indexed in terms of parental separation, low socioeconomic status, and familial psychopathology. Over the course of the study, 40 subjects had a depressive episode. Multilevel models indicated that childhood adversity promoted clustering of depression and inflammation. Among subjects exposed to high levels of childhood adversity, the transition to depression was accompanied by increases in both CRP and IL-6. Higher CRP values remained evident six months later, even after depressive symptoms had abated. These lingering effects were bidirectional; among subjects with childhood adversity, high IL-6 levels forecast depression six months later, even after concurrent inflammation was taken into account. This coupling of depression and inflammation was not apparent in those without childhood adversity.

According to the authors, the current findings suggest that childhood adversity promotes the formation of a neuro-immune pipeline in which inflammatory signaling between the brain and periphery is amplified. Once established, this pipeline appears to lead to a coupling of depression and inflammation, which may contribute to later affective difficulties and biomedical complications. (45 References)
RELATIONSHIP BETWEEN PROGRESSION OF BRAIN WHITE MATTER CHANGES AND LATE-LIFE DEPRESSION: 3-YEAR RESULTS FROM THE LADIS STUDY

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BR J PSYCHIATRY, 201:40-5, July 2012

While a converging body of evidence appears to implicate cerebral white matter changes (WMC) in the pathogenesis of late-life depression, the directionality of this association remains unclear. As part of a longitudinal, multicenter, pan-European study (Leukoaraiosis and Disability in the elderly), subjects between the ages of 65 and 84 underwent baseline magnetic resonance imaging (MRI) and clinical assessment. Repeat MRI scans were obtained at three years after baseline. Depressive outcomes were assessed in terms of depressive episodes and Geriatric Depression Scale (GDS) scores. The progression of WMC was measured by means of the modified Rotterdam Progression scale.

At three-year follow-up, repeat MRI data were obtained from 394 participants (210 women, 184 men). Of the remaining 185 individuals (104 women, 81 men) for whom no repeat MRI data were available, 38 had died, 63 had dropped out of the study, five had unsatisfactory or missing baseline scans, and 79 either refused or were unavailable for a second scan. The progression of WMC was found to be significantly associated with incident depression during year 3 of the study; this association remained significant even after the authors controlled for transition to disability, baseline WMC, and baseline history of depression. No significant association emerged between progression of WMC and GDS score, and no significant relationship was found between progression of WMC and history of depression at baseline.

According to the authors, the current results support the vascular depression hypothesis, i.e., that vascular disease changes to the brain predispose individuals to the development of depression by disrupting fiber tracts. These data also point to WMC as playing a causative role in the pathogenesis of late-life depression. (33 References)
TREATMENT COURSE WITH ANTIDEPRESSANT THERAPY IN LATE-LIFE DEPRESSION

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AM J PSYCHIATRY, 169:1185-93, November 2012

Late-life depression is a heterogeneous disorder that is associated with many adverse conditions, an elevated risk for comorbid medical disorders, and an elevated mortality rate. Gray matter structural changes are also implicated in late-life depression, especially the regions comprising the frontolimbic pathway. To assess the effect of gray matter volumes and cortical thickness in antidepressant treatment response in individuals with late-life depression, the authors examined the relationship between brain regions identified a priori and Montgomery-Asberg Depression Rating Scale (MADRS) scores over the course of an antidepressant treatment trial.

In a nonrandomized prospective trial, 168 patients who were at least 60 years of age and who met DSM-IV criteria for major depression underwent MRI scans and were enrolled in a 12-week treatment study. Exclusion criteria included cognitive impairment or having a severe mental disorder. The volumes or cortical thicknesses of regions of interest that differed between the depressed group and a comparison group (N=50) were determined. These regions of interest were used in analyses of the depressed group to predict antidepressant treatment outcome. Mixed-model analyses (adjusted for age, education, age at depression onset, race, baseline MADRS score, scanner, and interaction with time) examined predictors of MADRS scores over time. Smaller hippocampal volumes were found to predict a slower response to treatment. With the inclusion of white matter hyperintensity severity and neuropsychological factor scores, the best model included hippocampal volume and cognitive processing speed to predict rate of response over time. A secondary analysis showed that hippocampal volume and frontal pole thickness differed between depressed patients who achieved remission and those who did not.

According to the authors, the findings of the current investigation indicate that the primary variables of hippocampal volume and cognitive processing speed, subsuming other contributing factors (episodic memory, executive function, language processing), appear to predict response to antidepressant treatment. (41 References)
EFFICACY AND SAFETY OF DESVENLAFAXINE 50 MG/D FOR PREVENTION OF RELAPSE IN MAJOR DEPRESSIVE DISORDER: A RANDOMIZED CONTROLLED TRIAL

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J CLIN PSYCHIATRY, 74:158-66, February 2013

Major depressive disorder (MDD) is a chronic, disabling illness, and incomplete resolution of depressive symptoms is often associated with early relapse and recurrent episodes. Desvenlafaxine (administered as desvenlafaxine succinate) is a serotonin-norepinephrine reuptake inhibitor approved for the treatment of MDD in adults. The purpose of the present study was to evaluate the long-term (11 months) efficacy and safety of desvenlafaxine at the recommended 50 mg/d dose in preventing relapse in patients with MDD.

Adult outpatients (18 years of age or older) who met DSM-IV criteria for MDD and who had a 17-item Hamilton Depression Rating Scale (HDRS17) total score ≥ 20 at screening and baseline were enrolled in a multicenter, double-blind, placebo-controlled, randomized withdrawal trial conducted between June 2009 and March 2011. Those patients who responded to eight-week open-label treatment with desvenlafaxine 50 mg/d with a continuing stable response through week 20 were randomly assigned to receive placebo or desvenlafaxine 50 mg/d in a six-month, double-blind withdrawal period. The primary efficacy endpoint was time to relapse following randomization to double-blind treatment. Relapse was defined as HDRS17 total score ≥ 16, discontinuation for unsatisfactory response, hospitalization for depression, suicide attempt, or suicide. Safety and tolerability data were collected throughout the trial. A total of 874 patients were enrolled; 548 were randomly assigned to receive placebo (N=276) or desvenlafaxine 50 mg/d (N=272) in the double-blind withdrawal period. Time to relapse was significantly shorter for those on placebo than for those receiving desvenlafaxine. At the end of the six-month double-blind treatment phase, the estimated probability of relapse was 30.2% for the placebo group and 14.3% for the desvenlafaxine group. Safety and tolerability results were generally consistent with those in short-term studies of desvenlafaxine.

In the current study, long-term continuation treatment with desvenlafaxine 50 mg/d reduced the risk of relapse in those MDD patients who received the drug as compared with those who discontinued desvenlafaxine treatment (placebo patients). The authors conclude that the benefit/risk profile of desvenlafaxine 50 mg/d for the long-term treatment of individuals with MDD remains favorable. (47 References)
L-METHYLFOLATE AS ADJUNCTIVE THERAPY FOR SSRI-RESISTANT MAJOR DEPRESSION: RESULTS OF TWO RANDOMIZED, DOUBLE-BLIND, PARALLEL-SEQUENTIAL TRIALS

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AM J PSYCHIATRY, 169:1267-74, December 2012

Previous studies have suggested that low folate levels in patients with major depression may predict a poorer prognosis during treatment. L-Methylfolate is the biologically active form of folate, and the only form of folate that crosses the blood-brain barrier. The present authors conducted two multicenter sequential parallel comparison design trials in order to investigate the effect of L-methylfolate augmentation in the treatment of major depressive disorder in patients who had had a partial response or no response to selective serotonin reuptake inhibitors (SSRIs).

In the first trial, 148 outpatients with SSRI-resistant major depressive disorder were enrolled in a 60-day study divided into two 30-day periods. The patients were randomly assigned (in a 2:3:3 ratio) to receive L-methylfolate for 60 days (7.5 mg/day for 30 days followed by 15 mg/day for 30 days); placebo for 30 days followed by L-methylfolate (7.5 mg/day) for 30 days; or placebo for 60 days. SSRI dosages were kept constant throughout the study. In the second trial (75 patients), the design was identical to the first, except that the L-methylfolate dosage was 15 mg/day during both 30-day periods. In the first trial, no significant difference was seen in outcomes between the treatment groups. In the second trial, adjunctive L-methylfolate at 15 mg/day showed significantly greater efficacy than continued SSRI therapy plus placebo on both primary outcome measures (response rate and degree of change in depression symptom score) and on two secondary outcome measures of symptom severity. The number needed to treat for response was approximately six in favor of adjunctive L-methylfolate at 15 mg/day. The drug was well tolerated, with rates of adverse events no different from those reported with placebo.

According to the authors, adjunctive L-methylfolate at 15 mg/day may constitute an effective, safe, and relatively well tolerated treatment strategy for patients who have a major depressive disorder and who respond either partially or not at all to SSRIs. (35 References)
RELATIONSHIPS BETWEEN CHANGES IN SUSTAINED FRONTO-STRIATAL CONNECTIVITY AND POSITIVE AFFECT IN MAJOR DEPRESSION RESULTING FROM ANTIDEPRESSANT TREATMENT

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Deficits in positive affect and their neural bases have been associated with major depression. Whether reductions in positive affect result solely from an overall reduction in nucleus accumbens activity and fronto-striatal connectivity or the additional inability to sustain engagement of this network over time is unknown. In the present study, the authors attempted to determine whether treatment-induced changes in the ability to sustain nucleus accumbens activity and fronto-striatal connectivity during the regulation of positive affect would be associated with gains in positive affect.

Using fMRI, the researchers evaluated the ability to sustain activity in reward-related networks while attempting to increase positive emotion during performance of an emotion regulation paradigm (viewing a sequence of 72 positive and 72 negative images) in 21 depressed patients before and after two months of antidepressant treatment with either fluoxetine or venlafaxine. Fourteen healthy comparison subjects underwent scanning over the same interval. After two months of treatment, self-reported positive affect increased. Patients who demonstrated the largest increases in sustained nucleus accumbens activity over the two-month period were those who demonstrated the largest increases in positive affect. When negative affect was controlled, patients who demonstrated the largest increases in sustained fronto-striatal connectivity also were those who displayed the largest increases in positive affect. None of these associations were seen in the healthy comparison subjects.

According to the authors, the current results suggest that treatment-induced change in the sustained engagement of fronto-striatal circuitry tracks the experience of positive emotion in daily life. Future studies aimed at evaluating reduced positive affect in a variety of psychiatric disorders might benefit from an examination of the temporal dynamics of brain activity when attempting to understand changes in daily positive affect. (41 References)
SEXUAL SATISFACTION AND QUALITY OF LIFE IN
MAJOR DEPRESSIVE DISORDER BEFORE AND AFTER
TREATMENT WITH CITALOPRAM IN THE STAR*D STUDY

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Major depressive disorder (MDD) has a lifetime prevalence of 16.5% and a 12-
month prevalence of 6.7% in the adult population. MDD patients often experience impaired sexual satisfaction (ISS) and poor quality of life (QOL). Selective serotonin reuptake inhibitors (SSRIs), the first-line treatment for MDD, can cause sexual dysfunction, potentially worsening ISS and QOL. In the present study, the authors examined the impact of MDD and the SSRI citalopram on sexual satisfaction and QOL in level 1 of the Sequenced Treatment Alternatives to Relieve Depression trial (July 2001-September 2006).

The researchers conducted a retrospective analysis of the change in sexual satisfaction (as measured by item 9 of the Quality of Life Enjoyment and Satisfaction Questionnaire [the primary outcome measure]) in 2,280 patients who met DSM-IV-TR criteria for MDD and who were treated with citalopram for 12 weeks. The Quick Inventory of Depressive Symptomatology-Self Report was used to evaluate the impact of depression ratings on ISS and QOL. The results showed that ISS was present in 64.3% of the MDD patients at pretreatment, but this figure declined to 47.1% at posttreatment. Patients who achieved remission exhibited less ISS and better QOL. The prevalence of ISS was 21.2% in remitters and 61.3% in nonremitters. The mean deviation score increased from 2.32 to 3.44 in remitters but only from 1.99 to 2.19 in nonremitters. The difference between remitters and nonremitters proved to be highly significant. Regression analyses performed at pretreatment and posttreatment showed significant associations between depressive symptoms and ISS and between ISS and lower QOL, as well as an association between citalopram and an increased probability of ISS and a poorer QOL in patients who continued to suffer from moderate-to-severe depression.

According to the authors, a majority of MDD patients report ISS, a symptom associated with poor QOL. Despite the sexual side effects of the SSRI citalopram, treating depression to full remission with this drug appears to be associated with improvements in sexual satisfaction and QOL. (31 References)
ORAL SCOPOLAMINE AUGMENTATION IN MODERATE TO SEVERE
MAJOR DEPRESSIVE DISORDER: A RANDOMIZED,
DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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Since many patients do not respond to antidepressant therapy, augmentation
strategies may prove to be vitally important in the treatment of those with
depressive disorders. In the present randomized, double-blind, placebo-
controlled study, the authors evaluated the antidepressant effect of oral
scopolamine (an anticholinergic agent) as an adjunct to citalopram in patients
with moderate to severe major depressive disorder (MDD).

Study participants were drawn from the outpatient clinics of two large
hospitals and were assessed between November 2011 and January 2012. Forty
patients (age range, 18 to 55 years) who met DSM-IV-TR criteria for MDD and
who had 17-item Hamilton Depression Rating Scale (HDRS) scores of ≥ 22 were
randomly assigned to receive scopolamine hydrobromide 1 mg/d (N=20) or
placebo (N=20) in addition to citalopram for a period of six weeks. The HDRS
score was measured at baseline and on days 4, 7, 14, 28, and 42. In both the
scopolamine and the placebo groups, the primary outcome measure was HDRS
score change from baseline to week 6. Response was defined as a ≥ 50%
decrease in HDRS score, and remission as an HDRS score ≤ 7. Augmentation
with scopolamine proved to be significantly more effective than adjunctive
placebo. Patients receiving scopolamine showed higher rates of response (65%,
13/20 at week 4) and remission (65%, 13/20 at week 6) than those receiving
placebo (30%, 6/20 and 20%, 4/20, respectively). Dry mouth, dizziness, and
blurred vision were found to occur more frequently in the scopolamine group
than in the placebo group.

According to the authors, the current results indicate that adding oral
scopolamine to an antidepressant regimen in patients with moderate to severe
MDD is an effective and safe way to achieve high response and remission rates.
However, the researchers note, the long-term efficacy and safety profile of
scopolamine, as well as its optimal dosage, requires further investigation. (41
References)
PERSONALISED INTERVENTION FOR PEOPLE WITH DEPRESSION AND SEVERE COPD

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BR J PSYCHIATRY, 202:235-6, March 2013

Many older adults with chronic illnesses suffer from depression, a condition that may worsen outcome and undermine treatment adherence. Chronic obstructive pulmonary disease (COPD) with co-occurring depression exemplifies the challenge inherent in managing chronic illnesses that require active patient participation in care. The authors developed a personalized intervention for depression and COPD (PID-C) that focuses on both conditions. PID-C is administered by care managers who work with: (1) each patient to identify treatment barriers and to help him/her work on rehabilitation and adherence to prescribed antidepressants; and (2) the patient’s physicians in monitoring his/her treatment and progress. The researchers hypothesized that PID-C offered in the community would be more effective than treatment as usual (TAU) in remitting depression and reducing depressive symptoms and dyspnea-related disability over a period of 28 weeks.

The study participants were recruited from an acute inpatient pulmonary rehabilitation unit and were randomly assigned to PID-C or TAU in blocks of five. Subjects in the PID-C group had their first session of PID-C (30 minutes) at discharge, and the remainder in their own homes at weeks 3, 4, 8, 12, 16, 20, 24, and 26. PID-C targets patient-specific barriers to non-adherence in seven domains (misconceptions about COPD and depression, misunderstanding about drug regimen, misattribution of depressive symptoms, hopelessness, overestimation of exercise effort, dissatisfaction with care, and practical barriers). The results showed that compared with TAU, over a period of 28 weeks, PID-C led to a higher remission rate of depression and a greater reduction in depressive symptoms and dyspnea-related disability in 138 patients with major depression and COPD. These benefits lasted six months after the intervention ended. Even though COPD has a deteriorating course, dyspnea-related disability did not worsen in the PID-C group over the course of a year.

According to the author, if the current findings are replicated in future trials, PID-C may serve as a management model for the increasing number of people with both depression and a medical illness that requires active patient participation in care. (10 References)
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SOCIAL DISTANCE AND STIGMA TOWARD INDIVIDUALS WITH SCHIZOPHRENIA
Findings in an Urban, African-American Community Sample

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J NERV MENT DIS, 200:935-40, November 2012

Studies indicate that cultural characteristics and differences may have a significant impact on attitudes and stigma toward individuals with mental illnesses. Although schizophrenia is arguably one of the most stigmatized health conditions, few studies to date have closely examined correlates of attitudes toward schizophrenia, or mental illness in general, within the African-American community. The authors of the present investigation examined social distance and stigma among members of a specific cultural community, namely, predominantly Protestant, low-income, urban African-Americans residing in the Southeastern United States.

A survey was distributed to 282 patrons (174 males, 108 females; mean age, 46.5 years) of an inner city food court/farmers’ market. The participants had to be at least 18 years old and able to read and speak English. The greater part of the sample (N=163) earned less than $10,000 per year, and more than half (N=152) were unemployed. In all, 117 respondents had known someone with schizophrenia, and 66 reported having a family member with schizophrenia. Associations were assessed between two measures of stigma (an adapted version of the Social Distance Scale [SDS] and a Semantic Differential Measure [SDM] of attributes such as dangerousness, dirtiness, and worthlessness) and several key variables addressing sociodemographic characteristics and exposure to, or familiarity with, mental illnesses. Linear regression modeling was used to identify independently significant correlates of scores on the SDS and the SDM. The data indicated that a higher level of stigma (as measured by the SDM) was correlated with a family history of psychiatric treatment, whereas a lower level of stigma (as measured by the SDS) was correlated with a personal history of psychiatric treatment and a higher annual income.

The authors suggest that health literacy initiatives surrounding the topic of mental illness specifically target public-sector health care settings and socially disadvantaged communities. Such initiatives may serve to normalize mental illness by incorporating stories from community members and addressing misconceptions about dangerousness. Future research should examine family experiences, as well as the best approaches for increasing health literacy (and decreasing stigma) in the community. (35 References)
HIGH MORTALITY AND LOW ACCESS TO CARE FOLLOWING INCIDENT ACUTE MYOCARDIAL INFARCTION IN INDIVIDUALS WITH SCHIZOPHRENIA

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SCHIZOPHR RES, 142:52-7, December 2012

Individuals with schizophrenia have a life span that is approximately 20 years shorter than those in the general population. While mental health-related mortality factors, such as suicide, are likely to play a role in this reduced life span, early mortality also may be attributable to well-established modifiable risk factors that are more prevalent among those with schizophrenia (e.g., obesity, smoking, diabetes, cardiovascular disease). Previous studies have found that schizophrenic individuals are at increased risk of acute myocardial infarction (AMI). The present authors used a retrospective cohort study design to measure the risk of mortality following incident AMI among subjects with and without a diagnosis of schizophrenia in Ontario, Canada, where all residents have access to universal health care coverage.

The sample was composed of incident AMI patients who were discharged from hospital between January 1, 2002, and December 31, 2006. The main outcome measure was 30-day mortality post-discharge. Secondary outcomes were receipt of cardiac procedures (coronary artery bypass graft surgery or percutaneous transluminal coronary angiography) following index AMI and cardiologist visits within 30 days of discharge. After exclusions, a total of 71,668 subjects were included, among whom 842 had a diagnosis of schizophrenia. In all, 69,911 subjects were alive 30 days after hospital discharge, including 809 with a diagnosis of schizophrenia. After adjusting for key prognostic factors, the authors found that the risk of death 30 days post-discharge was 56% greater for schizophrenic patients than for those without schizophrenia. However, in the 30 days after hospital admission, individuals with schizophrenia were 50% less likely than non-schizophrenic patients to receive a cardiac procedure or have a follow-up visit with a cardiologist. Less than one in four (24.1%) schizophrenic patients underwent a cardiac procedure within 30 days of hospital admission, and only 12 out of every 100 (12%) schizophrenic patients had a follow-up visit with a cardiologist during this period.

According to the authors, the present findings indicate that schizophrenic individuals are at greater risk of dying after incident AMI than those without schizophrenia. Despite this elevated mortality risk, however, individuals with schizophrenia are less likely to receive cardiac procedures and specialist care following incident AMI. (38 References)
NICOTINE DEPENDENCE AND ILLNESS SEVERITY IN SCHIZOPHRENIA

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BR J PSYCHIATRY, 201:306-12, October 2012

While smoking is known to be common in patients with schizophrenia, prevalence studies examining the association between symptom domains and smoking have found conflicting results. To examine the relationships among clinical features, social adjustment, and nicotine dependence in a geographically defined population of individuals with schizophrenia, the present authors conducted a cross-sectional survey of clinical measures and measures of nicotine dependence in Nithsdale, Scotland.

In all, 131 individuals with a diagnosis of schizophrenia were interviewed. Of these, 70 (47 males, 23 females; mean age, 49.61 years) were current smokers, and 61 (25 males, 36 females; mean age, 57.79 years) were non-smokers. Of the 61 non-smokers, 21 had smoked at some point in the past. Of the 70 current smokers, 50 fulfilled criteria for severe nicotine dependence, and 20 met criteria for mild-moderate nicotine dependence. Compared with non-smokers, current smokers were significantly younger, were more likely to be male, and were three times more likely to be unemployed. Smokers with severe nicotine dependence had higher scores on the positive subscale of the Positive and Negative Syndrome Scale (PANSS) and were prescribed higher doses of antipsychotic medication. Those with mild-moderate nicotine dependence had higher scores on the PANSS negative subscale. Greater symptom severity was associated with poorer social adjustment. Psychopathology and social adjustment were similar in those who had quit smoking and those who had never smoked.

According to the authors, the current findings indicate that nicotine dependence is associated with symptom severity and outcome in individuals with schizophrenia. Although the present study does not establish a causal relationship between these variables, identifying and treating nicotine dependence may have some value in reducing morbidity and mortality among those with schizophrenia. (45 References)
EMPATHY IN ELECTRODERMAL RESPONSIVE AND NONRESPONSIVE PATIENTS WITH SCHIZOPHRENIA

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SCHIZOPHR RES, 142:71-6, December 2012

Skin conductance response (SCR) is an electrodermal response measure that has been used to investigate response to emotion-evoking stimuli since the late 19th century. In previous studies, the SCR to emotion-evoking stimuli among schizophrenic patients has suggested the existence of two subgroups, with one being characterized by absent SCR and the other by heightened or non-habituating SCR. Because subgroups of patients that differ in SCR responsiveness also may differ in social and emotional functioning, the present authors evaluated the association between SCR responsiveness and multiple aspects of social cognition in persons with schizophrenia.

The study sample was composed of 28 outpatients with schizophrenia or schizoaffective disorder and 24 matched healthy controls. SCR was measured while the subjects watched emotion-evoking and neutral video tapes. Using a variety of assessment tools, the researchers also evaluated symptoms, neurocognition, social cognition, and social function. Event-related potential (ERP) responses were recorded as subjects viewed pictures of people who were either experiencing or not experiencing pain. On the basis of SCR frequency, the subjects were divided into “SCR non-responder” and “SCR responder” groups. Fourteen schizophrenic patients and seven healthy controls were designated as SCR non-responders; 14 schizophrenic patients and 17 healthy controls were classified as SCR responders. As a whole, the patient group performed significantly poorer than the control group on almost all measures of neurocognition, general social cognition, and social function. Compared with the schizophrenia SCR non-responders and the healthy controls, the schizophrenia SCR responders had significantly higher self-reported personal distress in response to others in distress and lower P300 ERP responses to others in pain.

According to the authors, the current findings suggest that sensitivity to images of others in pain, perhaps through fear or through poor interpersonal boundaries and heightened empathic contagion, contributes to clinical instability in SCR (hyper) responsive patients. SCR responsiveness appears to be a potential marker of subgroups of schizophrenic patients that differ in pathophysiology, function, and prognosis. (51 References)
VOICE IDENTITY RECOGNITION FAILURE IN PATIENTS WITH SCHIZOPHRENIA

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J NERV MENT DIS, 200:784-90, September 2012

Auditory verbal hallucinations (AVHs) are one of the most striking symptoms of schizophrenia. Despite the vast body of research that has been carried out in this area, the mechanisms behind the formation of AVHs are still poorly understood. While some cognitive models have proposed that AVHs arise by means of inner speech misidentification, such models do not explain why the voices in hallucinations often have identities that differ from those of the hearer. The authors of the current study attempted to determine whether a general voice identity recognition difficulty is present in individuals with schizophrenia and whether that difficulty is related to AVHs.

Twenty-five outpatients who met DSM-IV-TR criteria for schizophrenia (20 men, five women) and 13 healthy control subjects (eight men, five women) were tested with regard to their ability to recognize famous voices. Signal detection theory was used to calculate perceptual sensitivity and response criterion measures. Twelve patients (10 men, two women) who were not currently experiencing hallucinations were assigned to the non-hallucinators’ group (NAVH), while the 13 patients (10 men, three women) who reported current hallucinations were allocated to the hallucinators’ group (AVH). The researchers found significant differences between groups in the percentage of hits obtained in the famous voices recognition task, as well as in the sensitivity measure A'. Compared with the controls, the patients with schizophrenia obtained a lower percentage of hits and showed less sensitivity to identifying famous voices. Analysis revealed that patients in the AVH group obtained significantly lower hit rates and sensitivity index A' than subjects in the control group. Patients in the AVH group also showed a trend toward obtaining lower hit rates and A' than patients in the NAVH group. The control group did not differ significantly from the NAVH group. There were no differences between the patients with schizophrenia and the healthy controls in false alarm rate or response criterion.

According to the authors, the current findings indicate that schizophrenia patients who experience hallucinations are impaired in voice identity recognition because of decreased sensitivity, which may result in inner speech misidentification. (40 References)
THALAMOCORTICAL DYSCONNECTIVITY IN SCHIZOPHRENIA

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AM J PSYCHIATRY, 169:1092-9, October 2012

Several neurobiological theories of schizophrenia have hypothesized that the pathophysiology of the disorder includes abnormal functional interactions between the cortex and the thalamus. Thalamocortical networks are organized topographically into parallel pathways that link distinct cortical areas to specific thalamic nuclei. Consequently, a dysfunction of thalamocortical networks may account for the wide array of clinical and cognitive symptoms seen in persons with schizophrenia. However, the topographical arrangement of reciprocal connections between the cortex and thalamus also raises the distinct possibility that thalamocortical networks may be differentially affected in schizophrenia. To explore this possibility, the authors of the present study used resting-state functional MRI (fMRI) and examined functional connectivity in intrinsic low-frequency blood-oxygen-level-dependent (BOLD) signal fluctuations between major divisions of the cortex and thalamus.

Seventy-seven healthy comparison subjects and 62 patients with schizophrenia underwent resting-state fMRI. To identify functional subdivisions of the thalamus, the researchers parceled the cortex into six regions of interest: prefrontal cortex, motor cortex/supplementary motor area, somatosensory cortex, temporal lobe, posterior parietal cortex, and occipital lobe. Mean BOLD time series were extracted for each region of interest and entered into a seed-based functional connectivity analysis. The results showed that activity in distinct cortical areas correlated with specific, largely non-overlapping regions of the thalamus in both healthy subjects and schizophrenia patients. Direct comparisons between the groups revealed reduced prefrontal-thalamic connectivity and increased motor/somatosensory-thalamic connectivity in the patients with schizophrenia. The changes in connectivity were not related to local gray matter content within the thalamus or to antipsychotic medication dosage. No differences were observed in temporal, posterior parietal, or occipital cortex connectivity with the thalamus.

According to the authors, the current findings establish differential abnormalities of thalamocortical networks in individuals with schizophrenia. The etiology of schizophrenia may disrupt the development of prefrontal-thalamic connectivity and the refinement of somato-motor connectivity with the thalamus that occurs during brain maturation. (41 References)
HIGHER GAMMA-AMINOBUTYRIC ACID NEURON DENSITY IN THE WHITE MATTER OF ORBITAL FRONTAL CORTEX IN SCHIZOPHRENIA

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BIOL PSYCHIATRY, 72:725-33, November 1, 2012

Schizophrenia is a devastating psychiatric illness characterized by social withdrawal, hallucinations, working memory impairments, and attention deficits. Because of these diverse symptoms, multiple cortical areas such as the dorsolateral prefrontal cortex, the orbitofrontal cortex (OFC), the anterior cingulate cortex, and the superior temporal gyrus have been implicated in the etiology of the disorder. The OFC is of particular interest because it is a core component of the social brain network, and multiple lines of evidence suggest that abnormalities of the OFC may play a role in the pathophysiology of schizophrenia. In the OFC of individuals with schizophrenia, reduced gray matter volume and reduced glutamic acid decarboxylase 67kDa isoform (GAD67) messenger RNA (mRNA) have been found; however it remains unclear how these alterations relate to the developmental pathology of interneurons. The authors of the present study attempted to determine whether increased interstitial white matter neuron (IWMN) density exists in the OFC; whether gamma-aminobutyric acid (GABA)ergic neuron density in OFC white matter is altered; and how IWMN density may be related to an early-expressed inhibitory neuron marker (Dlx1) in the OFC gray matter in schizophrenia.

In 38 patients with schizophrenia (25 men 13 women) and 38 normal control subjects (29 men, nine women), IWMN densities were determined for neuronal nuclear antigen (NeuN+) and 65/67kDa isoform of glutamic acid decarboxylase immunopositive (GAD65/67+) neurons. In situ hybridization was performed to determine Dlx1 and GAD67 mRNA expression in OFC gray matter. The results showed that NeuN and GAD65/67 immunopositive cell density was significantly increased in the superficial white matter of the schizophrenia patients. Gray matter Dlx1 and GAD67 mRNA expression were reduced in those with schizophrenia. Dlx1 mRNA levels were found to be negatively correlated with GAD65/67 IWMN density.

According to the authors, the findings of the present study indicate that the pathology of IWMNs in schizophrenia includes GABAergic interneurons and that increased IWMN density may be related to GABAergic deficits in the overlying gray matter. (72 References)
SHORT-TERM TROPISETRON TREATMENT AND COGNITIVE AND P50 AUDITORY GATING DEFICITS IN SCHIZOPHRENIA

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AM J PSYCHIATRY, 169:974-81, September 2012

Compromised neurocognitive function is a core feature of schizophrenia, as it affects processing speed, learning, memory, attention, executive function, and social cognition. The cognitive impairment associated with schizophrenia often is severe, widespread, and evident long before overt signs of psychosis emerge. The 7 nicotinic acetylcholine receptor (nAChR) is associated with cognitive and P50 gating deficits in schizophrenia, and 7 nAChR agonists potentially may reverse these deficits. Using a randomized, double-blind design, the authors of the present study examined multiple dosages of tropisetron (a high-affinity partial agonist of the nAChR) with regard to its short-term effects on cognition and P50 deficits in patients with schizophrenia.

The sample was composed of 40 nonsmoking schizophrenia patients who had P50 ratios greater than 0.5 and who were stabilized on 3-6 mg/day of risperidone. They were randomly assigned to receive placebo (N=10) or oral tropisetron 5 mg/day (N=10), 10 mg/day (N=10), or 20 mg/day (N=10). The researchers measured P50 inhibitory gating and administered the Chinese-language version of the Repeatable Battery for Assessment of Neuropsychological Status at baseline and after 10 days of treatment. The results indicated that after 10 days of treatment, all three daily doses of tropisetron significantly improved overall cognitive deficits, with 10 mg/day showing the greatest improvement for the immediate memory index score and 20 mg/day, for the delayed memory index score on the cognitive battery. The P50 deficits were also improved, and that improvement was significantly correlated with cognitive improvement. Two patients in the 20 mg/day group dropped out because of adverse effects, but the other dosage schedules were well tolerated.

According to the authors, the improvement of cognition with tropisetron appeared to be associated with normalization in P50 deficits. Thus, the researchers conclude, 7 nAChR agonists would seem to offer a promising therapeutic approach to the treatment of cognitive deficits that are related to abnormal P50 suppression in schizophrenia. (41 References)
IMPROVEMENT OF BRAIN REWARD ABNORMALITIES BY ANTIPSYCHOTIC MONOTHERAPY IN SCHIZOPHRENIA

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ARCH GEN PSYCHIATRY, 69:1195-204, December 2012

Dopamine is an essential neurotransmitter in the brain reward system. It appears that the symptoms of schizophrenia are linked to a dysfunction of dopamine neurotransmission and the brain reward system. However, it remains unclear whether antipsychotic treatment, which blocks dopamine transmission, improves, alters, or even worsens these reward-related abnormalities. In the present controlled, longitudinal study, the authors examined changes in reward-related brain activations in schizophrenia patients before and after antipsychotic monotherapy with a dopamine D2/D3 antagonist.

Twenty-three antipsychotic-naïve patients with first-episode schizophrenia (16 males, seven females) and 24 healthy controls (20 males, four females) initially matched in terms of age, sex, and parental socioeconomic status were examined with functional magnetic resonance imaging (fMRI) while playing a variant of the monetary incentive delay task. The patients were treated for six weeks with the antipsychotic compound amisulpride, while the controls were followed up without receiving any treatment. The main outcome variables were task-related blood oxygen level-dependent activations as measured by fMRI before and after antipsychotic treatment. At baseline, the patients (as compared with the controls) demonstrated an attenuation of brain activation during reward anticipation in the ventral striatum, bilaterally. After six weeks of antipsychotic monotherapy, the patients showed an increase in the anticipation-related fMRI signal and were no longer statistically distinguishable from the controls. Within the patient group, there was a correlation between the improvement in positive symptoms and the normalization of reward-related activation. Those patients who showed the greatest clinical improvement in positive symptoms also showed the greatest increase in reward-related activation after treatment.

According to the authors, the current results indicate that alterations in reward processing are fundamental to schizophrenia and are evident prior to any treatment. However, treatment with antipsychotic medication does appear to normalize the response of the reward system in schizophrenia patients. (45 References)
DOPAMINE SYNTHESIS CAPACITY IN PATIENTS WITH TREATMENT-RESISTANT SCHIZOPHRENIA

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AM J PSYCHIATRY, 169:1203-10, November 2012

Between 20% and 35% of patients with schizophrenia show only a limited response to antipsychotic treatment (Lindenmayer, 2000). There is substantial evidence to suggest that the efficacy of antipsychotic drugs is related to dopamine D2 receptor blockade (Kapur et al., 2000). All currently approved antipsychotic medications block dopamine receptors, and their relative clinical potency parallels their binding and blocking affinity for the dopamine D2 receptor subtype. Elevated presynaptic striatal dopaminergic function is a robust feature of schizophrenia. However, the relationship between this dopamine abnormality and the response to dopamine-blocking antipsychotic treatments is unclear. In the present investigation, the authors hypothesized that in patients with schizophrenia the response to antipsychotic treatment would be related to the severity of presynaptic dopamine dysfunction, as indexed through the use of [18F]-DOPA uptake positron emission tomography (PET).

Twelve patients with treatment-resistant schizophrenia, 12 schizophrenia patients who had responded to antipsychotic treatment, and 12 healthy volunteers underwent [18F]-DOPA PET scanning. The groups were matched in terms of gender, age, ethnicity, weight, and cigarette smoking. [18F]-DOPA influx rate constants (Kicer values) were measured in the striatum and its functional subdivisions. The patients who had responded to antipsychotic treatment showed significantly higher Kicerc striatal values than the patients with treatment-resistant illness and the healthy volunteers. The elevated [18F]-DOPA uptake was most marked in the associative and the limbic striatal subdivisions. There were no significant differences between the patients with treatment-resistant illness and the healthy volunteers in the whole striatum or any of its subdivisions.

According to the authors, the current data indicate that schizophrenia patients whose illness is resistant to antipsychotic treatment have relatively normal levels of dopamine synthesis capacity, as compared with those patients whose symptoms respond to treatment. This finding suggests either that patients with treatment-resistant illness start with a different underlying pathophysiology or that antipsychotics have an effect on their dopamine synthesis capacity, albeit one that does not reduce their symptoms. (40 References)
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A DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL OF FLUOXETINE FOR REPETITIVE BEHAVIORS AND GLOBAL SEVERITY IN ADULT AUTISM SPECTRUM DISORDERS
LOWER BIRTH WEIGHT INDICATES HIGHER RISK OF AUTISTIC TRAITS IN DISCORDANT TWIN PAIRS

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PSYCHOL MED, 42:1091-102, May 2012

Autism spectrum disorder (ASD) is a neurodevelopmental disorder of complex etiology that affects approximately one in 100 children. Although the cause of ASD is not known definitively, there is strong evidence to suggest a causal role for genetic factors, and environmental factors have also been implicated. Previous studies have supported a possible association between birth weight and ASD; however the mechanisms underlying this potential relationship are not straightforward. For example, low birth weight (and other environmental factors) could act independently or could interact with underlying genetic predisposition as part of a liability threshold model of complex disorders (Falconer, 1981). It is also possible that low birth weight could be the result of an underlying genetic liability to ASD. In the present investigation, the authors used a co-twin-control design to examine low birth weight as a potential risk factor for ASD.

The population-based sample was composed of 3,715 same-sex twin pairs who were participating in the Child and Adolescent Twin Study of Sweden. ASD was assessed by means of a structured parent interview designed to screen for ASD and related developmental disorders (based on DSM-IV criteria). Birth weights were obtained from medical birth records maintained by the Swedish Medical Birth Registry. Twins lower in birth weight among ASD-discordant twin pairs (N=34) were more than three times as likely to meet criteria for ASD than heavier twins (Odds Ratio=3.25). Analyses of birth weight as a continuous risk factor showed a 13% reduction in risk of ASD for every 100-g increase in birth weight (N=78). Analysis of the effect of birth weight on ASD symptoms in the entire population (most of whom did not have ASD) revealed a modest association. Thus, for every 100-g increase in birth weight, a 2% decrease in severity of ASD (as indexed by scores on the Autism-Tics, attention-deficit hyperactivity disorder, and other Comorbidities inventory) would be expected in the sample as a whole.

According to the authors, the findings of the current investigation are consistent with the hypothesis that low birth weight confers a risk for ASD. Although genetic effects are of major importance, the researchers conclude, a non-genetic influence associated with birth weight may contribute to the development of ASD. (66 References)
DIFFERENCES IN WHITE MATTER FIBER TRACT DEVELOPMENT PRESENT FROM 6 TO 24 MONTHS IN INFANTS WITH AUTISM

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AM J PSYCHIATRY, 169:589-600, June 2012

Autism spectrum disorders (ASDs) are complex neurodevelopmental disorders characterized by impaired social communication and restricted, repetitive behaviors. Evidence from prospective studies of high-risk infants suggests that early symptoms of autism usually emerge late in the first year or early in the second year of life after a period of relatively typical development. Autism is increasingly being considered as a disorder partly characterized by aberrant neural circuitry. The present authors examined white matter fiber tract organization from the ages of six to 24 months in high-risk infants who developed ASDs by 24 months of age.

The sample was composed of 92 high-risk infant siblings who were drawn from an ongoing imaging study of autism. All participants underwent diffusion tensor imaging at six months and behavioral assessments at 24 months; a majority contributed additional imaging data at 12 and/or 24 months. At 24 months of age, 28 infants met criteria for ASDs, and 64 infants did not. Microstructural properties of white matter fiber tracts reported to be associated with ASDs or related behaviors were characterized by fractional anisotropy and radial and axial diffusivity. The fractional anisotropy trajectories for 12 of 15 fiber tracts differed significantly between the infants who developed ASDs and those who did not. Development for most fiber tracts in the infants with ASDs was characterized by higher fractional anisotropy values at six months followed by slower changes over time relative to infants without ASDs. Thus, by 24 months of age, infants with ASDs had lower values.

According to the authors, the current results suggest that aberrant development of white matter pathways may precede the manifestation of autistic symptoms in the first year of life. They conclude that longitudinal data are critical to characterizing the dynamic age-related brain and behavior changes underlying the development of autism. (63 References)
**INCREASED RATE OF AMYGDALA GROWTH IN CHILDREN AGED 2 TO 4 YEARS WITH AUTISM SPECTRUM DISORDERS**  
A Longitudinal Study

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ARCH GEN PSYCHIATRY, 69:53-61, January 2012

Autism is a neurodevelopmental disorder characterized by impairments in social behavior and communication and by the presence of repetitive or restricted interests. Precocious amygdala enlargement is frequently seen in young children with autism; however, the age at which such abnormal enlargement begins and the relative growth trajectories of amygdala and the total brain remain unclear. The present authors conducted a longitudinal structural magnetic resonance imaging (MRI) study in an attempt to determine whether the rate of amygdala growth is abnormal and disproportionate to total brain growth in very young children with autism spectrum disorders (ASDs).

Participants were recruited from the community, with neuroimaging and diagnostic assessments being performed at an academic medical center. Baseline MRIs were acquired in 132 boys (85 with ASD and 47 with typical development [TD]) when they were between two and four years of age (mean age, 37 months). Longitudinal MRIs were collected one year later in a subset of 70 boys (45 with ASD and 25 with TD). Amygdala volumes and total cerebral volumes (TCVs) were evaluated at both time points, and one-year growth rates were calculated. The amygdala was found to be larger in the children with ASD at both time points, but the magnitude of enlargement was greater at time 2. TCV was also enlarged by the same magnitude at both time points in the children with ASD. When the researchers controlled for TCV, amygdala enlargement remained significant at both time points. Over the one-year interval, the rate of amygdala growth was faster in the children with ASD than in those with TD. The rate of TCV growth did not differ between the two groups. Post hoc exploratory analyses revealed three patterns of amygdala and TCV growth rates within the ASD group (rapid amygdala, normal TCV growth [42%]; slow amygdala, rapid TCV growth [16%]; and typical rates of amygdala and TCV growth [42%]).

According to the authors, the findings of the present investigation indicate that disproportionate amygdala enlargement is present by 37 months of age in children with ASDs. While the amygdala continues to grow at an increased rate, substantial heterogeneity appears to exist in both amygdala and TCV growth patterns. *(30 References)*
BRAIN ANATOMY AND ITS RELATIONSHIP TO BEHAVIOR IN ADULTS WITH AUTISM SPECTRUM DISORDER
A Multicenter Magnetic Resonance Imaging Study

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ARCH GEN PSYCHIATRY, 69:195-209, February 2012

Autism spectrum disorder (ASD) is a life-long neurodevelopmental condition characterized by impaired social communication and repetitive/stereotypical behavior. While it is thought that ASD is accompanied by differences in neuroanatomy, the neural substrates of ASD in adults (and how they relate to behavioral variation) remain poorly understood. To identify brain regions and systems associated with ASD in adults, the present authors, using quantitative magnetic resonance imaging, conducted a multicenter, case-control study.

The sample was composed of 89 men with ASD (mean age, 26 years; full-scale IQ, 110) and 89 male control subjects (mean age, 28 years; full-scale IQ, 113). The main outcome measures were: (1) between-group differences in regional neuroanatomy as assessed by voxel-based morphometry, and (2) distributed neural systems maximally correlated with ASD, as identified by partial least-squares analysis. The results showed that the adults with ASD did not differ significantly from the controls in terms of overall brain volume. However, voxel-wise comparisons between the groups revealed that the men with ASD had significantly increased gray matter volume in the anterior temporal and dorsolateral prefrontal regions as well as significant reductions in the occipital and medial parietal regions. These regional differences were significantly correlated with the severity of specific autistic symptoms. The large-scale neuroanatomic networks maximally correlated with ASD as identified by partial least-squares analysis included the regions identified by voxel-based analysis, as well as the cerebellum, basal ganglia, amygdala, inferior parietal lobe, cingulate cortex, and various medial, orbital, and lateral prefrontal regions. Spatially distributed reductions in white matter volume were also seen in those with ASD.

Adults with ASD appear to have distributed differences in brain anatomy and connectivity that are associated with specific autistic features and traits. The current data are compatible with the concept of autism as a syndrome characterized by atypical neural “connectivity.” (127 References)
EPIGENETIC SIGNATURES OF AUTISM
Trimethylated H3K4 Landscapes in Prefrontal Neurons

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Autism spectrum disorders are complex and etiologically heterogeneous illnesses. Studies have found that neurons residing in the prefrontal cortex (PFC) and other cortical association areas in autistic subjects are affected by subtle defects in connectivity patterns, cytoarchitecture, and other structural alterations. While the role of such disordered neural circuitry within the context of neurodevelopmental disease is well understood (including impairment of higher cognition and social communication), very little is known about the molecular pathology of PFC neurons in the autistic brain. The authors attempted to characterize epigenetic signatures of autism in PFC neurons by comparing the trimethylated H3K4 (H3K4me3) epigenomes of the PFC neurons of autistic individuals with a panel of controls across a wide range of ages (0.5 to 70 years).

The researchers performed fluorescence-activated sorting and separating of neuronal and non-neuronal nuclei from postmortem PFC; digested the chromatin with micrococcal nuclease; and deeply sequenced the DNA from the mononucleosomes with H3K4me3, a histone mark associated with transcriptional regulation. Approximately 15 billion base pairs of H3K4me3-enriched sequences were collected from 32 brains (16 autistic subjects and 16 control subjects). The brains of the autistic subjects showed no evidence of generalized disruption of the developmentally regulated remodeling of the H3K4me3 landscape that defines PFC neurons in early infancy. However, excess spreading of H3K4me3 from the transcription start sites into downstream gene bodies and upstream promoters was specifically observed in neuronal chromatin from four of the 16 autism cases but not in any of the controls. Variable subsets of autism cases exhibited altered H3K4me3 peaks at numerous genes regulating neuronal connectivity, social behaviors, and cognition (often in conjunction with altered expression of the corresponding transcripts). Autism-associated H3K4me3 peaks were found to be significantly enriched in genes and loci implicated in neurodevelopmental diseases.

The authors conclude that PFC neurons from individuals with autism show changes in chromatin structures at hundreds of loci genome-wide, revealing considerable overlap between genetic and epigenetic risk maps of developmental brain disorders. (64 References)
A MULTISITE STUDY OF THE CLINICAL DIAGNOSIS OF DIFFERENT AUTISM SPECTRUM DISORDERS

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Best-estimate clinical (BEC) diagnoses of specific autism spectrum disorders (autistic disorder, pervasive developmental disorder-not otherwise specified, and Asperger syndrome) have been used as the diagnostic gold standard, even when information from standardized instruments was available. The authors attempted to determine whether the relationships between behavioral phenotypes and clinical diagnoses of different autism spectrum disorders (ASDs) would vary across 12 university-based sites. Clinical phenotype data (diagnostic, developmental, and demographic) were collected, and classification trees were used to identify characteristics that predicted diagnosis across and within sites.

The sample consisted of 2,102 probands (1,814 males and 288 females) between the ages of four and 18 years (mean, 8.93 years). All met autism spectrum criteria on the Autism Diagnostic Interview-Revised and the Autism Diagnostic Observation Schedule; all had a clinical diagnosis of an ASD. The main outcome measure was BEC diagnosis predicted by standardized scores from diagnostic, cognitive, and behavioral factors. Although distributions of scores on standardized measures were similar across sites, significant site differences emerged in BEC diagnoses of specific ASDs. Relationships between clinical diagnoses and standardized scores, particularly verbal IQ, language level, and core diagnostic features, varied across sites with regard to weighing of information and cutoffs.

The current data support the move from existing subgroups of ASDs to dimensional descriptions of core features of social affect and fixed, repetitive behaviors, together with characteristics such as language level and cognitive function. (36 References)
FACTORS ASSOCIATED WITH DRIVING IN TEENS WITH AUTISM SPECTRUM DISORDERS

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J DEV BEHAV PEDIATR, 33:70-4, January 2012

Little is known about driving experiences among teenagers with autism spectrum disorders (ASDs). Among those without a concurrent intellectual disability, subtle deficits in social interaction, communication, and motor/coordination skills could directly impair driving. In the present investigation, the authors compared the characteristics of driving and nondriving teens with higher functioning ASDs (HFASDs) and also explored the driving outcomes among driving teens with HFASD. Teens with HFASD were defined as those with a parent-reported diagnosis of ASD and without a diagnosis of intellectual disability.

Eligible subjects for this cross-sectional study were those parents of teens (age range, 15 to 18 years) who had a diagnosis of ASD and who were enrolled in the Interactive Autism Network, an online research registry. Data were collected by means of an online survey. A total of 297 surveys were completed (response rate, 26%). Of the 83% of teens who were old enough to drive in their state of residence (age-eligible teens), 29% were currently driving, and 34% planned to drive. Compared with age-eligible but nondriving teens, a greater proportion were engaged in full-time regular education, planned to attend college, and held a paid job outside the home. A greater proportion of parents of driving teens had taught one or more teenagers to drive previously. There were no differences in gender, autism subtype, attention deficit/hyperactivity disorder diagnosis, parental age/education, or access to public transportation. Driving predictors included individualized education plans with driving goals; indicators of functional status (classroom placement, college aspiration, and job experience); and parental experience in teaching teenagers to drive. In all, 63% of driving teens held a permit. Over the previous 12 months, 12% of independent drivers (those with restricted or unrestricted licenses) were reported to have been in at least one motor vehicle crash as the driver at fault, and 12% were reported to have received a citation for a moving violation.

According to the authors, in the present study a significant proportion of teenagers with HFASDs were interested in driving. However, the majority of driving teens did not have driving goals included in their individualized education plans, a fact that suggests an area of opportunity for improvement in transition planning. (27 References)
LONGITUDINAL FOLLOW-UP OF CHILDREN WITH AUTISM RECEIVING TARGETED INTERVENTIONS ON JOINT ATTENTION AND PLAY

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 51:487-95, May 2012

Young children with autism spectrum disorders (ASDs) are noted for a constellation of developmental difficulties that differentiate them from other children. These early difficulties center primarily around social and communication skills, such as joint attention, imitation, affective sharing, and object play skills. The authors of the present investigation examined the cognitive and language outcomes of children with an ASD over a period of five years after the children had received targeted early interventions that had focused on joint attention and play skills.

Of 58 children who originally participated in a randomized controlled trial, 40 (33 boys, 7 girls; mean age=8 years, 8 months) returned for five-year follow-up assessments. In the original study, three- to four-year-old children were randomized to a joint attention, symbolic play, or control condition within the same intensive early intervention program. At follow-up, the Autism Diagnostic Interview Schedule (ADOS) was re-administered to the 40 returning children; 26 met criteria for autism, eight met criteria for ASD, and six did not meet criteria for autism or ASD, but displayed elevated scores on the ADOS indicative of the broader autism phenotype. The results showed that 80% of the children tested at follow-up had achieved functional use of spoken language, with baseline play level predicting spoken language at the five-year point. With regard to the children who were using spoken language at eight years of age, several baseline behaviors predicted their later ability, including beginning intervention at an earlier age, initiating more joint attention, demonstrating higher play levels, and being assigned to either the joint attention or symbolic play intervention group. Only baseline play diversity predicted cognitive scores at age 8 years.

According to the authors, the current investigation is one of the few long-term follow-up studies of children who participated in preschool early interventions designed to target core developmental difficulties. The present findings suggest that focusing on joint attention and play skills in comprehensive treatment models is important with regard to long-term spoken language outcomes. (36 References)
EFFECTS OF LARGE DOSES OF ARACHIDONIC ACID ADDED TO DOCOSAHEXAENOIC ACID ON SOCIAL IMPAIRMENT IN INDIVIDUALS WITH AUTISM SPECTRUM DISORDERS
A Double-Blind, Placebo-Controlled, Randomized Trial

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J CLIN PSYCHOPHARMACOL, 32:200-6, April 2012

Autism spectrum disorders (ASDs), believed to be neurodevelopmental in origin, appear to have reduced cortical functional connectivity that is related to social cognition. The polyunsaturated fatty acids arachidonic acid (ARA) and docosahexaenoic acid (DHA) may play key roles in brain network maturation. ARA in particular is thought to be important in signal transduction related to neuronal maturation. Therefore, the present authors state, supplementation with larger ARA doses added to DHA may serve to mitigate social impairment. They conducted a double-blind, randomized, placebo-controlled trial to determine whether the addition of larger doses of ARA to DHA supplementation would improve social withdrawal and communication symptoms in persons with ASDs.

The study population was composed of 13 autistic individuals (12 males, one female; age range, 16 to 28 years; mean age, 14.6 years). All were assigned to 16 weeks of supplementation with large doses of ARA added to DHA (N=7) or placebo (N=6). To explore possible mechanisms underlying the effect of the supplementation regimen, the researchers examined plasma levels of the antioxidants transferrin and superoxide dismutase, both of which are useful markers of signal transduction. Main outcome measures were the Social Responsiveness Scale and the Aberrant Behavior Checklist-Community. Repeated-measures analyses of variance revealed that the supplementation regimen significantly improved social withdrawal (as measured by the Aberrant Behavior Checklist-Community) and communication (as measured by the Social Responsiveness Scale). Effect sizes were more favorable for the treatment group than for the placebo group (social withdrawal: treatment group, 0.88 and placebo group, 0.54; communication: treatment group, 0.87 and placebo group, 0.44). There was a significant difference between the two groups with regard to change in plasma transferrin levels and a trend toward a significant difference in terms of change in plasma superoxide dismutase levels.

According to the authors, the findings of the current preliminary investigation suggest that supplementation with larger doses of ARA added to DHA improves impaired social interaction in individuals with ASDs by up-regulating signal transduction. (53 References)
A DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL OF FLUOXETINE FOR REPETITIVE BEHAVIORS AND GLOBAL SEVERITY IN ADULT AUTISM SPECTRUM DISORDERS

Eric Hollander, MD (e-mail: eholland@montefiore.org); Latha Soorya, PhD; William Chaplin, PhD; Evdokia Anagnostou, MD; Bonnie P. Taylor, PhD; Casara J. Ferretti, MS; Stacy Wasserman, MD; Erika Swanson, MA; and Cara Settipani, BA
AM J PSYCHIATRY, 169:292-9, March 2012

Autism spectrum disorders ASDs) are defined by three core symptom areas: impairments in social relatedness, deficits in social communication, and restricted, repetitive behaviors and interests. Among children with ASDs, between 75% and 80% continue to meet criteria for these disorders in adolescence and adulthood, with ASDs in adults being characterized by persistent functional deficits in core and associated symptom domains. In the present study, the authors compared the effects of fluoxetine and placebo on repetitive behaviors and global severity in a sample of adults with ASDs.

Subjects who were between the ages of 18 and 60 years and who met DSM-IV criteria for an ASD were enrolled in a 12-week, double-blind, placebo-controlled fluoxetine trial. In all, 37 were randomly assigned to receive fluoxetine (N=22) or placebo (N=15). Medications were dispensed according to a fixed schedule, starting at 10 mg/day and increasing as tolerated up to a maximum of 80 mg/day. Repetitive behaviors were measured with the compulsion subscale of the Yale-Brown Obsessive Compulsive Scale. The Clinical Global Impression (CGI) improvement scale was used to rate improvement in obsessive-compulsive symptoms and overall severity. A significant treatment-by-time interaction was found whereby (across time) there was a significantly greater reduction in repetitive behaviors among fluoxetine-treated adults than among placebo-treated subjects. When overall response was defined as a CGI global improvement score of 2 or less, at week 12 significantly more responders were found in the fluoxetine group than in the placebo group. The risk ratio was 1.5 for CGI global improvement (responders: fluoxetine, 35%; placebo, 0%) and 1.8 for CGI-rated improvement in obsessive-compulsive symptoms (responders: fluoxetine, 50%; placebo, 8%). Fluoxetine was well tolerated, with only mild to moderate side effects being observed, including insomnia, dry mouth, and headaches.

According to the authors, the present study is the first randomized, placebo-controlled trial of the safety and efficacy of fluoxetine as a treatment for adults with ASDs. The most robust findings were those indicating significant improvement in the core symptom domain of repetitive behaviors. In addition, greater improvements in overall severity and autistic symptoms were seen in the fluoxetine group than in the placebo group. (27 References)
Abstracts and Reviews of Selected Literature in Psychiatry, Neurology, and their Allied Fields

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Childhood maltreatment encompasses a spectrum of sexual, physical, and emotional abuse, as well as physical and/or emotional neglect. It is highly prevalent in Western countries, and it is estimated that between 30% and 40% of the adult population have experienced some form of maltreatment during childhood. Since childhood maltreatment has been found to represent a strong risk factor for the development of depression and posttraumatic stress disorder (PTSD) in later life, the authors of the present study investigated the underpinnings of this association. Because both depression and PTSD have been seen to be associated with increased amygdala responsiveness to negative stimuli and reduced hippocampal gray matter volume, the researchers postulated that childhood maltreatment would result in similar functional and structural alterations in previously maltreated but otherwise healthy adults.

In all, 148 healthy subjects were enrolled in the study via public notices and newspaper announcements and were carefully screened for psychiatric disorders. Amygdala responsiveness was measured by means of functional magnetic resonance imaging and an emotional face-matching paradigm specifically designed to activate the amygdala in response to threat-related faces. Voxel-based morphometry was used to examine morphological alterations. Childhood maltreatment was assessed with the 25-item Childhood Trauma Questionnaire (CTQ). A positive association was found between CTQ scores and amygdala responsiveness to negative facial expressions. In subjects with high CTQ scores, morphometric analysis yielded reduced gray matter volumes in the hippocampus, insula, orbitofrontal cortex, anterior cingulate gyrus, and caudate. These results were not influenced by trait anxiety, depression level, age, intelligence, education level, or more recent stressful life events.

According to the authors, the current data may suggest that limbic hyperresponsiveness and reduced hippocampal volumes could be mediators between adversities experienced during childhood and the later development of emotional disorders. (85 References)
CHILD ABUSE AND NEGLECT, MAOA, AND MENTAL HEALTH OUTCOMES: A PROSPECTIVE EXAMINATION

Valentina Nikulina (Psychology Dept., John Jay College, City University of New York, 899 Tenth Ave., Suite 631, New York, NY 10019; e-mail: vnikulina@jjay.cuny.edu); Cathy Spatz Widom; and Linda M. Brzustowicz

Research has shown that adults who were abused and/or neglected as children are at increased risk for a variety of negative consequences, including depression, alcohol abuse, and violent/criminal behavior. At the same time, several studies have found that some children prove to be resilient despite having suffered adversities, including maltreatment. Some researchers have begun to examine gene by environment interactions by focusing on monoamine oxidase A (MAOA) as a moderator between the environmental stressors of child maltreatment and subsequent outcomes such as depressive symptomatology and alcohol abuse; however, findings have been inconclusive. For example, both high- and low-activity allele combinations have been shown to be protective in maltreated children, with the direction of results varying according to the methodology employed and the sex of the participants. The present authors examined the interaction of child maltreatment and the MAOA genotype in relation to three adult mental health outcomes (major depressive disorder, dysthymia, and alcohol abuse).

Participants in a prospective cohort design study involving court-substantiated cases of child abuse and neglect and matched comparison subjects were followed into adulthood and interviewed (N=802). Eighty-two percent consented to provide blood, 631 gave permission for DNA extraction and analyses, and 575 were included in the final sample, which included male, female, white, and nonwhite (primarily black) participants. Symptoms of dysthymia, major depression, and alcohol abuse were assessed by means of the National Institutes of Mental Health Diagnostic Interview Schedule-III-R. Significant three-way interactions (MAOA genotype by abuse by sex) were found to predict dysthymic symptoms. Low-activity MAOA genotype served as a buffer against symptoms of dysthymia in physically abused and multiply-maltreated women. Significant three-way interactions (MAOA genotype by sexual abuse by race) predicted all outcomes. Low-activity MAOA genotype served as a buffer against symptoms of dysthymia, major depressive disorder, and alcohol abuse in sexually abused white participants. The high-activity genotype proved to be protective in the nonwhite sexually abused group.

According to the authors, the current data provide evidence that the MAOA genotype may act as a moderator of the relationship between childhood maltreatment and mental health outcomes. (73 References)
CHILD AND ADULT OUTCOMES OF CHRONIC CHILD MALTREATMENT

Melissa Jonson-Reid, PhD (George Warren Brown School of Social Work, Washington University, Campus Box 1196, One Brookings Drive, St. Louis, MO 63130; e-mail: jonsonrd@wustl.edu); Patricia L. Kohl, PhD; and Brett Drake, PhD

PEDIATRICS, 129:839-45, May 2012

To describe how child maltreatment chronicity is related to negative outcomes in later childhood and early adulthood, the authors attempted to determine: (1) whether a relationship existed between chronicity of maltreatment and adverse behavioral, emotional, and health outcomes before age 18; and (2) whether chronicity would predict young adult outcomes once adverse childhood outcomes were controlled. In an attempt to characterize the shape of a possible dose-response relationship, the researchers also tried to determine whether a certain number of maltreatment reports would be necessary before an increased risk was seen (flat initial response) or whether a ceiling effect (reduction in slope over time) would mitigate the impact of reports beyond a certain point.

The study sample was composed of 5,994 low-income children who were from a large Midwestern city and who were followed from 1993-1994 through 2009. At the time of initial sampling, the children were 11 years of age or younger. Data were gleaned from administrative and treatment records that contained information on substance abuse, mental health treatment, brain injury, sexually transmitted disease, suicide attempts, and violent delinquency before age 18 and child maltreatment perpetration, mental health treatment, and substance abuse in adulthood. Multivariate analysis was used to control for potential confounders. The primary independent variable was the number of maltreatment reports a child received before age 18. In all, 41% of the sample had no reported maltreatment by age 18, 19% had only one report, 12.7% had two reports, 7.9% had three reports, and 19.1% had between four and 22 reports. Child maltreatment chronicity predicted negative childhood outcome in a linear fashion. For example, 29.7% of those with at least one negative outcome had no reports of maltreatment, 39.5% had one report, and 67.1% had four reports. Suicide attempts before age 18 showed the largest proportionate increase with repeated maltreatment. The dose-response relationship was reduced when controls for other adverse childhood outcomes were added in multivariate models of child maltreatment, perpetration, and mental health issues. The relationship between adult substance abuse and maltreatment report history disappeared after the researchers controlled for adverse childhood outcomes.

The current findings suggest that although any report of child maltreatment is undesirable, chronic maltreatment appears to predict poorer outcomes across a number of domains. (27 References)
Among adolescents and adults in the general population, the risk of suicide is elevated in those with a history of childhood physical, sexual, and/or emotional abuse. Street youth (young people who live on the street full- or part-time) show early mortality and an excess risk of suicide when compared with their mainstream peers. However, it is not known to what extent childhood abuse and neglect may be related to risk of suicide in this highly marginalized group. In the present study, the authors examined the possible relationship between childhood trauma and subsequent attempted suicide during adolescence and young adulthood among street youth.

Between October 2005 and November 2007, 495 young people (age range, 14 to 26 years) were recruited for the At Risk Youth Study (ARYS), which follows a cohort of youth with extensive street involvement in Vancouver, Canada. Many of the ARYS youth are homeless, have not completed high school, and are heavily involved in the drug scene. Self-reported attempted suicide in the preceding six months was examined in relation to childhood abuse and neglect, as measured by the Childhood Trauma Questionnaire (CTQ). Logistic regression was employed, with recent suicide attempt as the dependent variable and total CTQ score as an independent variable. To adjust for possible confounders, the researchers explored bivariate associations between recent suicide attempts and a range of sociodemographic, drug use, and behavioral variables. Of the 495 young people who provided data on history of attempted suicide, 182 (36.8%) reported a lifetime history of suicidal ideation, and 46 (9.3%) reported having made an actual suicide attempt during the preceding six months. Childhood physical and sexual abuse were highly prevalent, with 201 (40.6%) of the cohort reporting a history of childhood physical abuse, and 131 (26.5%) reporting a history of childhood sexual abuse. An increasing CTQ score was found to be related to risk for suicide attempt, despite adjustments made for confounders.

According to the authors, the current data suggest that a strong and graded association exists between childhood trauma and subsequent attempted suicide among street youth, an otherwise “hidden” population. (14 References) EAF
Prior research suggests that various types of childhood maltreatment frequently co-occur and confer risk for multiple psychiatric diagnoses. This may mean that childhood maltreatment increases vulnerability to numerous specific psychiatric disorders through diverse, specific mechanisms or that it engenders a generalized liability to dimensions of psychopathology. The authors used a latent variable approach to estimate the associations of childhood maltreatment with underlying dimensions of internalizing and externalizing psychopathology and with specific disorders (after accounting for latent dimensions).

Data were drawn from a nationally representative survey of 34,653 U.S. adults (14,564 men and 20,089 women). Lifetime DSM-IV psychiatric disorders were assessed by means of the Alcohol Use Disorder and Associated Disabilities Interview Schedule, DSM-IV version. Physical, sexual, and emotional abuse and neglect were assessed through use of validated measures. Analyses were designed to control for other childhood adversities and sociodemographic variables. The results showed that the relationship between childhood maltreatment and psychiatric disorders was fully mediated through the associations of maltreatment with estimated latent internalizing and externalizing dimensions rather than through specific disorders. When all types of maltreatment and other childhood adversities were controlled, all forms of abuse (physical, emotional, and sexual) were found to be associated with at least one dimension of psychopathology, whereas emotional and physical neglect were not associated with either internalizing or externalizing dimensions. Specific types of maltreatment exhibited specific patterns of association with internalizing or externalizing dimensions. For example, sexual abuse was related more strongly to internalizing than to externalizing dimension in both men and women. Patterns of association between maltreatment and underlying psychopathology dimensions were found to differ by gender. Physical abuse was associated only with externalizing liability in men and only with internalizing liability in women.

The current results emphasize the pernicious consequences of childhood maltreatment for mental health across the life span. (80 References)
CHILDHOOD MALTREATMENT AND DSM-IV ADULT MENTAL DISORDERS: COMPARISON OF PROSPECTIVE AND RETROSPECTIVE FINDINGS

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BR J PSYCHIATRY, 200:469-75, June 2012

Previous studies have found stronger associations between childhood maltreatment and adult psychopathology when maltreatment is assessed retrospectively rather than prospectively, thereby casting doubt on the mental health risk conferred by childhood maltreatment as well as on the validity of retrospective reports. In the present investigation, the authors compared mental disorder outcomes between adults whose maltreatment histories were prospectively ascertained (via child protection agency records) and adults whose histories were retrospectively ascertained (via subjects’ retrospective reports).

A nationally representative sample of respondents (N=1,413; age range, 16 to 27 years) in New Zealand completed a retrospective assessment of maltreatment and DSM-IV mental disorders. The survey data were linked with a national child protection database to identify those respondents with maltreatment records. Of the 1,413 respondents, 887 had no history of childhood maltreatment, 358 had retrospectively ascertained histories of maltreatment in childhood, and 168 had prospectively ascertained histories of maltreatment in childhood. The researchers found that a history of childhood maltreatment conferred a considerably higher risk of developing a range of mental disorders (mood, anxiety, and drug use disorders) in young adulthood, but there was no difference in the strength of associations as a function of whether maltreatment history was prospectively or retrospectively ascertained. Prospectively ascertained maltreatment was found to be predictive of major depressive disorders characterized by earlier onset, higher frequency of episodes, and greater associated impairment.

According to the authors, the results of the current investigation indicate that associations between childhood maltreatment and mental disorders are similar across both retrospective and prospective maltreatment ascertainment; this finding serves to confirm the substantive risk conferred by childhood abuse for later mental health. The present data also provide evidence of a link between prospectively ascertained childhood maltreatment and a more unfavorable course of depressive disorder. (29 References)
EMOTION REGULATION PREDICTS ATTENTION BIAS IN MALTREATED CHILDREN AT-RISK FOR DEPRESSION

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J CHILD PSYCHOL PSYCHIATRY, 53:120-7, February 2012

Child maltreatment is a prevalent problem in the United States and has been linked to a heightened risk for depression; however, not all individuals who experience maltreatment develop depression. Previous research has shown that maltreated children exhibit alterations in emotional reactivity and regulation, and that these behaviors are associated with altered attention to emotional information. In the present study, the authors examined attention patterns for sad, depression-relevant cues in children with and without maltreatment experiences. They also attempted to determine whether individual differences in physiological reactivity and emotion regulation in response to a sad emotional state would predict heightened attention to sad cues associated with depression.

Sixty-one children (31 males, 30 females; age range, 11 to 14 years) participated in the study. The Children’s Response Styles Scale was used to assess trait rumination (repetitive thinking about the causes and consequences of negative events and emotions), and the Child Depression Inventory was used to measure current depressive symptoms. One-way analyses of variance indicated that there was no association between any attention bias measures and the following: participant’s sex, age, and race/ethnicity or parental diagnoses. Linear regression analyses revealed no associations between child symptoms of depression or other psychopathology and any attention bias measures. The results indicated that children who experienced high levels of maltreatment showed an increase in attention bias for sad faces throughout the course of the study, such that they exhibited biased attention for sad faces following the initiation of a sad emotional state. Maltreated children who had high levels of trait rumination demonstrated an attention bias toward sad faces across all time points.

According to the authors, the current data suggest that maltreated children show heightened attention for depression-relevant cues in certain contexts (e.g., after the experience of a sad emotional state). In addition, maltreated children who tend to engage in rumination show a relatively stable pattern of heightened attention for depression-relevant cues. These patterns, the researchers note, may identify which maltreated children could be most likely to exhibit biased attention for sad cues and to be at heightened risk for depression. (38 References)
IMPACT OF PHYSICAL AND SEXUAL ABUSE ON TREATMENT RESPONSE IN THE TREATMENT OF RESISTANT DEPRESSION IN ADOLESCENTS STUDY (TORDIA)

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 50:293-301, March 2011

The relationship between a history of physical abuse (PA) or sexual abuse (SA) and an increased risk of adverse mental health outcomes, including depression, is well established. However, there are few studies that have examined the association between history of abuse and response to treatment in depressed patients, particularly adolescents. The present authors previously reported that a history of abuse was associated with a poorer response to combination treatment in the Treatment of Resistant Depression in Adolescents study (TORDIA). In the current study, they examine the nature and correlates of abuse that might explain their previous findings.

The study sample was composed of 334 depressed youth who had not benefited from an adequate selective serotonin reuptake inhibitor (SSRI) trial. They were randomly assigned to one of the following for a period of 12 weeks: an alternative SSRI, an alternative SSRI plus cognitive behavior therapy (CBT), venlafaxine, or venlafaxine plus CBT. The effects of abuse history on response to pharmacotherapy or combination therapy were analyzed. Of the 334 participants, 43 had a history of PA, and 55 had a history of SA; of these, 17 had a history of both. Those without a history of PA or SA had a higher response rate to combination therapy (62.8%) than to medication monotherapy (37.6%). Those with a history of SA had similar response rates to combination treatment (48.3%) and medication monotherapy (42.3%), whereas participants with a history of PA had a much lower rate of response to combination therapy (18.4%) than to medication monotherapy (52.4%). Even after adjustments were made for other clinical predictors, adolescents with a history of PA were still 10 times more likely to have an adequate response to medication monotherapy than to combination treatment.

According to the authors, the current findings suggest that the negative impact of a history of abuse on response to combination treatment relative to medication monotherapy found in the TORDIA study may be mostly attributable to a history of physical abuse. (45 References)
CHILDHOOD MALTREATMENT AND DIFFERENTIAL TREATMENT RESPONSE AND RECURRENCE IN ADULT MAJOR DEPRESSIVE DISORDER

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J CONSULT CLIN PSYCHOL, 80:342-53, June 2012

Cognitive-behavioral therapy, interpersonal psychotherapy, and antidepressant medication have shown superior efficacy relative to placebo in several randomized controlled trials of unipolar major depressive disorder (MDD). However, a substantial number of patients with MDD do not respond to treatment, and recurrence rates remain high. The purpose of the present study was to evaluate a history of severe childhood abuse as a moderator of response following a 16-week acute treatment trial, and of recurrence over a 12-month follow-up period.

The participants included 203 adult outpatients with MDD (74 men, 129 women; age range, 18 to 60 years). They were enrolled in a 16-week, single-center, randomized, open-label trial of interpersonal psychotherapy, cognitive-behavioral therapy, or antidepressant medication, with a 12-month naturalistic follow-up, conducted at a university psychiatry center in Canada. The main outcome measure was Hamilton Depression Rating Scale score at treatment end point. Childhood maltreatment was assessed at the completion of treatment by means of an interview-based contextual measure of childhood physical, sexual, and emotional abuse. Multiple imputation was adopted to estimate missing values. Complete case data for the acute phase of treatment were available for 112 patients. Complete case data for the follow-up phase were available for 65 patients (i.e., 75 who completed follow-up minus 10 who were missing childhood maltreatment data). Patients with histories of severe maltreatment were significantly less likely to respond to interpersonal psychotherapy than to cognitive-behavioral therapy or medication. There were no differences across treatment modalities in the responses of those with no history of maltreatment. In addition, a history of maltreatment significantly predicted a shorter time to recurrence during follow-up across all treatment conditions. These findings were replicated in those with complete case data.

According to the authors, the current results suggest that patients with a history of childhood abuse may benefit more from antidepressant medication or cognitive-behavioral therapy than from interpersonal psychotherapy. However, they note, these patients appear to remain vulnerable to recurrence, regardless of treatment modality. (70 References)
THE INTERACTIVE EFFECT OF BLAME ATTRIBUTION WITH CHARACTERISTICS OF CHILD SEXUAL ABUSE ON POSTTRAUMATIC STRESS DISORDER

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J NERV MENT DIS, 200:329-35, April 2012

Victims of child sexual abuse (CSA) are at high risk for developing interpersonal and psychological problems over both the short- and long-term, with one of the most prevalent risks being the development of posttraumatic stress disorder (PTSD). The direction of blame attribution for a traumatic event such as CSA (e.g., toward one’s self, toward the perpetrator, toward non-perpetrator family members) has consequences for how a victim reacts to that trauma. In the present study, the authors examined the role of attributions of blame for CSA with regard to the development of PTSD symptoms.

The sample was composed of 151 female victims of CSA (mean age, 19.67 years); 78.1% were from intact families, 9.3% were from families with divorced parents, 6% had experienced the death of one or both parents, 4.6% were from stepfamilies, 1.3% were from adoptive families, and 0.7% were from families with cohabiting parents. The participants were asked to complete (anonymously) a retrospective self-report questionnaire that was designed to elicit sociodemographic data, CSA experiences, and other maltreatment incidents. The Attributions of Responsibility and Blame Scale was used to assess attributions made about CSA. The Severity of Symptoms of PTSD Scale was also administered. The results indicated that self-blame and family blame were related to higher PTSD scores. However, perpetrator blame was not found to be related to PTSD symptoms. The strength of the relationship between blame attribution and PTSD score was greater in cases of more severe, isolated, and extra-familial abuse.

According to the authors, the current data point to a number of areas that could be altered through the treatment of CSA victims during childhood. Diminishing self-blame attributions may be particularly advantageous in cases of isolated and extra-familial CSA, whereas diminishing family blame may be more advantageous in cases of more severe abuse. In addition, the researchers note, encouraging perpetrator blame attributions may not prove to be helpful in the treatment of CSA survivors. (42 References)
DIGEST of NEUROLOGY and PSYCHIATRY

Abstracts and Reviews of Selected Literature in Psychiatry, Neurology, and their Allied Fields

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PATHOLOGICAL GAMBLING AND THE STRUCTURE OF COMMON MENTAL DISORDERS

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J NERV MENT DIS, 199:956-60, December 2011

Using a nationally representative mental health survey, in 1999 Krueger published a seminal paper on the structure of common mental disorders in which he basically proposed a three-factor model. The first was a higher-order externalizing factor composed of drug and alcohol dependence and antisocial personality disorder (ASPD). The second and third were part of a higher-order internalizing factor that included lower-order factors of fear (panic disorders, social phobia, simple phobia, and agoraphobia) and anxious-misery (major depression, dysthymia, and generalized anxiety disorder). In the present study, the authors assessed the fit of Krueger’s original three-factor structure in the National Epidemiologic Survey of Alcohol and Related Conditions (NESARC; N=43,093). They also evaluated the inclusion of pathological gambling (PG) in the three-factor model to determine whether PG would load more strongly on the higher-order externalizing factor.

The results indicated a good fit for the original Krueger model to the NESARC data, and the model’s fit was retained after the inclusion of the new diagnosis of PG. The findings confirmed that PG loaded most strongly onto the externalizing factor (drug and alcohol dependence and ASPD). While the data revealed that PG was externalizing in nature for both men and women, in women the best fit was found when PG was allowed to load onto the externalizing factor as well as the lower-order internalizing factor of anxious-misery (according to a chi-square difference test and model modification indices), indicating that PG appears to be related to externalizing factors and mood disorders in women.

According to the authors, the current data support findings from previous studies that have demonstrated that the original Krueger model can be replicated in other samples, with the present results extending the replication to another nationally representative sample. However, they note, further research is needed to explore the possible differences between men’s and women’s gambling behavior. It could be that PG in women results from an attempt to deal with negative emotions, whereas PG in men may have a stronger externalizing element. (33 References)
PATHOLOGICAL GAMBLING IN A PSYCHIATRIC SAMPLE

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COMPR PSYCHIATRY, 53:9-14, January, 2012

Previous studies aimed at investigating prevalence rates of gambling difficulties in patients with various psychiatric disorders have found a higher percentage of pathological gambling (PG) in these patients than that seen in members of the general population. The purpose of the present observational report was to determine the prevalence of problem gambling and PG in a sample of psychiatric inpatients and compare it with that found in a nonpsychiatric patient sample. In addition, the authors analyzed the prevalence of gambling across all psychiatric diagnoses.

The study was conducted between March 2006 and May 2007 in a 300-bed general teaching hospital. The psychiatric group consisted of 100 patients consecutively admitted to the psychiatric unit. The nonpsychiatric group was composed of 100 age- and sex-matched psychiatrically healthy inpatients who had been admitted to other units of the hospital (e.g., gynecology, orthopedic surgery, internal medicine, general surgery). The mean age of the sample as a whole was 38.2 years, and 50% were men. The National Opinion Research Center Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Screen for Gambling Problems was used to screen for gambling behavior. In the psychiatric group, 9% experienced gambling difficulties (8% PG and 1% problem gambling); their mean age was 41.11 years, and 78% were men. In the nonpsychiatric group, 3% experienced gambling difficulties (2% PG and 1% problem gambling); their mean age was 55.33 years, and all were men. The difference in gambling prevalence between the two groups was not statistically significant. There was a significant difference in gambling behavior between patients with psychotic disorders (17%) and patients with any other psychiatric diagnosis (5%). A significantly larger number of psychiatric patients with psychotic disorders were men, had no stable partner, and had a substance use disorder, particularly cannabis use.

In the current investigation, a higher prevalence of gambling disorders was found in psychiatric inpatients than in nonpsychiatric inpatients. The authors suggest that clinicians routinely assess for the presence of gambling difficulties as part of the psychiatric evaluation. (31 References)
A NEUROCOGNITIVE COMPARISON OF COGNITIVE FLEXIBILITY AND RESPONSE INHIBITION IN GAMBLERS WITH VARYING DEGREES OF CLINICAL SEVERITY

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PSYCHOL MED, 41:2111-9, October 2011

Pathological gambling is a significant public health problem that is estimated to affect approximately 1% of the U.S. population. As behavioral addictions with clinical and phenomenological features similar to those of substance addiction, recreational and pathological gambling represent valuable models for studying the neurobiology of addiction, without the potential confounding pernicious brain effects from chronic alcohol or illicit substance abuse. The authors of the present study examined clinical features, response inhibition, and cognitive flexibility in gamblers with varying degrees of clinical severity.

A community sample of individuals (age range, 18 to 65 years) who had gambled in any form at least five times during the past year was recruited through newspaper advertising. The subjects were divided a priori into three groups (no-risk, at-risk, and pathological gamblers) on the basis of a diagnostic interview. All subjects underwent a psychiatric clinical interview and neurocognitive tests designed to assess motor impulsivity and cognitive flexibility. Those subjects with a current axis I disorder, a history of brain injury/trauma, or implementation or dose changes of psychoactive medication within six weeks of study enrollment were excluded. A total of 135 no-risk, 69 at-risk, and 46 pathological gambling subjects were assessed. Compared with non-gamblers, pathological gamblers were significantly older and exhibited significant deficiencies in motor impulse control (stop-signal reaction times), response speed (median “go” trial response latency), and cognitive flexibility (total intra-dimensional/extra-dimensional errors). The finding of impaired impulse control and cognitive flexibility proved to be robust in the analysis of an age-matched subgroup of pathological gamblers. There were no significant differences between the no-risk and at-risk gambling groups in terms of task performance. Elevated rates of psychiatric comorbidity were found in pathological (69.6%) and at-risk (34.8%) gamblers compared with no-risk (17%) gamblers.

According to the authors, the current data indicate that when compared with no-risk and at-risk gamblers, pathological gamblers appear to exhibit impaired response inhibition and deficits in cognitive flexibility. (40 References) EAF
SEROTONIN AND DOPAMINE PLAY COMPLEMENTARY ROLES IN GAMBLING TO RECOVER LOSSES

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NEUROPSYCHOPHARMACOLOGY, 36:402-10, January 2011

Pathological gambling is a source of enormous personal and family distress and represents a significant public health issue. Continued gambling to recover losses (loss chasing) is a prominent feature of social and pathological gambling. However, very little is known about the neuromodulators that influence this behavior. The present authors conducted three separate experiments in which they investigated the influence of serotonin activity, D_{2}/D_{3} receptor activity, and beta-adrenoceptor activity on the loss-chasing behavior of age- and IQ-matched healthy adults who were randomly assigned to receive treatment or an appropriate control/placebo.

In Experiment 1 (N=34), the participants consumed amino-acid drinks that did or did not contain the serotonin precursor tryptophan. In Experiment 2 (N=30), the participants received a single dose (176 µg) of the D_{2}/D_{3} receptor agonist pramipexole, or placebo. In Experiment 3 (N=28), the participants received a single dose (80 mg) of the beta-adrenoceptor blocker propranolol, or placebo. Following treatment, the participants completed a computerized loss-chasing game. Mood and heart rate were measured at baseline and after treatment. Tryptophan depletion significantly reduced the number of decisions made to chase losses and the number of consecutive decisions to chase, in the absence of any marked mood changes. On the other hand, pramipexole significantly increased the value of losses chased and diminished the value of losses surrendered. Propranolol markedly reduced heart rate, but produced no significant changes in loss-chasing behavior.

According to the authors, loss chasing may be thought of as an aversively motivated escape behavior, controlled, in part, by the marginal value of continued gambling relative to the value of already accumulated losses. The current findings suggest that the general persistence of gamblers in playing to recover losses is modulated by serotonin activity, whereas the evaluation of losses that gamblers judge to be worth chasing is mediated by the activity of the D_{2}/D_{3} receptor system. (68 References)
Pathological gambling (PG) and anxiety disorders both have considerable health implications and may be associated with suicidality and disrupted social and financial domains. PG and anxiety disorders frequently co-occur. However, the extent to which the co-occurrence is related to genetic or environmental factors across PG and anxiety disorders is not known. In the present study, the authors examined data from the Vietnam Era Twin Registry (7,869 male twins) by means of bivariate models in order to estimate genetic and shared and unique environmental contributions to PG and generalized anxiety disorder (GAD) and to PG and panic disorder (PD). The participants were interviewed in 1992 for the purpose of ascertaining DSM-III-R diagnoses. The mean age of the respondents was 42 years, and the majority (93.4%) were white.

The data revealed that lifetime criteria for PG, GAD, and PD were met by 112 (1.4%), 966 (12.3%), and 473 (6%) participants, respectively. In unadjusted models, PG was found to frequently co-occur with both GAD and PD. While both genetic and unique environmental factors contributed individually to PG, GAD, and PD, the best fitting model indicated that the relationship between PG and GAD was attributable predominantly to shared genetic contributions. On the other hand, substantial correlations were seen between both the genetic and unique environmental contributions to PG and PD.

According to the authors, the existence of shared genetic contributions between PG and both GAD and PD suggests that specific genes (perhaps those involved in affect regulation or stress responsiveness) may contribute to PG and anxiety disorders. Overlapping environmental contributions to the co-occurrence of PG and PD indicate that common life experiences (e.g., early life trauma) may contribute to both PG and PD. Conversely, the data suggest that distinct environmental factors may contribute to PG and GAD (e.g., early onset of gambling in PG. The researchers recommend that future studies examine the relationship between PG and anxiety disorders in other populations (women and adolescents) in order to identify specific genetic and environmental influences that may account for the manifestation of these disorders and their co-occurrences. (32 References)
GAMBLING, DISORDERED GAMBLING AND THEIR ASSOCIATION WITH MAJOR DEPRESSION AND SUBSTANCE USE: A WEB-BASED COHORT AND TWIN-SIBLING STUDY

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PSYCHOL MED, 42:497-508, March 2012

Pathological gambling (PG) is a persistent and recurrent maladaptive pattern of gambling behavior characterized by increased preoccupation with gambling activities, loss of control, and continued gambling despite problems in social or occupational functioning. It is associated with significant financial losses, legal problems, and disrupted interpersonal and familial relationships. Previous studies have found that PG is part of a broader continuum of gambling-related problems that is often referred to as disordered gambling (DG) and that includes less severe forms of the disorder. Relatively little is known about the genetic and environmental contributions to DG and gambling frequency. To address this issue, the present authors conducted a survey in which a web-based cohort (N=43,799) were assessed with regard to number of lifetime gambling episodes; DSM-IV criteria for PG; alcohol, nicotine, and caffeine intake; nicotine dependence (ND); and DSM-III-R criteria for lifetime major depression (MD). The sample included both members of 609 twin and 303 sibling pairs.

Of the total sample, 30.2% denied ever gambling in their lives; 25.3% reported gambling between one and five times, 16% between six and 15 times, 6.3% between 16 and 24 times, 10.3% between 25 and 50 times, and 11.9% more than 50 times. When the entire cohort was considered, symptoms of DG indexed a single dimension of liability. Symptoms of DG were weakly related to caffeine intake and moderately related to MD, consumption of cigarettes and alcohol, and ND. Among the twin and sibling pairs, familial resemblance for number of times having gambled resulted from both familial-environmental and genetic factors. For symptoms of DG, resemblance resulted solely from genetic factors. Bivariate analyses indicated a low genetic correlation between symptoms of DG and MD, whereas genetic correlations with DG were substantially higher with use of alcohol, caffeine, and nicotine, and ND. Results were invariant across genders.

The authors conclude that while participation in gambling seems to be determined by shared environmental and genetic factors, DG appears to constitute a single latent dimension that is largely genetically determined and that is more closely related to externalizing behaviors rather than internalizing behaviors. Because the current findings seem to be invariant across genders, they suggest that the etiological factors of DG are likely to be similar in men and women. (48 References)
LONGITUDINAL LINKS BETWEEN IMPULSIVITY, GAMBLING PROBLEMS AND DEPRESSIVE SYMPTOMS:
A TRANSACTIONAL MODEL FROM ADOLESCENCE TO EARLY ADULTHOOD

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J CHILD PSYCHOL PSYCHIATRY, 52:130-8, February 2011

Previous research has found a high degree of comorbidity between gambling problems and depressive symptoms in both adolescents and adults; however, the directionality of this link is unclear. Moreover, the present authors state, the co-occurrence of gambling problems and depressive symptoms could be spurious and explained by common underlying risk factors, such as impulsivity and socio-family risk (e.g., poverty, divorce, teen parenthood). The goals of the current study were to determine (1) whether common antecedent factors explain the concurrent links between depressive symptoms and gambling problems, and (2) whether possible transitional links between depressive symptoms and gambling problems exist from late adolescence into early adulthood.

A total of 1,004 males from low socioeconomic areas participated in the study. The ongoing investigation began when the boys were attending kindergarten. Socio-family risk data were collected when the boys were 10 years old. Impulsivity data were gathered when the subjects were 14 years of age. Information on gambling and depression were collected when the participants were 17 and 23 years old. Analyses revealed a positive predictive link between impulsivity at age 14 and depressive symptoms and gambling problems at age 17. In turn, gambling problems at age 17 predicted an increase in depressive symptoms from age 17 to age 23, while depressive symptoms at age 17 predicted an increase in gambling problems from age 17 to age 23.

The current results suggest that a common antecedent risk factor (i.e., impulsivity) contributes to the early development of both gambling and depressive symptoms and explains their co-occurrence in adolescence. However, once gambling problems and depressive symptoms have emerged, their escalation appears to be better explained by a mutual direct influence between the two sets of disorders. These findings seem to reconcile two opposing theoretical perspectives regarding the developmental interplay between gambling problems and depressive symptoms, with one maintaining that gambling problems precede depressive symptoms and the other affirming that depressive symptoms precede gambling problems. (47 References)
CORRELATES OF AT-RISK/PROBLEM INTERNET GAMBLING IN ADOLESCENTS

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 50:150-9, February 2011

Internet gambling represents a relatively new and growing phenomenon, with online gambling sites increasing from 160 in 1999 to over 1,800 in 2002. The widespread availability of Internet gambling sites presents young people with multiple opportunities to gamble online. Despite these circumstances, relatively few studies have examined Internet gambling among adolescents. The purpose of the present investigation was to examine the correlates of at-risk or problem gambling in adolescents who either acknowledged or denied Internet gambling.

Using chi-square and logistic regression analyses, the authors evaluated survey data drawn from a statewide investigation of gambling and other risk-taking behaviors among Connecticut high-school students. The study sample was composed of 2,006 students who reported past-year gambling and who completed all questions targeting DSM-IV criteria for pathological gambling. Respondents who reported past-year gambling but did not acknowledge any DSM-IV criteria were classified as low-risk gamblers (LRGers), while those who endorsed one or more DSM-IV criteria were classified as at-risk/problem gamblers (ARPGers). Of the 2,006 adolescent gamblers, 412 (20.5%) reported Internet gambling; of these, 57.5% were classified as ARPGers and 42.5% as LRGers. Among non-Internet gamblers (N=1,594), 27.7% were classified as ARPGers and 72.3%, as LRGers. Compared with ARPG in the non-Internet gambling group, ARPG in the Internet gambling group was more strongly associated with poor academic performance and substance use (particularly current heavy alcohol use) and less strongly associated with gambling with friends. ARPG in the Internet and non-Internet gambling groups, respectively, was associated, each with multiple adverse measures, including dysphoria/depression (odds ratios 1.76 and 1.96); getting into serious fights (odds ratios 2.50 and 1.93); carrying weapons (odds ratios 2.11 and 1.90); and use of tobacco (odds ratios 2.05 and 1.88 for regular use), marijuana (odds ratios 2.02 and 1.39), and other drugs (odds ratios 3.24 and 1.67).

According to the authors, the differences found between Internet gamblers and non-Internet gamblers highlight the importance of considering specific forms of gambling when evaluating the health implications related to the severity of problem gambling in adolescents. (42 References)
ALTERED NEURAL REWARD REPRESENTATIONS IN PATHOLOGICAL GAMBLERS REVEALED BY DELAY AND PROBABILITY DISCOUNTING

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ARCH GEN PSYCHIATRY, 69:177-86, February 2012

Pathological gambling is classified as an impulse control disorder in DSM-IV, characterized by such core features as diminished self-control, compulsive gambling behavior, craving before gambling, and continuing to gamble despite negative consequences. A hallmark of pathological gambling is an increased discounting of delayed rewards. Recent neuroimaging studies have revealed the neural basis underlying delay discounting and probability discounting; however, only a few have examined reward processing among pathological gamblers. Using a computational model of intertemporal (delay discounting) and risky (probability discounting) decision-making, the authors examined subjective neural reward representations in pathological gamblers and normal controls.

Study participants were recruited from the local community through advertisements and self-help groups. The sample was composed of 16 pathological gamblers (15 men, one woman; age range, 21-48 years) and 16 healthy controls (15 men, one woman; age range, 22-50 years). Gamblers and controls were matched in terms of age, sex, smoking status, income, educational level, and handedness. During functional magnetic resonance imaging, the subjects participated in a computer-based paradigm whereby they made choices between a fixed immediate reward and larger delayed (delay discounting) or risky (probability discounting) rewards. Compared with controls, pathological gamblers showed increased discounting of delayed rewards and a trend toward decreased discounting of probabilistic rewards. At the neural level, a significant group condition interaction indicated that reward representations in the gamblers were modulated in a condition-specific manner, such that they exhibited increased (delay discounting) and decreased (probability discounting) neural value correlations in the reward system. In addition, throughout the reward system, neuronal value signals for delayed rewards were negatively correlated with gambling severity.

The current results extend previous reports of a generally hypoactive reward system in pathological gamblers by showing that, even when subjective reward valuation is taken into account, gamblers still show altered reward representations. The data point toward a gradual degradation of mesolimbic reward representations for delayed rewards during the course of pathological gambling. (67 References)
DISCOUNTING OF PROBABILISTIC REWARDS IS ASSOCIATED WITH GAMBLING ABSTINENCE IN TREATMENT-SEEKING PATHOLOGICAL GAMBLERS

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J ABNORM PSYCHOL, 121:151-9, February 2012

Behavioral economic theories of discounting are increasingly being applied to the study of addictive behaviors. It has been found that individuals with addictive disorders, including substance abusers and pathological gamblers, discount or devalue rewards delayed in time more than control subjects. Theoretically, preference for probabilistic rewards is directly related to gambling; however, there is limited empirical research directed at examining probabilistic discounting in individuals with pathological gambling. In the present study, the author evaluated probability and delay discounting in treatment-seeking pathological gamblers and their association with gambling treatment outcomes during and after treatment.

Upon study entry, 226 pathological gamblers completed probability and delay discounting tasks and then were randomly assigned to one of the following three treatment conditions: referral to Gamblers Anonymous (N=59); referral to Gamblers Anonymous plus cognitive-behavioral therapy via workbook (N=84); and referral to Gamblers Anonymous plus professionally delivered cognitive-behavioral therapy (N=83). Gambling behavior was measured throughout treatment, and at a one-year follow-up assessment. After possible confounding variables and treatment conditions were controlled, the results indicated that more shallow probability discounting was associated with greater reductions in amounts wagered during treatment and likelihood of gambling abstinence at the end of treatment and throughout the follow-up period. No associations were found between delay discounting and gambling treatment outcomes.

According to the author, the current results suggest that probability discounting may be an important construct in understanding pathological gambling and its treatment. For example, treatment-seeking pathological gamblers who discount probabilistic rewards less steeply may recognize that they will be unable to stop gambling once they start, and so may gravitate toward an abstinence goal. Contrastingly, pathological gamblers who discount probabilistic reinforcers relatively more steeply may be more prone toward gambling after initiating treatment, perhaps assuming that they will be able to stop gambling once they start. (46 References)
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BOOKS RECEIVED FOR REVIEW
FRONTAL BRAIN OSCILLATORY COUPLING IN CHILDREN OF PARENTS WITH SOCIAL PHOBIA: A PILOT STUDY

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J NEUROPSYCHIATRY CLIN NEUROSCI, 23:111-4, Winter 2011

Brain oscillations in specific frequency bandwidths reflect the arousal of functionally-distinct neural systems. Recent studies have suggested that cross-frequency interactions seen in evoked and spontaneous oscillations reflect relationships among different neuroanatomical levels. Spectral coupling between delta and beta frequency bands provides an electrophysiological correlate of cortico-subcortical cross-talk that is sensitive to motivational states and neuroendocrine patterning. This spectral coupling between delta and beta oscillations has been found to be related to anxiety. In the present pilot study, the authors compared resting frontal brain oscillatory coupling in children born to socially phobic parents with that of children born to healthy parents.

The participants were as follows: six right-handed children (three boys, three girls; mean age, 10.67 years) who had a biological parent with a primary DSM-IV diagnosis of social phobia and 10 typically developing right-handed children (five boys, five girls; mean age, 10.25 years) whose parents were free of any psychiatric or neurological illness. Regional EEG data were collected during a two-minute resting condition. Delta-beta coupling was estimated by means of Spearman’s rank-order correlations. The children of socially phobic parents showed stronger coupling than children of healthy parents in both the left and right frontal leads. Compared with children of nonphobic parents, children of socially phobic parents exhibited significantly greater delta-beta coupling in the right, but not the left, frontal lead. There were no between-group differences in terms of parental perceptions of their children’s shyness.

According to the authors, the current pilot study provides preliminary evidence that offspring of parents clinically diagnosed with social phobia differ in patterns of oscillatory EEG coupling during early school-age years when compared with children of healthy parents. The increased frontal coupling of delta and beta oscillations exhibited by the children of socially phobic parents is related to elevated anxiety, behavioral inhibition, and cortisol concentrations, the researchers note. (14 References)
SOCIAL PHOBIA AND SUBTYPES IN THE NATIONAL COMORBIDITY SURVEY ADOLESCENT SUPPLEMENT: PREVALENCE, CORRELATES, AND COMORBIDITY

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 50:870-80, September 2011

While social phobia typically develops during adolescence, no nationally representative studies in the United States have examined the rates and features of this condition among young people who fall in this age range. The objectives of the current investigation were as follows: (1) to present the lifetime prevalence, comorbidity, and sociodemographic and clinical correlates of social phobia in a large, nationally representative sample of United States adolescents; and (2) to examine differences in the rates and features of social phobia across the proposed DSM-5 diagnostic subtypes.

Data for the present study were drawn from the National Comorbidity Survey Replication Adolescent Supplement, which is a nationally representative face-to-face survey of 10,123 adolescents (age range, 13 to 18 years) residing in the continental United States. The results revealed that 8.6% of the adolescents met criteria for any social phobia during their lifetime. Of this group of adolescents, 55.8% were affected with the generalized subtype of social phobia, and 44.2% exhibited nongeneralized social phobia. Only 0.7% met criteria for the proposed DSM-5 performance-only subtype. Generalized social phobia was more common in female adolescents, and risk for this subtype increased with age. Compared with those who had nongeneralized forms of the disorder, adolescents with generalized social phobia had a younger age of onset, higher levels of disability and clinical severity, and a greater degree of comorbidity.

According to the authors, the present findings indicate that social phobia is a highly prevalent, persistent, and impairing psychiatric disorder seen in adolescent youth and that it appears to closely resemble social phobia conditions found in adults in terms of magnitude and severity. The current data also provide evidence for the clinical utility of the generalized subtype of the disorder and highlight the importance of considering the heterogeneity of social phobia among adolescents. (47 References)
RELATIONSHIP BETWEEN SOCIAL PHOBIA AND DEPRESSION DIFFERS BETWEEN BOYS AND GIRLS IN MID-adoLESCENCE

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J AFFECT DISORD, 133:97-104, September 2011

Previous reports have indicated that social phobia (SP) and depression (DEP) often have their onset in adolescence and are highly comorbid, with SP usually preceding DEP. However, there is a lack of population-based, prospective studies that focus on adolescents who are vulnerable to both disorders and that take into account possible gender differences in the relationship between the two. The aim of the present investigation was to study the prevalence of SP, DEP, and the comorbidity between these two disorders in adolescents at age 15 and again at age 17. The authors examined the course of SP and DEP and the development of their comorbidity over the course of a two-year follow-up, while closely evaluating any between-sex differences.

The current report is part of the prospective Adolescent Mental Health Cohort study. The subjects were secondary school students who responded to a survey conducted in two Finnish cities during 2002-2003 (T1) and again during 2004-2005 (T2). A total of 2,038 students completed the survey at both T1 and T2 (two-year follow-up). The mean age of the participants was 15.5 years at T1 and 17.6 years at T2. Social phobia was measured by the Social Phobia Inventory and depression, by the 13-item Beck Depression Inventory. At T1 and T2, prevalences were calculated as simple frequencies for SP without DEP, DEP without SP, and comorbid SP and DEP. Between ages 15 and 17, there was a significant increase in the prevalence of SP without DEP among girls, but not among boys. There was a significant decrease in the prevalence of DEP without SP in the total cohort. Between T1 and T2, the prevalence of comorbid SP and DEP increased significantly only among boys. Of those who had SP at age 15, 42.9% also presented with DEP, with girls doing so more frequently than boys. Of those who had DEP at age 15, 42.5% had comorbid SP, with no significant between-sex differences. Of those with SP at age 17, 42.5% had comorbid DEP (girls and boys equally frequently). Of those with DEP at age 17, 54.9% also presented with SP (girls and boys equally as often). The course of both disorders was unstable, but recovery was common.

According to the authors, the current findings suggest that the relationship between social phobia and depression appears to differ greatly between adolescent boys and girls. (62 References)
BECOMING THE CENTER OF ATTENTION IN SOCIAL ANXIETY DISORDER: 
STARTLE REACTIVITY TO A VIRTUAL AUDIENCE 
DURING SPEECH ANTICIPATION

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J CLIN PSYCHIATRY, 72:942-8, July 2011

Social anxiety disorder (SAD) is a common, impairing psychiatric illness that 
involves a persistent fear of situations in which the individual is scrutinized (e.g., 
public speaking). There is a lack of detailed information with regard to the ways 
persons diagnosed with SAD respond physiologically under social-evaluative 
threat. In the present study, the authors assessed startle reactivity within a 
virtual reality (VR) context to demonstrate heightened physiologic reactivity in 
persons with SAD and to identify components of social-evaluative contexts that 
would discriminate between healthy individuals and those with SAD.

Between December 2005 and March 2008, 16 individuals who 
met DSM-IV-TR criteria for SAD (ten men, six women; mean age, 35 years) and 16 healthy 
individuals (nine men, seven women; mean age, 31 years) were enrolled in the 
study. The subjects were asked to prepare and deliver a short speech in a VR 
environment, which simulated standing center stage before a live audience and 
allowed for the gradual introduction of social cues during speech anticipation. 
Startle eye-blink responses were elicited periodically by white noise bursts 
presented during anticipation, speech delivery, and recovery in VR, as well as 
outside VR during an initial habituation phase, with startle reactivity being 
measured by electromyography. The subjects used a 0-10 scale to rate their level 
of distress at four time points in VR, with anchors ranging from “not distressed” 
to “highly distressed.” State anxiety was measured before and after VR with the 
Spielberger State-Trait Anxiety Inventory. Compared with healthy individuals, 
those with SAD reported consistently greater distress and anxiety throughout 
the procedure. Subjects with SAD also showed a robust increase in state 
reactivity when the virtual audience became silent and directed their eye gaze 
toward the participants. Persons with SAD were considerably more distressed 
than healthy individuals during anticipation outside and inside VR and during 
and after speech delivery. State anxiety was also higher in those with SAD before 
and after the VR procedure.

According to the authors, the current data indicate that the VR environment 
is sufficiently realistic to provoke fear and anxiety in individuals who are highly 
vulnerable to socially threatening situations. (46 References)
ANXIETY, EMOTIONAL SECURITY AND THE INTERPERSONAL BEHAVIOR OF INDIVIDUALS WITH SOCIAL ANXIETY DISORDER

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PSYCHOL MED, 41:545-54, March 2011

Interpersonal functioning is central to social anxiety disorder (SAD), a condition in which anxiety symptoms impair social performance. Empirical studies of interpersonal behaviors in persons with SAD frequently have relied on analog samples, global retrospective reports, and laboratory observations. In addition, much of the research has focused on avoidance and safety behaviors while neglecting potential links between SAD and affiliative behaviors. Using a naturalistic, repeated-measures methodology, the authors of the present study examined the influence of situational anxiety and emotional security on interpersonal behaviors in 40 individuals with SAD (20 men, 20 women) and 40 normal controls (20 men, 20 women). The control sample did not differ from the SAD group in terms of age, education, or employment status. The participants monitored their behavior and affect in naturally occurring social interactions by using an event-contingent recording procedure.

The results revealed that individuals with SAD reported higher levels of submissive behavior and lower levels of dominant behavior than the control subjects. Consistent with cognitive-behavioral and evolutionary theories, elevated anxiety during specific events was found to predict increased submissiveness among those with SAD. Consistent with attachment theory, elevations in event-level emotional security were found to be associated with increased affiliative behaviors (increased agreeable behavior and decreased quarrelsome behavior) in the SAD subjects. The results could not be accounted for by concurrent elevations in sadness or between-group differences in the distribution of social partners.

According to the authors, the current data suggest that the interpersonal manifestations of SAD extend beyond behavioral inhibition, avoidance, and sensitivity to negative cues; socially anxious individuals may also respond to positive appraisals with increased affiliation. In the treatment of individuals with SAD, the researchers note, clinical interventions should focus on the identification of contextual and relational features that enhance perceived emotional security rather than target only those factors likely to elicit anxiety and avoidance. (41 References)
OCCUPATIONAL IMPAIRMENT AND SOCIAL ANXIETY DISORDER IN A SAMPLE OF PRIMARY CARE PATIENTS

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J AFFECT DISORD, 130:209-12, April 2011

Social Anxiety Disorder (SAD) is the second most prevalent psychiatric disorder in the United States. Because of the social impairments associated with SAD, individuals with this disorder may experience increased occupational impairment as compared to persons with other anxiety disorders. Among those with SAD who are employed, the disorder may lead to decreased work productivity, increased absences, and other occupational impairments. In the present study, the authors attempted to refine the understanding of SAD’s effects on occupation by comparing employment rates and workplace functioning in primary care patients with SAD with those in patients with other anxiety disorders and comorbid Major Depressive Disorder (MDD).

Data were gathered from the Primary Care Anxiety Project, a naturalistic, longitudinal study of anxiety disorders in 539 primary care patients. Of these patients, 182 met DSM-IV criteria for SAD. Seventy-one percent met criteria for at least one other psychiatric disorder at intake, and 100% met criteria for additional comorbid disorders at some point during their lifetime. In a multivariate linear regression model that controlled for educational attainment, the results indicated that SAD and MDD were unique predictors associated with lower workplace functioning, whereas all other disorders were not (according to the interviewer-administered Longitudinal Interval Follow-up Evaluation). Individuals with SAD were over two times more likely to be unemployed, while those with other anxiety disorders were likely to be employed. However, MDD was not found to be predictive of unemployment status. Patients with SAD and MDD were significantly more impaired in workplace functioning than all other individuals, regardless of educational level. Patients with SAD were 2.25 more likely to be unemployed (but expected to work) than patients with any other psychiatric condition.

According to the authors, the current findings highlight the need to assess individuals with SAD for the presence of undereducation and underperformance in the workplace, as they are at most risk for these impairments. In addition, the researchers note, early detection and intervention in persons with (or at risk for) SAD may serve to curb the future impact of social anxiety on occupational attainment. (23 References)
Social phobia is a common anxiety disorder that often imposes persistent functional impairment on its sufferers. Some studies have suggested the existence of a continuity of social anxiety symptomatology that runs from childhood into adulthood. Behavioral inhibition (BI), a heritable childhood temperament defined by a tendency to restrict exploration and avoid novelty, has been proposed as a risk factor for the development of social phobia. Recent investigations have indicated that BI may also be a precursor to anxiety, as well as to depressive and alcohol-related disorders, all of which have been found to co-occur frequently with social phobia. In the present study, the authors explored the possible relationships between BI and psychiatric disorders in 256 adults with a primary diagnosis of social phobia.

The study sample was composed of 113 men and 143 women, all of whom had suffered from social phobia for an average of 20.7 years. BI severity was assessed by means of the Retrospective Self-Report of Inhibition (RSRI), with subjects being instructed to think about themselves as they had been in elementary school. The severity of social phobia and the presence of comorbid diagnoses were evaluated with the Liebowitz Social Anxiety Scale (LSAS) and the Mini-International Neuropsychiatric Interview, respectively. Upon study entry, these socially phobic individuals suffered from one or more of the following comorbid mental disorders: major depressive disorder (N=63), panic disorder (N=56), agoraphobia (N=70), generalized anxiety disorder (N=78), obsessive-compulsive disorder (N=20), alcohol abuse (N=13), alcohol dependence (N=21), substance abuse (N=10), and substance dependence (N=8). The RSRI score was found to be significantly and positively correlated with both the LSAS score and the occurrence of a major depressive disorder. Thus, the severity of childhood BI was associated with the severity of social anxiety as well as the occurrence of lifetime avoidant personality disorder and major depressive disorder in adults with social phobia. No significant association was found between BI and other lifetime psychiatric comorbidities.

The present findings indicate that a childhood history of BI may be associated with an increased risk of depression and avoidant personality disorder comorbidity in adults with social phobia. (19 References)
WORKING MEMORY CAPACITY IN GENERALIZED SOCIAL PHOBIA

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There is a large body of research suggesting that individuals with generalized social phobia have biased cognitive processes that may maintain and exacerbate their symptoms. While some social information processing occurs rapidly and automatically, complex forms of social decoding may be dependent on the availability of higher-level cognitive resources, such as executive control. Thus, abnormalities in executive control could contribute to incorrect evaluations of social cues. In spite of the research indicating that persons who suffer from generalized social phobia are characterized by aberrant social information processing, relatively few studies have examined executive control in these individuals. Using an operation span task with threat-relevant and neutral stimuli, the authors of the present investigation assessed working memory capacity (WMC) in individuals with generalized social phobia and in nonanxious control subjects.

The final study sample was composed of 32 individuals who met DSM-IV criteria for current generalized social phobia and 30 nonanxious controls who did not meet criteria for any past or present Axis I disorder. When WMC performance was tested with neutral stimuli, individuals in the nonanxious control group performed better than individuals in the generalized social phobia group. The WMC performance of the socially anxious and nonanxious groups did not differ when presented with social threat words. Individuals with generalized social phobia demonstrated better WMC when presented with social threat stimuli relative to neutral stimuli.

According to the authors, the present results provide support for the conclusion that socially anxious individuals demonstrate different patterns of WMC performance relative to nonanxious individuals, depending on the type of information that is being processed. This pattern may be the result of differential allocation of attentional resources to social threat information in persons with social anxiety relative to nonanxious persons. Therefore, the researchers conclude, deficits in this cognitive capacity may partially account for the cognitive biases that are characteristic of those with generalized social phobia. (47 References)
COGNITIVE THERAPY VS INTERPERSONAL PSYCHOTHERAPY
IN SOCIAL ANXIETY DISORDER
A Randomized Controlled Trial

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ARCH GEN PSYCHIATRY, 68:692-700, July 2011

Social anxiety disorder (SAD) is a common mental illness that is associated with considerable vocational and psychosocial handicaps and an increased risk for the presence of comorbid disorders. Cognitive therapy (CT) focuses on the modification of biased information processing and the dysfunctional beliefs of those with SAD. Interpersonal psychotherapy (IPT) is geared toward changing problematic interpersonal behavior patterns that may play important parts in the maintenance of SAD. To compare the efficacy of CT, IPT, and a waiting-list control (WLC) condition in the treatment of SAD, the present authors conducted a randomized, controlled trial at two academic outpatient treatment sites.

Of 254 potential participants who were screened for the study, 117 had a primary diagnosis of SAD and were eligible for randomization; 106 participants completed the treatment (CT or IPT) or waiting-list phase. Treatment comprised 16 individual sessions of either CT or IPT and one booster session. Twenty weeks after randomization, posttreatment assessment was conducted, and participants in the WLC condition were then assigned to either CT or IPT. The primary outcome was treatment response on the Clinical Global Impression Improvement Scale as assessed by independent masked evaluators. Secondary outcome measures were independent assessor ratings on the Liebowitz Social Anxiety Scale (LSAS) and the Hamilton Rating Scale for Depression and the patient-completed Social Phobia and Anxiety Inventory. At the posttreatment assessment, response rates were 65.8% for CT, 42.1% for IPT, and 7.3% for WLC. LSAS ratings indicated that CT performed significantly better than IPT, and both treatments were superior to WLC. At a one-year follow-up, the differences between CT and IPT were largely maintained, with significantly higher response rates being seen in the CT group (68.4%) than in the IPT group (31.6%); better outcomes were also seen as assessed by the LSAS.

The authors conclude that in the current study both CT and IPT led to considerable improvements that were maintained one year after treatment; however, CT appeared to be more effective than IPT in reducing social phobia symptoms. (55 References)
PREDICTORS OF RESPONSE TO AN ATTENTION MODIFICATION PROGRAM IN GENERALIZED SOCIAL PHOBIA

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J CONSULT CLIN PSYCHOL, 79:533-41, August 2011

A number of randomized, double-blind, placebo-controlled studies have supported the efficacy of computerized attention modification programs (AMPs) in reducing symptoms of anxiety in patients with diagnosed anxiety disorders. AMP is based on cognitive theories of anxiety that propose a causal role for selective attention to threat-relevant information in the maintenance of anxiety. In the current investigation, the authors examined patient characteristics that would predict response to AMP in a large sample of individuals diagnosed with generalized social phobia.

The study sample was composed of 112 individuals who were seeking treatment for generalized social phobia and who completed a randomized clinical trial comparing AMP (N=55) with a placebo condition (attention control condition, N=57). The researchers evaluated the following domains of baseline predictors of treatment response: demographic characteristics (gender, age, ethnicity, years of education), clinical characteristics (Axis I comorbidity, trait anxiety, depression), and cognitive disturbance factors (attentional bias for social threat, social interpretation bias). The primary outcome measure was the clinician-rated Liebowitz Social Anxiety Scale, a 24-item scale that separately assesses fear and avoidance of social interaction and performance situations. The results revealed that ethnicity predicted treatment response across both interventions; participants who self-identified as non-Caucasian displayed better overall responses than Caucasian participants. The only prescriptive variable to emerge was attentional bias for social threat at pre-assessment. Participants in the AMP group who exhibited higher attentional bias scores displayed significantly greater reductions in clinician-rated social anxiety symptoms than their counterparts in the placebo group (attention control condition).

According to the authors, the findings of the current study point to a particular subgroup of individuals with generalized social phobia for whom AMP may be most effective; these data also serve to illustrate the boundaries within which attentional retraining procedures may yield the greatest clinical benefit. (48 References)
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NEUROLOGY, 76:822-9, March 1, 2011

Late-onset Alzheimer disease (AD) is a neurodegenerative disorder caused by complex genetic and environmental mechanisms. Age is the most significant risk factor for developing AD, followed by a family history of AD, with maternal transmission being found significantly more frequently than paternal transmission. In the current longitudinal brain imaging study, the authors attempted to determine whether different patterns of regional gray matter atrophy would be seen in cognitively healthy elderly subjects with and without a family history of late-onset AD.

As part of the University of Kansas Brain Aging Project, cognitively intact individuals who were 60 years of age or older underwent MRI examinations at baseline and at two-year follow-up. The subjects were similar in age, gender, education level, and Mini-Mental State Examination scores and were grouped as follows: 11 with a maternal history of AD, 10 with a paternal history of AD, and 32 with no parental history of AD. \textit{APOE} genotypes were determined by means of restriction enzyme isotyping. While controlling for age, gender, and \textit{APOE} status, the researchers used a custom voxel-based morphometry processing stream to examine regional differences in atrophy between family-history groups. A secondary analysis was performed to evaluate regional atrophy differences between the 14 subjects who carried an \textit{APOE}4 allele and the 39 who did not. Compared with the subjects without a family history of late-onset AD, those with a family history had significantly increased whole-brain gray matter atrophy and CSF expansion. When the subjects with a maternal and paternal family history were considered separately, only maternal family history was found to be associated with longitudinal measures of brain change. Voxel-based analysis also revealed that subjects with a maternal family history had significantly greater atrophy in the precuneus and parahippocampus/hippocampus regions than subjects with a paternal history and those with no family history; this finding was independent of \textit{APOE}4 status, gender, and age. Subjects who carried an \textit{APOE}4 allele had more regional atrophy in the frontal cortex than those who were noncarriers of the allele.

According to the authors, cognitively normal individuals with a maternal family history of late-onset AD appear to have progressive gray matter volume reductions in select AD-vulnerable brain regions, specifically the precuneus and parahippocampal gyrus. (40 References)
THE SYMPTOM OF LOW MOOD IN THE PRODROMAL STAGE OF MILD COGNITIVE IMPAIRMENT AND DEMENTIA: A COHORT STUDY OF A COMMUNITY DWELLING ELDERLY POPULATION

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J NEUROL NEUROSURG PSYCHIATRY, 82:788-93, July 2011

Subclinical syndromes of depression and isolated depressive symptoms are more common than clinical depression in both mild cognitive impairment (MCI) and dementia. The most prevalent symptom of depression seen in those with MCI is low mood. Taking into account MCI severity, time of assessment, and interaction with other factors, the authors investigated the symptom of low mood as a predictor of MCI and its progression to dementia. Low mood was defined as a report of perceived sadness.

The study sample was composed of 764 cognitively healthy elderly subjects (75 years of age or older) living in the community. The participants were assessed by means of direct interviews to detect low mood. The subjects were then followed for a period of six years to identify those who developed MCI. Those with incident MCI were followed for a further three years to assess progression to dementia. During follow-up, 160 individuals developed MCI; of these, 40 were classified as having amnestic MCI (aMCI) and 120 as having global cognitive impairment (other cognitive impairment no dementia [oCIND]). After adjusting for sociodemographic factors, the researchers found that low mood detected at baseline substantially increased the risk of developing MCI. More specifically, low mood was associated with a 5.8-fold increased risk of aMCI, a 2.2-fold increased risk of oCIND, and a 2.7-fold increased risk of overall MCI. The APoE-4 allele interacted with low mood in a synergistic fashion, increasing the risk of aMCI; however, no interaction with psychiatric, vascular, frailty-related, or psychosocial factors was observed. As opposed to low mood co-occurring with MCI, low mood at baseline was found to be associated with a 5.3-fold increased risk of progression to dementia in subjects with aMCI; no such association was found in those with oCIND.

According to the authors, the current findings revealed that low mood was more strongly associated with amnestic MCI than with global cognitive impairment. Progression toward dementia was predicted only by low mood that was manifest in the prodromal stage of MCI. The researchers conclude that low mood appears to be particularly prominent in the very early stages of cognitive decline. (41 References)

EAF
COGNITIVE DECLINE IN PRODROMAL ALZHEIMER DISEASE 
AND MILD COGNITIVE IMPAIRMENT

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By definition, dementia due to Alzheimer disease (AD) is preceded by a minimum of six months of cognitive decline. However, there have been relatively few studies of this prodromal phase of the disease, and estimates of its duration range from approximately one year to more than 10 years. In the present investigation, the authors examined changes in cognitive function during the prodromal phase of AD and before the onset of mild cognitive impairment (MCI).

The sample was drawn from two longitudinal cohort studies (the Religious Orders Study and the Rush Memory and Aging Project). For up to 16 years, more than 2,000 older individuals underwent annual clinical evaluations that included detailed testing of cognitive function and clinical classification of MCI, dementia, and AD. At baseline, there were 2,071 persons without dementia and 1,511 without cognitive impairment. During follow-up, 462 individuals developed AD; 20 persons with dementia solely due to another condition were excluded from the analyses. Those who developed AD were older than those who did not (81.3 years vs. 76.3 years), but the groups were similar in years of education (16.4 vs. 16.2 years) and sex distribution (72.7% female vs. 71.9% male). The data revealed that five to six years before diagnosis, the rate of global cognitive decline accelerated more than 15-fold. The acceleration in cognitive decline occurred slightly earlier for semantic memory (76 months before diagnosis) and working memory (75 months before diagnosis) than for other cognitive functions. MCI was also preceded by years of cognitive decline that began earlier (80 months before diagnosis) and proceeded more rapidly (annual loss of 0.102 unit) in the amnestic than in the nonamnestic (62 months, 0.072 unit) subtype.

According to the authors, the findings of the present investigation indicate that dementia due to AD is preceded by approximately five to six years of accelerated decline in multiple domains of cognitive functioning. By the time that individuals meet clinical criteria for a diagnosis of AD, they have already experienced many years of progressive cognitive decline. On the other hand, however, little cognitive decline is evident in those individuals who do not develop AD. (38 References)
IMPACT OF IMPAIRMENT IN INSTRUMENTAL ACTIVITIES OF DAILY LIVING AND MILD COGNITIVE IMPAIRMENT ON TIME TO INCIDENT DEMENTIA: RESULTS OF THE LEIPZIG LONGITUDINAL STUDY OF THE AGED

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PSYCHOL MED, 41:1087-97, May 2011

Mild cognitive impairment (MCI) has been found to be associated with a high risk for the development of dementia. In addition, some studies have shown that impairments in cognitively demanding instrumental activities of daily living (IADL) may serve as early indicators for the development of dementia. The aim of the current investigation was to determine the impact of MCI and IADL impairment on the time to incident dementia diagnosis in a large population-based sample of subjects who were 75 years of age or older.

The data were derived from the Leipzig Longitudinal Study of the Aged. The study covered a period of eight years and included a baseline assessment and five follow-up assessments, conducted on an average of every 1.4 years. Kaplan-Meier survival analysis was used to determine time to incident dementia. Cox proportional hazards models were applied to determine the impact of MCI and IADL impairment on the time to incident dementia. In all, 180 (22%) of 819 initially dementia-free subjects had developed dementia by the end of the study. The mean time to incident dementia was 6.7 years. A significant association was found between MCI and IADL impairment. The presence of MCI in combination with impaired IADL was associated with a higher conversion rate to dementia, a shorter time to clinically manifested diagnosis, and a lower chance of reversibility to cognitively normal functioning. The highest conversion rate and the shortest time to incident dementia was found in those subjects with both the amnestic subtype of MCI and impaired IADL.

The authors conclude that subject with both MCI and IADL impairment constitute a high-risk population for future dementia. The consideration of IADL impairment, in addition to MCI, could help to improve the prediction of dementia, especially with regard to an estimation of the time to clinical manifestation. IADL impairment in particular could aid in improving the prediction of dementia, because it reflects the development of dementia in real situations of daily life and can be assessed by less extensive methods than biological markers. (33 References)
FUNCTIONAL IMPAIRMENT IN ELDERLY PATIENTS WITH MILD COGNITIVE IMPAIRMENT AND MILD ALZHEIMER DISEASE

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ARCH GEN PSYCHIATRY, 68:617-26, June 2011

The term mild cognitive impairment (MCI) is used to identify a stage of impairment that demonstrates considerable heterogeneity, with MCI being displayed by individuals at high risk for conversion to dementia. While original MCI criteria excluded substantial functional deficits, recent research reports have suggested otherwise. Identifying the extent, severity, type, and correlates of functional deficits that occur in MCI and mild Alzheimer disease (AD) may aid in the early detection of incipient dementia and may help in the identification of potential mechanistic pathways to disrupted instrumental activities of daily living (IADLs). Using baseline data from the Alzheimer’s Disease Neuroimaging Initiative, the authors examined the number, type, and severity of functional impairments and attempted to identify the clinical characteristics associated with functional impairment in patients with amnestic MCI (aMCI) and in patients with mild AD.

The study sample was composed of 394 patients with aMCI, 193 patients with mild AD, and 229 healthy, cognitively intact individuals (control group). The 10-item Pfeffer Functional Activities Questionnaire (FAQ) was used to assess functioning. Self-reports of functional deficits were collected for the control group, but informant reports were collected for the aMCI and AD groups. Informant-reported FAQ deficits were common in patients with aMCI (72.3%) and AD (97.4%), but were rarely self-reported by control subjects (7.9%). The average severity per FAQ deficit did not differ between patients with aMCI and controls; both were less impaired than patients with AD. Two FAQ items (remembering appointments, family occasions, holidays, and medications; and assembling tax records, business affairs, or other papers) were specific in terms of differentiating the control group from the combined aMCI and AD groups; only 34% of patients with aMCI and 3.6% of those with AD had no difficulty with these two items. The severity of FAQ deficits in the combined aMCI and AD group was associated with poorer Trail Making Test, Part A scores and with smaller hippocampal volumes.

The authors conclude that mild deficits in IADLs appear to be common in individuals with aMCI and should be incorporated into MCI criteria. (53 References)
CLINICAL FEATURES AND APOE GENOTYPE OF PATHOLOGICALLY PROVEN EARLY-ONSET ALZHEIMER DISEASE

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NEUROLOGY, 76:1720-5, May 17, 2011

Alzheimer Disease (AD) is the most frequent cause of degenerative dementia in developed countries. The typical clinical pattern starts with episodic memory dysfunction and then progresses to other cognitive domains. The diagnosis of early-onset AD (EOAD) presents a challenge because it frequently presents with atypical clinical manifestations such as visual, executive, behavioral, or language impairments. The purpose of the present study was to describe the clinical features of a group of patients with pathologically confirmed EOAD (onset before age 60), investigate the frequency of nonmemory presentations in EOAD, and identify features that led to misdiagnoses.

The authors conducted a retrospective review of clinical data (age at onset, family history, clinical presentation, diagnostic delay, diagnosis) and APOE genotype for 40 cases (25 male, 15 female) with neuropathologically confirmed EOAD. The mean age at onset was 54.5 years (range, 46-60). The mean disease duration was 11 years, with a mean diagnostic delay of 3.1 years. Twenty-five patients (62.5%) presented with typical episodic memory dysfunction as the first symptom, while the other 15 patients (37.5%) had an atypical presentation. Behavioral/executive dysfunction was the most prevalent atypical presentation. Incorrect initial clinical diagnoses were common (53%) in patients with atypical presentations, but were rare when anterograde amnesia was the presenting symptom (4%). Incorrect initial clinical diagnoses were as follows: behavioral variant frontotemporal lobar degeneration (N=2), normal pressure hydrocephalus (N=2), semantic dementia (N=1), primary progressive aphasia (N=1), corticobasal degeneration (N=1), pseudodementia with depression (N=1), and unclassifiable dementia (N=1). The APOE genotype was 3/3 in 59%, with no significant differences between typical and atypical presentations. APOE 4 was found 3.3 times more frequently in subjects with a family history of AD. In all, 97.5% of the cases presented with advanced neurofibrillary pathology.

In the current study, one third of patients with pathologically confirmed EOAD presented with atypical symptoms. The authors conclude that EOAD patients with nonamnestic presentations often receive incorrect clinical diagnoses. (32 References)
INTERPERSONAL TRAITS CHANGE AS A FUNCTION OF DISEASE TYPE AND SEVERITY IN DEGENERATIVE BRAIN DISEASES

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J NEUROL NEUROSURG PSYCHIATRY, 82:732-9, July 2011

Personality (an individual’s habitual pattern of cognition, emotion, and behavior) may change dramatically in people with traumatic brain injuries or degenerative brain diseases. Different degenerative brain diseases result in distinct personality changes because of divergent patterns of brain damage; however, little is known about the natural history of these personality changes throughout the course of each disease. The aim of the present study was to determine how interpersonal traits change as a function of degenerative brain disease type and severity.

Using the Interpersonal Adjective Scales, the authors collected annually for one to four years informant ratings of retrospective premorbid and current scores for dominance, extraversion, warmth, and ingenuousness on the following: 188 patients (67 with behavioral variant frontotemporal dementia [bvFTD], 40 with semantic dementia [SemD], 81 with Alzheimer’s disease [AD]) and 65 older healthy controls. Through the use of random coefficient models, interpersonal behavior scores at very mild, mild, or moderate-to-severe disease states were compared within and between patient groups. The results showed that bvFTD, SemD, and AD patients demonstrated changes in specific personality traits at a very mild stage of disease, and these traits changed with disease progression. For example, bvFTD and SemD patients could be differentiated from AD patients on the basis of their progressively decreasing levels of extraversion, warmth, and ingenuousness (i.e., interpersonal traits associated with emotional affiliation) and their increasing interpersonal rigidity. Among these behaviors, lack of warmth best differentiated bvFTD and SemD patients from AD patients at all disease stages.

The authors conclude that interpersonal trait changes in bvFTD, SemD, and AD patients occur as a function of disease type and severity, thereby providing further evidence of direct brain-behavior relationships for some aspects of personality. While patients in all three disease categories experienced loss of social dominance early, only bvFTD and SemD patients showed progressive alterations in their capacity for affiliative social behavior, which is consistent with the severity of damage known to occur in the emotion-related frontoinsular and anterior frontal cortex. (42 References)
PREDICTING SURVIVAL IN FRONTOTEMPORAL DEMENTIA WITH MOTOR NEURON DISEASE

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Frontotemporal dementia (FTD) encompasses clinical syndromes characterized by progressive and insidious behavioral changes and language deficits. Clinical symptoms of motor neuron disease (MND) can develop in patients with FTD, and patients with MND may manifest behavioral or language symptoms over the course of the disease. In the present study, the authors attempted to determine whether clinical and demographic features are associated with prognosis in patients with both FTD and MND, i.e., FTD-MND.

A database search of the Mayo Clinic electronic medical record system was used to identify all patients diagnosed with both dementia and MND between January 2000 and July 2010. Those with FTD-MND were classified according to the existence of behavioral- or language-dominant symptoms at presentation and throughout the course of illness. Demographic, clinical, imaging, and survival data were analyzed with respect to dominant FTD-MND type. Voxel-based morphometry was used to assess and compare regional patterns of atrophy in behavioral- and language-dominant FTD-MND types. Of 56 patients identified with FTD-MND, 31 had dominant behavioral symptoms, and 25 had dominant language symptoms; 53 patients had died. A survival difference was found between types; patients with behavioral-dominant symptoms survived 506 days longer than patients with language-dominant symptoms (mean, 1,397 days vs. 891 days; \( p = 0.002 \)). There was also a difference between groups in time from diagnosis to death. Patients with language-dominant disease were more likely to have bulbar-onset than limb-onset MND. There was a similar pattern of frontal and temporal lobe atrophy in both types, although there was some evidence indicating that patients with the behavioral type had more frontal atrophy, while those with the language type had more left temporal atrophy.

According to the authors, the results of the current study suggest that patients with behavioral-dominant FTD-MND but without bulbar onset have the best survival rates, whereas those with language-onset FTD-MND and bulbar onset have the poorest survival rates. It appears that patients with FTD-NMD can be categorized according to behavioral or language dominance through the use of clinical features outlined in the consensus criteria and that this categorization has implications for survival in counseling patients and their families. (34 References)
DISEASE-MODIFYING PROPERTIES OF LONG-TERM LITHIUM TREATMENT FOR AMNESTIC MILD COGNITIVE IMPAIRMENT: RANDOMISED CONTROLLED TRIAL

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BR J PSYCHIATRY, 198:351-6, May 2011

The findings of two recent clinical studies support the feasibility of conducting trials aimed at evaluating the disease-modifying properties of lithium in Alzheimer’s disease, although no benefits were found with regard to short-term treatment. In the present single-center, double-blind, placebo-controlled study, the authors attempted to evaluate the effects of long-term, low-dose lithium treatment on cognitive and biological outcomes in a group of community-dwelling outpatients with amnestic mild cognitive impairment (aMCI).

To be enrolled in the trial, subjects had to be 60 years of age or older; have a diagnosis of aMCI according to Mayo Clinic criteria; and have no evidence of ongoing psychiatric disorders. Forty-five participants with aMCI were randomly assigned to receive lithium (N=24) or placebo (N=21) for a period of 12 months. The primary outcome measures were modifications in cognitive and functional test scores and concentrations of cerebrospinal fluid (CSF) biomarkers (amyloid-beta peptide, total tau, and phosphorylated-tau). Forty-one participants (91% of the total sample) completed one year of follow-up (21 in the lithium group and 20 in the placebo group). Eleven participants (24% of the total sample) progressed to Alzheimer’s disease after 12 months of follow-up. Long-term lithium treatment was associated with a significant decrease in CSF concentrations of phosphorylated-tau as well as better performances on attention tasks and on the cognitive subscale of the Alzheimer’s Disease Assessment Scale. In general, tolerability to lithium was good, and the adherence rate was 91%.

According to the authors, the findings of the current investigation reinforce the notion that in an individual at risk for Alzheimer’s disease, lithium treatment may have a protective effect with regard to the progression from cognitive impairment to dementia. In the researchers’ opinion, this is probably a consequence of the effect of lithium on glycogen synthase kinase 3 beta and possibly on other pivotal cascades involved in the pathophysiology of Alzheimer’s disease. (27 References)
IMPROVED LANGUAGE PERFORMANCE IN ALZHEIMER DISEASE FOLLOWING BRAIN STIMULATION

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J NEUROL NEUROSURG PSYCHIATRY, 82:794-7, July 2011

Alzheimer disease (AD) is a progressive disorder that impacts memory, language, and several other cognitive functions. Given the limited effectiveness of pharmacological treatments for AD, non-pharmacological interventions have gained attention in recent years, and there are currently many different approaches under investigation, ranging from multistrategy interventions to cognitive training. For example, repetitive transcranial magnetic stimulation (rTMS) has been proposed as a possible treatment for the cognitive deficits associated with AD. The aim of the present study was to assess the long-term effects (on cognitive performance) of rTMS applied to the left dorsolateral prefrontal cortex (DLPFC) in patients with AD.

The study sample was composed of ten outpatients who met diagnostic criteria for probable moderate AD. A multiple-baseline design was used, and the patients were randomly assigned to one of two groups. The first group underwent a four-week real rTMS stimulation protocol, while the second group underwent two weeks of placebo treatment, followed by two weeks of real rTMS stimulation. Each session consisted of the application of rhythmic high-frequency rTMS over the DLPFC for 25 minutes. Sessions were conducted once a day, five days a week. The main outcome measure was the change in cognitive test performance at two and four weeks after rTMS treatment initiation, with follow-up performed eight weeks after the end of rTMS (compared with baseline performance). A significant difference was found between groups over sessions in terms of the percentage of correct responses on auditory sentence comprehension. Only real treatment induced an improvement in performance with respect to baseline or placebo. Moreover, both groups exhibited a lasting effect on the improved performance eight weeks after the end of treatment.

According to the authors, the results of the present study provide initial evidence for the persistent beneficial effects of rTMS on sentence comprehension in patients with AD. The current findings may reflect an rTMS-induced modulation of short- and/or long-range cortical synaptic efficacy and connectivity that potentiates the system within the language network, leading to more effective processing. Rhythmic rTMS, in conjunction with other therapeutic interventions, may represent a novel approach to the treatment of language dysfunction in patients with AD. (15 References)
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Several recent studies have found an increase in the prevalence of alcohol use among older adults, suggesting that alcohol disorders are a growing public health concern in late life. One indicator of problematic alcohol use that may have adverse health consequences is binge drinking (consumption of more than three drinks per occasion in older individuals). The objectives of the present three-year, prospective, population-based investigation were to: (1) identify the sociodemographic correlates of binge drinking status in the year preceding the 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) among adults 50 years of age and older; and (2) provide estimates of the risks posed by the status of binge drinking in the year prior to 2001-2002 NESARC for the subsequent occurrence of specific Axis I psychiatric disorders and use of illicit drugs three years later during Wave 2 of NESARC (2004-2005).

The sample consisted of 13,489 community-dwelling middle-aged and older adults (50 years of age and older) who participated in both Wave 1 and Wave 2 of the NESARC. The authors found that 15.6% of the men and 5.7% of the women reported binge drinking in the year prior to the 2001-2002 baseline assessment. After adjustments were made for covariates, the data showed that both men who were occasional binge drinkers and men who were frequent binge drinkers were significantly more likely than current male drinkers without binge drinking to have alcohol abuse disorder and alcohol dependence disorder. Similarly, after adjusting for covariates, the researchers found that women who were occasional binge drinkers and women who were frequent binge drinkers were significantly more likely than current female drinkers without binge drinking to have alcohol abuse disorder and alcohol dependence disorder. Among the female subjects, occasional binge drinking was also associated with an increased risk for panic disorder without agoraphobia and for posttraumatic stress disorder.

According to the authors, the current data serve to provide preliminary evidence that binge drinking is positively linked to the occurrence of alcohol use disorders and a few specific anxiety disorders. The strong and persistent relationship found between binge drinking and alcohol use disorders indicates that binge drinking may lead to alcoholism in middle adulthood as well as in old age. (60 References)
SIX-MONTH CHANGES IN SPIRITUALITY AND RELIGIOUSNESS IN ALCOHOLICS PREDICT DRINKING OUTCOMES AT NINE MONTHS

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Although spiritual change is hypothesized to contribute to recovery from alcohol dependence, few studies have employed prospective data to investigate this theory. In addition, previous investigations have been limited to treatment-seeking and Alcoholics Anonymous (AA) samples. To examine the effect of spiritual and religious (SR) change on subsequent drinking outcomes (independent of AA involvement), the present authors conducted a longitudinal panel study of alcohol-dependent individuals, some of whom were receiving treatment and some of whom were not.

The total sample was composed of 364 alcoholics; 157 were recruited from a university-affiliated outpatient treatment program, 80 were recruited from a Veterans Affairs outpatients treatment clinic, 34 were recruited from a moderated drinking program, and 93 were untreated and recruited from the larger community. After controlling for baseline drinking and AA involvement, the researchers used quantitative measures of SR change between baseline and six months to predict nine-month drinking outcomes. Of the 364 participants who completed the baseline interview, 316 completed the six-month interview. At nine months, valid drinking data were obtained for 283 respondents. Significant changes were found in eight of 12 SR measures: private SR practices, beliefs, daily spiritual experiences, three indices of forgiveness (overall, of self, and of others), negative religious coping, and purpose in life. Increases in private SR practices (e.g., prayer, meditation) and forgiveness of self proved to be the strongest predictors of improvements in drinking outcomes. Changes in daily spiritual experiences, purpose in life, a general measure of forgiveness, and negative religious coping also predicted favorable drinking outcomes.

According to the authors, the current data indicate that SR change reinforces and supports subsequent reductions in drinking among alcohol-dependent individuals. SR variables, broadly defined, warrant attention in fostering change, even among those alcoholics who do not affiliate with AA or with religious institutions. Future research is needed to determine how change in SR dimensions, particularly that involving various types of forgiveness, affects dependence and recovery among alcoholics. (48 References)
PREVALENCE AND CORRELATES OF ALCOHOL MISUSE AMONG RETURNING AFGHANISTAN AND IRAQ VETERANS

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ADDICT BEHAV, 36:801-6, August 2011

Over 1.6 million military service members have served in the ongoing conflicts in Afghanistan and Iraq, referred to as Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF), respectively. Several studies have reported high rates of alcohol misuse and low rates of substance abuse treatment among OEF/OIF military service members. In the present investigation, the authors examined the proportion of recently returned National Guard service members who reported misusing alcohol and the associations between demographics, mental health symptoms, years in the military, number of deployments, and recent combat exposure with alcohol misuse. The researchers also studied the proportion of National Guard service members who reported receiving mental health and substance use services, concerns that affected their decision to receive care, and factors that facilitated their pursuit of care.

The study sample was composed of 585 National Guard members who volunteered to complete an anonymous survey assessing mental health and substance use problems, functional status, and past treatment experiences. The majority were white (75%), male (87%), and between 18 and 30 years of age (58%). More than half (55%) had been in the military for at least five years; 38% reported two or more deployments, and 41% reported recent combat exposure. Thirty-six percent of the service members met criteria for alcohol misuse. Of those misusing alcohol, 31% reported receiving some type of mental health service in the past year, and 2.5% reported receiving specific substance abuse treatment during that time. Concerns affecting the decision to receive mental health treatment most commonly endorsed by service members misusing alcohol were concern that this information would appear in their records (30%), concern that they would be seen as weak (24%), concern that the unit leadership might treat them differently (22%), and concern that they would be embarrassed (22%). Among those who misused alcohol and who received services, spouses were most commonly cited as facilitating the pursuit of care.

The current study found high rates of alcohol misuse among OEF/OIF National Guard service members. However, among those who misused alcohol, rates of mental health and substance use treatment utilization were low. Additional research is needed to identify means of overcoming barriers to care and to establish more effective ways to facilitate linkage to care and receipt of appropriate interventions. (19 References)
EVALUATION OF TWO WEB-BASED ALCOHOL INTERVENTIONS IN THE U.S. MILITARY

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J STUD ALCOHOL DRUGS, 72:480-9, May 2011

The U.S. military traditionally has seen high rates of alcohol misuse and alcohol-related problems among its members, thereby emphasizing the need for effective treatment programs that minimize participant burden. Web-based interventions have shown promise as viable treatment options for college students and adults but have not been widely evaluated in the military. The purpose of the present study was to evaluate the efficacy of two web-based alcohol interventions that were originally created for civilians and then adapted for U.S. military personnel. The first intervention was Alcohol Savvy, a universal, primary prevention program aimed at adults in the workplace. The second was the Drinker’s Check-Up, a brief motivational intervention designed to reduce alcohol misuse in adult high-risk drinkers.

The convenience sample of 3,070 active-duty personnel were drawn from eight military installations (two Army, two Navy, two Air Force, and two Marine Corps). Participation was voluntary and was open to all active-duty personnel assigned to the selected installations. Following a baseline survey, the participants were assigned to one of three conditions: Alcohol Savvy, Drinker’s Check-Up, or control (no program participation). Follow-up surveys were completed by 1,072 participants one month after baseline and by 532 participants six months after baseline. At the one-month follow-up, participants who completed the Drinker’s Check-Up intervention demonstrated significant reductions in multiple measures of alcohol use relative to controls. Positive outcomes were found for average number of drinks consumed per occasion, frequent heavy episodic drinker status, and estimated peak blood alcohol concentrations. These reductions in alcohol use were still being maintained at the six-month follow-up. There were no statistically significant changes in alcohol use for participants who completed the Alcohol Savvy program.

According to the authors, the current data suggest that military versions of civilian web-based alcohol intervention programs show promise in reducing alcohol misuse in active-duty military personnel. (35 References)
INTERNET THERAPY VERSUS INTERNET SELF-HELP VERSUS NO TREATMENT FOR PROBLEMATIC ALCOHOL USE: A RANDOMIZED CONTROLLED TRIAL

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J CONSULT CLIN PSYCHOL, 79:330-41, June 2011

Problematic alcohol use is the third leading contributor to the global burden of disease; this is partly due to the fact that most problem drinkers do not receive any form or treatment. While Internet-based alcohol interventions may attract an otherwise untreated population, their effectiveness has not yet been established. In the current study, the authors examined the efficacy of Internet-based therapy (therapy alcohol online [TAO]) and Internet-based self-help (self-help alcohol online [SAO]) for the treatment of problematic alcohol users.

The sample was composed of 205 adult problem drinkers (101 men, 104 women; mean age, 42 years; mean Alcohol Use Disorders Identification Test score, 20) who were randomly assigned to TAO (N=68), SAO (N=68), or an untreated waiting-list (WL) control group (N=69). Participants in the TAO arm received seven individual text-based chat-therapy sessions. Both the TAO and SAO interventions were based on cognitive-behavioral therapy and motivational interviewing techniques. Assessments were conducted at baseline and at three and six months after randomization. The primary outcome measures were alcohol consumption and treatment response. Secondary outcome variables included measures of quality of life. In all three arms, participants reported less alcohol consumption at the three-month follow-up than at baseline. Through the application of generalized estimating equation regression models, intention-to-treat analyses showed significant effects for TAO versus WL and for SAO versus WL on alcohol consumption at three months post-randomization. The differences between TAO and SAO were not significant at the three-month follow-up but were significant at the six-month follow-up, with larger effects being obtained with TAO. A similar pattern of results was seen for treatment response and quality-of-life outcome measures.

According to the authors, the results of the current investigation support the effectiveness of Internet-based therapy and Internet-based self-help for problematic alcohol users. It appears that Internet-based interventions are able to attract a new population of problematic drinkers into treatment, including men and women who are gainfully employed but who have a clear need for assistance in addressing their drinking problems. (73 References)
ALCOHOL AND DRUG USE AMONG PATIENTS PRESENTING TO AN INNER-CITY EMERGENCY DEPARTMENT: A LATENT CLASS ANALYSIS

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ADDICT BEHAV, 36:793-800, August 2011

Nationally, the prevalence of substance use disorders is quite high. The inner-city Emergency Department (ED) is a crucial location for interventions with drug-using individuals, since patients who use inner-city EDs often do not have a primary care physician, do not routinely receive medical care other than in the ED setting, are members of a minority population, and are of a lower socioeconomic group. In the present study, the authors used latent class analyses to characterize substance use/substance use disorders (SUDs) among adults who were between 19 and 60 years of age and who presented to the ED of a large, inner-city hospital with medical complaints or injuries.

In all, 14,557 participants (45% male; 54% African-American) completed a computerized survey designed to assess demographics, health functioning, and substance use/SUDs; 9,823 patients had presented to the ED with a medical complaint, and 4,734 had presented with an injury. Although injured patients were significantly more likely to use tobacco, alcohol, and marijuana and were more likely to have an alcohol use disorder, their presenting complaint was not related to other drug use/diagnoses. Five latent classes were identified: (1) low users/SUDs (65.9%), (2) binge drinkers (24.3%), (3) marijuana users/SUDs (3.5%), (4) cocaine users/SUDs (2.9%), and (5) poly-drug users (3.3%). Compared with individuals in Class 1, participants in the other classes were more likely to be younger, to be male, to have no health insurance, to exhibit poor mental health functioning, to be tobacco users, and to have had prior treatment for substance use. African-Americans were most likely to fall in Class 3 or Class 4. Employed participants were most likely to be found in Class 2. Compared to those in Class 1, participants in Class 2 and Class 3 reported better physical health. Patients in Class 2 were more likely to present to the ED with an injury, while those in Class 5 were more likely to present with a medical complaint.

According to the authors, an ED visit for care related to either an injury or a medical complaint may provide an ideal opportunity to target screening, brief interventions and linkage to treatment for individuals with substance use/SUDs. Given the current findings regarding substance use among ED patients, research is needed to develop and test tailored multiple risk interventions aimed at reducing poly-substance use and increasing substance use treatment entry among this vulnerable population. (57 References) EAF
PROBLEM DRINKING AND LOW-DOSE NALTREXONE-ASSISTED OPIOID DETOXIFICATION

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J STUD ALCOHOL DRUGS, 72:507-13, May 2011

While alcohol use is common among opioid-dependent individuals, little is known about the effects of alcohol consumption on opioid withdrawal and on the efficacy of specific detoxification approaches. In a previous study (Mannelli et al., 2009), the authors found that the addition of very-low-dose naltrexone (VLNTX) to methadone attenuated opioid withdrawal severity and craving during inpatient detoxification. In a secondary analysis of these data, the researchers attempted to determine whether problem drinking before detoxification affects opioid withdrawal severity and treatment completion and whether the addition of VLNTX is safe and effective in improving treatment outcome.

By means of a double-blind, randomized design, 174 opioid-dependent patients received naltrexone 0.125 mg per day and methadone taper (N=59), naltrexone 0.250 mg per day and methadone taper (N=58), or placebo and methadone taper (N=57) during a six-day inpatient detoxification. Alcohol consumption was assessed at admission through the use of the Addiction Severity Index and self-reports. Outcome measures were opioid withdrawal intensity, craving, and retention in treatment. The problem-drinking opioid-dependent patients (N=79) showed episodic heavy alcohol use, reported increased subjective opioid withdrawal intensity and craving, and had a significantly lower rate of retention in treatment. The problem-drinking opioid-dependent individuals who were treated with VLNTX (N=55) exhibited reduced withdrawal and a lower rate of treatment discontinuation, resuming alcohol intake in smaller numbers on the day following discharge. VLNTX (0.250 mg) was significantly more effective than placebo in decreasing anxiety, perspiration, shakiness, nausea, stomach cramps, and craving.

According to the authors, the current data indicate that heavy episodic alcohol use is associated with negative outcomes in opioid-dependent patients who discontinue opioid-agonist treatment. The administration of VLNTX appears to be a safe and effective way to reduce withdrawal severity and facilitate treatment retention. Future studies should explore the use of VLNTX in the detoxification and long-term treatment of combined alcohol-opioid dependence and alcohol dependence alone. (42References)
SEX DIFFERENCES AMONGST DEPENDENT HEROIN USERS: HISTORIES, CLINICAL CHARACTERISTICS AND PREDICTORS OF OTHER SUBSTANCE DEPENDENCE

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ADDICT BEHAV, 36:27-36, January/February 2011

Previous studies of heroin-dependent individuals have described a chronic disorder strongly associated with polydrug use, poor mental and physical health, increased mortality risk, and poor legal, social, and economic outcomes. Evidence suggests that there are at least some clinical and family background differences between male and female dependent heroin users. The authors of the current investigation explored differences in the characteristics and histories of male and female heroin-dependent individuals and also examined between-sex differences in the clinical diagnoses associated with multiple substance dependence diagnoses.

The study sample was composed of 1,513 heroin-dependent participants (914 males, 599 females; median age, 36 years), all of whom completed a structured interview designed to elicit information on substance use and dependence, psychiatric history, childhood maltreatment, family background, adult violence, and criminal history. Family backgrounds, demographic variables, and clinical characteristics were analyzed by sex. Ordinal regression was used to determine whether there was a relationship between number of substance dependence diagnoses and other clinical variables. The results showed that women were more likely to experience most forms of childhood maltreatment, to first use heroin with a boyfriend or partner, to experience ongoing adult violence at the hands of a partner, and to have a poorer psychiatric history. Men had more prevalent lifetime substance dependence diagnoses and criminal histories and were more likely to meet the criteria for antisocial personality disorder. Predictors of multiple substance dependence diagnoses for both sexes were mental health variables, antisocial behavior, childhood sexual abuse, victim of adult violence, younger age at first cannabis use, and overdose. As the number of dependence diagnoses increased, clinical and behavioral problems also increased. Childhood emotional neglect was related to increasing dependence diagnoses for females but not males, whereas posttraumatic stress disorder was a significant predictor for men but not women.

The authors conclude that dependent heroin users are not a homogeneous group in terms of lifetime substance dependence diagnoses. They also suggest that the path to heroin and multiple substance dependence may be different for males and females. (88 References)
CONTEXTUAL PROFILES OF YOUNG ADULT ECSTASY USERS: A MULTISITE STUDY

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ADDICT BEHAV, 36:190-6, March 2011

Among the “club drugs” (those popular at parties, clubs, raves, and concerts), ecstasy (3,4 methylenedioxymethamphetamine or MDMA) is widely used by adolescents and young adults throughout the world. Ecstasy is responsible for many drug-related deaths and emergency room visits and can cause various long-term physical, psychological, and neurotoxic effects. The authors of the present study assessed the possible contextual factors influencing ecstasy use in young adults from three diverse sites (St. Louis, Missouri; Miami, Florida; and Sydney, Australia).

The sample was composed of 612 ecstasy users who were between 18 and 30 years of age. Assessment instruments were the Washington University-Risk Behavior Assessment-Club Drug Version and the Club Drug Substance Abuse Module. Bivariate analyses were used to assess different contextual factors influencing ecstasy use. Nearly all ecstasy users at all three sites reported that they obtained the drug from roommates or friends (94%-96%). In addition, strangers emerged as a major source of ecstasy (60%-69%) at all the sites. In St. Louis and Miami, ecstasy use occurred mostly in homes, apartments, or dorms; whereas, in Sydney, ecstasy use occurred most often in bars, clubs, or restaurants. Ecstasy consumption at public places and in cars, trains, or ferries was significantly higher in Miami (89% and 77%) than in St. Louis (67% and 65%) or Sydney (67% and 61%). At all three sites, nearly all users reported consuming ecstasy with roommates or friends, and more than 75% reported using ecstasy with a spouse or a partner. In Sydney, alcohol was the substance most commonly used in conjunction with ecstasy. Ecstasy users in St. Louis and Miami most commonly reported the concomitant use of marijuana. Most users at all three sites reported using ecstasy out of curiosity, with those in St. Louis being the most likely to cite this reason. Approximately 70% of the ecstasy users at all three sites reported using the drug for no reason and to bond with friends.

According to the authors, the current data provide evidence of similarities and differences in the contexts of ecstasy use among young adults in two cities in the United States as well as in the capital of Australia. These differences appear to reflect local cultures as well as current trends in drug use. The present findings may highlight the changing contextual factors of ecstasy use over time, and prevention programs should take these newly emerging factors into account, the researchers note. (47 References)
NON-MEDICAL USE OF PRESCRIPTION DRUGS IN A NATIONAL SAMPLE OF COLLEGE WOMEN

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ADDICT BEHAV, 36:690-5, July 2011

Because of the complex interactions between individual variables and environmental factors that are unique to the college experience, college students are at high risk for substance use. One of the fastest growing forms of illicit drug use is the non-medical use of prescription drugs (NMUPD). Some researchers have suggested that college students may be at higher risk for NMUPD than other groups, given the degree of accessibility of different classes of prescription drugs in the college/university setting and the likelihood of students sharing their prescriptions with other students. The authors of the present study examined demographic characteristics, health/mental health, substance misuse, and rape experiences as potential risk correlates of NMUPD among a national sample of 2,000 college women.

The women were interviewed by means of a computer-assisted telephone interviewing system. The participants were asked about past year non-medical use of various prescription drugs, including tranquilizers, sedatives, stimulants, steroids, and pain medicines. Those who endorsed at least one instance of non-medical use of a prescription drug in the past year met criteria for NMUPD. Logistic regression analyses were used to identify variables within each predictor set that were associated with NMUPD. Significant predictors that emerged from these analyses were entered into a final multivariable logistic regression model predictive of unique variance in NMUPD use over the past year. NMUPD was endorsed by 7.8% of the sample (N=155). None of the demographic variables examined were associated with increased odds of ever misusing prescription drugs. Although incapacitated rape and drug- and/or alcohol-facilitated rape were found to be associated with NMUPD in the initial model, the final multivariable model showed that only a lifetime history of major depression and other forms of substance use/abuse were significantly and uniquely associated with an increased likelihood of NMUPD.

According to the authors, the current data reinforce the concern that college students are at risk for multiple substance use. Targeted assessment, prevention, and psycho-education among college students ultimately may assist in reducing the risk for NMUPD and other forms of substance abuse in this at-risk population. (38 References)
DIGEST
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Abstracts and Reviews of Selected Literature in Psychiatry, Neurology, and their Allied Fields

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THE BURDEN OF ANXIETY DISORDERS ON THE FAMILY

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J NERV MENT DIS, 198:876-80, December 2010

There is currently an extensive body of literature dealing with the increased burden experienced by families of mentally ill individuals. Most of the studies designed to assess the burden of mental illness on family members has been limited to severe psychiatric disorders, such as schizophrenia. While it is well established that individuals with anxiety disorders experience significant impairments in social and occupational functioning, the impact of anxiety disorders on family members has received relatively little attention. The purpose of the present investigation was to explore the nature and degree of burden experienced by family members of anxiety-disordered individuals.

The study sample consisted of 74 outpatients with a primary anxiety disorder diagnosis (23 men, 51 women; mean age, 36.5 years) and 74 family members (43 men, 31 women; mean age, 43 years). The family members included 46 spouses, 17 parents, and 11 others. The family members completed measures that were designed to assess the impact of having an anxiety-disordered relative. The results indicated that family members of patients with anxiety disorders experience a significant degree of burden. This burden encompassed several domains and included negative effects on physical health, psychological well-being, and family functioning. The severity of the patient’s illness was positively correlated with overall burden, burden on family health, and family closeness. Furthermore, the presence of a comorbid major depressive disorder or comorbid dysthymia in the patient was found to be associated with increased overall burden in family members.

According to the authors, the current data indicate that there is a significant amount of burden placed on family members of anxiety-disordered individuals. Living with, or taking care of, persons with anxiety disorders appears to have a negative impact on both the physical and mental health of family members. The present findings suggest that health-care professionals should assess the impact of the patient's anxiety disorder on his/her family and should attempt to provide support and easily accessible treatment interventions that would not only reduce the burden experienced by family members but improve the quality of their life as well. (35 References)
CHILDHOOD ADVERSITY MODIFIES THE RELATIONSHIP BETWEEN ANXIETY DISORDERS AND CORTISOL SECRETION

Esther J. M. van der Vegt; Jan van der Ende; Anja C. Huizink; Frank C. Verhulst; and Henning Tiemeier (Erasmus MC-Sophia Children’s Hospital, Dept. of Child and Adolescent Psychiatry, PO Box 2060, 3000 CB Rotterdam, The Netherlands; e-mail: h.tiemeier@erasmusmc.nl)

BIOL PSYCHIATRY, 68:1048-54, December 1, 2010

Although internalizing psychiatric disorders and early childhood adversities both have been associated with altered basal cortisol secretion, most research has focused on only one of these factors at a time in relation to cortisol secretion. In the present investigation, the authors attempted to determine whether early childhood adversity (e.g., abuse and/or neglect) modifies the relationship between anxiety and mood disorders and cortisol secretion.

The study sample was composed of 429 international adoptees (191 males, 238 females) who were followed from childhood to adulthood. During childhood, their adoptive parents provided information about abuse and neglect suffered by the adoptees before their adoption. As adults, the adoptees completed a standardized psychiatric interview designed to assess internalizing disorders; they also collected saliva samples four times over the course of a day (directly after awakening, half an hour after awakening, at 3:00 PM, and just before going to bed). The results showed that the relationship between anxiety disorders and cortisol secretion during one day, as measured by the area under the curve, was dependent on the experience of severe early maltreatment. In adoptees with an anxiety disorder, severe childhood maltreatment was associated with lower daily cortisol secretion. In adoptees without an anxiety disorder, no difference in cortisol secretion was found between persons who did and did not experience severe maltreatment early in life. Severe early maltreatment was found to have no modifying effect on the relationship between the presence of mood disorders and daily cortisol secretion.

According to the authors, the results of the current investigation add to the existing body of literature providing information about the long-term consequences of early childhood maltreatment. Maltreatment experienced early in life may have long-lasting effects and may modify the association between internalizing disorders and basal cortisol secretion in adulthood. To understand the relationship between internalizing psychiatric disorders and cortisol secretion, the researchers note, early maltreatment should be taken into account, even in those individuals in whom such maltreatment is less pervasive. (46 References)
ANXIETY DISORDERS IN CHILDREN AND ADOLESCENTS IN THE FIRST SIX MONTHS AFTER TRAUMATIC BRAIN INJURY

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Traumatic brain injury (TBI) in children and adolescents has become a major public health problem, and recent research has indicated that TBI is associated with an increase in the occurrence of psychiatric disorders. The objective of the present study was to assess the nature, rate, predictive factors, and neuroimaging correlates of novel (new-onset) definite anxiety disorders and novel definite/subclinical anxiety disorders (in a broader group of children with at least subclinical anxiety disorders) after TBI.

In all, 177 children (age range, five to 14 years) who had suffered a TBI between 1998 and 2003 were recruited from five different trauma centers. The participants were evaluated with psychiatric interviews soon after injury (baseline) and again at six months post-injury. Of the original 177 children, 141 (80%) returned for the six-month psychiatric assessment. Novel definite anxiety disorder and novel definite/subclinical anxiety disorders occurred in 12 (8.5%) and 24 (17%) children, respectively, in the first six months after injury. Of those with mild TBI (N=70), 11% developed a definite anxiety disorder and 20%, a definite/subclinical anxiety disorder. Of those with moderate TBI (N=17), none developed a definite anxiety disorder, and 24% developed a definite/subclinical anxiety disorder. Of those with a severe TBI (N=54), 7% developed a definite anxiety disorder and 11%, a definite/subclinical anxiety disorder. Novel definite anxiety disorder was significantly associated with younger age at injury and tended to be associated with novel depressive disorder, as well as with lesions of the superior frontal gyrus. Novel definite/subclinical anxiety disorder was significantly associated with concurrent psychiatric problems of personality change due to TBI and novel definite/subclinical depressive disorder, as well as with lesions of the superior frontal gyrus and a trend-association with frontal lobe white-matter lesions.

According to the authors, the current findings suggest that anxiety after childhood TBI may be part of a broader problem of affective dysregulation related to damaged dorsal frontal lobe and frontal white-matter systems, with younger children being at greatest risk for developing a novel anxiety disorder after suffering a TBI. (34 References)
HEALTH-RELATED QUALITY OF LIFE ACROSS THE ANXIETY DISORDERS: RESULTS FROM THE NATIONAL EPIDEMIOLOGIC SURVEY ON ALCOHOL AND RELATED CONDITIONS (NESARC)

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Anxiety disorders are the most prevalent class of mental health disorders, and collectively they impose a substantial public health burden on society. Although clinical studies have shown that specific anxiety disorders are associated with impaired psychosocial functioning, little is known about their comparative effects on health-related quality of life within a general population. Drawing on data gathered from a US nationally representative adult sample, the current analysis assesses the absolute and comparative severity of impairment in health-related quality of life across four common anxiety disorders (social anxiety disorder, generalized anxiety disorder [GAD], panic disorder, and specific phobia).

From 2001 to 2002, face-to-face interviews were conducted with 43,093 randomly selected adults who were 18 years of age or older and who were residing in households and group homes. The prevalence of DSM-IV anxiety disorders and relative associations with health-related quality of life indicators were examined. The Short-Form 12-item (SF-12) Health Survey was used to measure health-related quality of life. Roughly one in 10 of the respondents (9.8%) met diagnostic criteria for at least one 12-month DSM-IV anxiety disorder. Compared with non-anxiety-disordered respondents, adults with anxiety disorders tended to have lower personal incomes, higher rates of 12-month physical conditions, and greater numbers of Axis I and Axis II DSM-IV psychiatric disorders. After adjusting for sociodemographic and clinical correlates, including other anxiety disorders, the researchers found that GAD was associated with significant decrements in the SF-12 mental component summary score. In similar models, GAD and (to a lesser extent) panic disorder were significantly associated with impairment on the following SF-12 subscales: social functioning, role emotional, and mental health.

According to the authors, the current findings serve to underscore the magnitude of the burden of disease associated with anxiety disorders. Clinical efforts aimed at redressing the problems of individuals affected by DSM-IV anxiety disorders should include health-related quality of life assessments in order to detect cases, identify treatment targets, and evaluate effectiveness of therapeutic interventions. (78 References)
FUNCTIONING AND DISABILITY LEVELS IN PRIMARY CARE OUT-PATIENTS WITH ONE OR MORE ANXIETY DISORDERS

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PSYCHOL MED, 40:2059-68, December 2010

Anxiety disorders are among the most prevalent mental health disorders in the United States and are associated with substantial disability and reduced well-being. However, it is not known whether the relative impact of different anxiety disorders is due to the specific anxiety disorder itself or to the co-occurrence with other anxiety disorders. In the present study, the authors compared the functional impact of combinations of anxiety disorders in outpatients seen in primary care settings.

A total of 1,004 primary care patients (mean age, 43 years) with panic disorder (PD), generalized anxiety disorder (GAD), social anxiety disorder (SAD), or posttraumatic stress disorder (PTSD) completed a baseline telephone questionnaire and provided data on their mental and physical functioning and disability status. Linear multivariate regression models were used to compare functional levels in patients with different numbers and combinations of disorders. Of the 1,004 patients, 421 (42%) had one anxiety disorder only, 387 (38%) had two, 162 (16%) had three, and 34 (3%) had all four anxiety disorders. The results revealed few relative differences in functioning among the patients with only one anxiety disorder, although those with SAD were the most restricted in terms of their work, social life, and home activities, and those with GAD were the least impaired. As the number of anxiety disorders increased, so did the percentage of patients with comorbid depression. For example, 56% of the patients with only one anxiety disorder had comorbid depression, as compared with 88% of those with four anxiety disorders. The prevalence of comorbid depression varied from 64% in patients with PD to 85% in patients with PTSD (with or without another anxiety disorder) Functioning levels tended to deteriorate as comorbidity increased.

According to the authors, of the four anxiety disorders examined in the current investigation, GAD appeared to be the least disabling, although all four (PD, GAD, SAD, and PTSD) seemed to have more in common than in distinction with regard to functional impairment. A focus on the unique effects of specific anxiety disorders is inadequate, the researchers note, because such an approach fails to address the more pervasive impairment associated with the presence of multiple anxiety disorders, which is the modal presentation in primary care patients. (47 References)
GENERALIZED ANXIETY DISORDER, WITH OR WITHOUT CO-MORBID MAJOR DEPRESSIVE DISORDER, IN PRIMARY CARE: PREVALENCE OF PAINFUL SOMATIC SYMPTOMS, FUNCTIONING AND HEALTH STATUS

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J AFFECT DISORD, 127:160-8, December 2010

Generalized anxiety disorder (GAD) is the most prevalent anxiety disorder seen in primary care (PC), with GAD patients often exhibiting marked impairments in overall functioning and quality of life. Painful physical symptoms (PPS) have received little attention in patients with GAD, particularly in the PC setting. In the present cross-sectional, multi-center, epidemiological study carried out in the PC setting, the authors assessed the prevalence of PPS in the following groups: patients with GAD, patients with GAD and comorbid major depressive disorder (MDD), and controls (patients with neither GAD nor MDD).

The study consisted of a three-stage design: a screening to identify patients at high risk for GAD, a diagnostic confirmation of GAD (as per DSM-IV-TR criteria), and a clinical evaluation for the presence of PPS. Patients were considered to have PPS if their Visual Analog Scale overall pain score was greater than 30. Relationships between the presence of PPS and level of functioning and health status were analyzed, with results being adjusted for confounding factors. Of a total of 7,152 patients, 1,546 (22%) screened positive for GAD, and 981 (14%) had a confirmed GAD diagnosis; of these patients, 559 had GAD with comorbid MDD, and 422 had GAD alone. Of the 5,292 patients who screened negative for GAD, 336 were confirmed as controls. PPS in the patients with GAD were found to be twice as prevalent as those in the control group (59% versus 28.3%). Among the patients with GAD, the presence of comorbid MDD was found to be associated with a significantly higher prevalence of PPS (78% versus 59%). In both the patients with GAD alone and in those with GAD and comorbid MDD, a significant association was found between PPS and impairments in overall functioning and health status.

According to the authors, the present findings contribute new insights into what is already known about the relationship between GAD and PPS in the primary care setting. It appears that patients with GAD, regardless of the presence of comorbid MDD, have higher rates of PPS. The current data also suggest that the presence of PPS is independently associated with both worsening of a patient’s overall functioning and worsening of his/her health status. (34 References)
ZIPRASIDONE TREATMENT OF REFRACATORY GENERALIZED ANXIETY DISORDER
A Placebo-Controlled, Double-Blind Study

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J CLIN PSYCHOPHARMACOL, 30:185-9, April 2010

Generalized anxiety disorder (GAD) is a chronic psychiatric condition that is characterized by excessive and uncontrollable anxiety and worry and that is associated with symptoms of irritability, restlessness, fatigue, insomnia, concentration difficulties, and muscle tension. GAD affects approximately 3% to 5% of the general population in the United States, is twice as prevalent in women as in men, and typically follows a chronic episodic pattern of remission and relapse. In the present eight-week, randomized, double-blind, placebo-controlled, flexible-dose trial, the authors assessed the efficacy, safety, and tolerability of ziprasidone in adults with treatment-resistant GAD.

In all, 73 subjects with treatment-resistant GAD were recruited, and 62 were randomly assigned to treatment with either ziprasidone (N=41) or placebo (N=21) at a ratio of 2:1, with a flexible dosing strategy (20 mg-80 mg daily) being employed. Randomization was stratified into two subtypes of patients: those in whom ziprasidone was used to augment their current drug regimen (augmented group, N=18), and those who had discontinued their ineffective medications before entering the trial (nonaugmented group, N=44). Clinical status was monitored weekly throughout the course of the study. Assessment tools included the Hamilton Anxiety Scale (primary outcome measure), the Clinical Global Impression Improvement and Severity of Illness scales, the Hamilton Depression Scale, the Sheehan Disability Scale, the Hospital Anxiety and Depression Scale, and the Abnormal Involuntary Movements Scale. The dropout rate was 24% (two placebo patients and 13 ziprasidone patients). Most of the ziprasidone (88%) and placebo (86%) patients reported at least one adverse event. There was no statistically significant difference in the Hamilton Anxiety Scale score reduction between the ziprasidone and placebo groups. However, statistical trends were observed for an augmentation-study medication interaction effect, with ziprasidone patients showing more improvement in the nonaugmented group than in the augmented group.

On the basis of the data obtained in this trial and the subsequent power analyses, the authors state, a future double-blind, placebo-controlled trial should include at least 150 treatment-resistant GAD nonaugmented patients randomized to ziprasidone and placebo in a 1:1 ratio. (26 References) EAF
TIME TO RELAPSE AFTER 6 AND 12 MONTHS’ TREATMENT OF GENERALIZED ANXIETY DISORDER WITH VENLAFAXINE EXTENDED RELEASE

Karl Rickels, MD (Mood and Anxiety Disorders Section, Dept. of Psychiatry, University of Pennsylvania School of Medicine, 3535 Market St., Ste. 670, Philadelphia, PA 19104; e-mail: krickels@mail.med.upenn.edu); Bijan Etemad, MD; Sarosh Khalid-Khan, MD; Falk W. Lohoff, MD; Moira A. Rynn, MD; and Robert J. Gallop, PhD
ARCH GEN PSYCHIATRY, 67:1274-81, December 2010

Generalized anxiety disorder (GAD) is a chronic psychiatric illness that is characterized by excessive and uncontrollable worry, apprehension, and anxiety and by symptoms of irritability, restlessness, fatigue, insomnia, concentration difficulties, and muscle tension. The present 18-month, single-center, relapse prevention study was designed to clarify the role of long-term anxiolytic therapy in the treatment of chronically anxious patients with GAD. The main objectives were: (1) to examine the long-term efficacy of venlafaxine extended release (XR) in chronically ill GAD patients who responded therapeutically to an initial six-month course of venlafaxine XR and were followed up for another six months on venlafaxine XR or placebo; and (2) to determine whether patients treated with venlafaxine XR for 12 months rather than six months would show lower relapse rates over a six-month placebo period.

The study was composed of three treatment phases: a six-month, open-label, venlafaxine XR, flexible dose phase (phase 1); a six-month, randomized, double-blind, placebo-controlled relapse phase (phase 2); and a final six-month, randomized, double-blind, placebo-controlled relapse phase (phase 3). Of 268 GAD patients who entered phase 1, 158 (59%) completed six months of treatment, and 136 (50.7%) entered phase 2 (six-12 months). Of these 136 patients, 59 (43.4%) entered phase 3 (12-18 months). After six months of venlafaxine XR treatment, patients who continued on the active drug for 12 months experienced a significantly lower relapse rate (9.8%) than patients who switched to placebo (53.7%). Patients who were treated with venlafaxine XR for 12 months before being shifted to placebo experienced a lower relapse rate (32.4%) than patients who were shifted to placebo after being on venlafaxine XR for only six months (53.7%).

According to the authors, many patients with chronic GAD need prolonged pharmacotherapy in order to maintain any clinical improvement they have achieved. Treatment with an antidepressant should continue for at least 12 months at the highest tolerated and most effective daily dose. Preliminary data indicate that improved patients who relapse while off their anti-anxiety medication after at least six months of therapy may well respond to a second course of treatment with the same drug. (40 References)
A RANDOMIZED CONTROLLED TRIAL OF COGNITIVE-BEHAVIORAL THERAPY FOR GENERALIZED ANXIETY DISORDER WITH INTEGRATED TECHNIQUES FROM EMOTION-FOCUSED AND INTERPERSONAL THERAPIES

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J CONSUL CLIN PSYCHOL, 79:171-81, April 2011

Cognitive-behavioral therapy (CBT) currently stands as the only psychotherapy to meet criteria as an empirically supported treatment for generalized anxiety disorder (GAD). Nevertheless, a marked percentage of CBT clients continue to experience clinically significant symptoms of anxiety after treatment and fail to demonstrate a sustained reduction in GAD symptoms. Recent models have suggested that GAD symptoms may be maintained by emotional processing avoidance and interpersonal problems. The present study is the first randomized controlled trial designed to directly determine whether CBT could be augmented with the addition of a module formulated to target interpersonal problems and emotional processing.

In all, 83 individuals (mean age, 37 years) with a principal diagnosis of GAD were recruited from the community. Through use of an additive study design, the participants were randomly assigned to a course of CBT plus supportive listening (N=40) or to a program of CBT plus interpersonal and emotional processing therapy (N=43). The participants were treated in an outpatient clinic by doctoral-level psychologists with full-time private practices. Assessors blind to treatment status evaluated the participants at the following time points: pretreatment, posttreatment, six-month follow-up, one-year follow-up, and two-year follow-up. A composite of self-report and assessor-rated GAD symptom measures was used as were indices of clinically significant change. Assessment tools included the Penn State Worry Questionnaire, the Hamilton Anxiety Rating Scale, and the State–Trait Anxiety Inventory–Trait Version. The results showed that both treatment modalities led to significant improvement from pretreatment to posttreatment, as well as maintenance of therapeutic gains from posttreatment to two-year follow-up. Within-treatment effect sizes were very large for both treatment models. Chi-square analysis revealed no statistical difference between the compared treatments in terms of clinically significant change.

According to the authors, the findings of the current study indicate that interpersonal and emotional processing techniques may not augment CBT for all individuals with GAD. (55 References)
THERAPEUTIC INTERVENTIONS RELATED TO OUTCOME IN PSYCHODYNAMIC PSYCHOTHERAPY FOR ANXIETY DISORDER PATIENTS

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J NERV MENT DIS, 199:214-21, April 2011

Anxiety disorders are the most prevalent mental illnesses in the United States and are associated with severe functional impairment. While psychodynamic therapy has a well-articulated and efficacious model of psychotherapeutic change for sufferers of anxiety, there is little empirical research addressing the specific treatment factors related to such change. The authors of the present study examined specific therapeutic techniques related to change in patients with anxiety disorders during a course of short-term psychodynamic psychotherapy.

The study participants were drawn from a group of patients who had been admitted to a community outpatient clinic for individual psychotherapy. Of 25 who were diagnosed with an anxiety disorder, 21 (three men, 18 women; mean age, 27.67 years) completed treatment. Treatment consisted of once or twice weekly sessions of short-term psychodynamic psychotherapy. Treatment was not of a fixed duration, but was determined by the clinician’s judgment, the patient’s decision, progress toward goals, and life changes. All 21 patients attended a minimum of nine sessions and completed (at least) a ninth-session assessment battery. The mean number of sessions attended was 29. Examination of the effectiveness of short-term psychodynamic psychotherapy revealed significant and positive pre-/post-treatment changes on both patient self-ratings and independent clinical ratings for anxiety and global symptomatology as well as for relational, social, and occupational functioning. At treatment termination, most patients (76%) reported anxiety symptoms that were within a normal distribution. Psychodynamic interventions rated early in treatment (third/fourth session) were positively related to changes in anxiety symptoms. Finally, several individual psychodynamic techniques were found to be meaningfully related to outcome, including the following: (1) focusing on wishes, fantasies, dreams, and early memories; (2) linking current feelings or perceptions to the past; (3) highlighting patients’ typical relational patterns; and (4) helping patients to understand their experiences in new ways.

According to the authors, the current results suggest that there are certain specific therapeutic interventions, such as the four mentioned above, that may be positively related to change in the psychodynamic treatment of patients with anxiety disorders. (58 References)
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A COHORT STUDY OF THE PREVALENCE AND IMPACT OF COMORBID MEDICAL CONDITIONS IN PEDIATRIC BIPOLAR DISORDER

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J CLIN PSYCHIATRY, 71:1518-25, November 2010

Pediatric bipolar disorder (BP) is a relatively virulent phenotype that is associated with mixed mood states, rapid cycling, substance abuse, adverse psychosocial adjustment, childhood abuse, and high rates of attempted suicide. In the present study, the authors attempted to identify the association (if any) between medical or psychiatric comorbidities, clinical characteristics, and course of illness/recovery in pediatric BD.

Data from the South Carolina Medicaid program (covering all medical services and medication prescriptions between January 1996 and December 2005) were used to analyze the temporal onset of 12 comorbid medical or psychiatric conditions in a cohort of 1,841 children and adolescents diagnosed with BD (according to DSM-IV-TR criteria) and in a random sample of 4,500 children not treated for any psychiatric disorder (control group). Primary outcome measures were diagnostic codes and regression analyses of patterns of acute and outpatient treatment services for BD over time. Ten conditions examined were significantly more prevalent in the BD cohort: obesity, type 2 diabetes mellitus, endocrine disorders, migraine headaches, central nervous system (CNS) disorders/epilepsy, organic brain disorders/mental retardation, cardiovascular disorders, attention deficit/hyperactivity disorder (ADHD), asthma, and substance abuse. In terms of clinical characteristics within the BD cohort, an adolescent-onset diagnosis of BD (age ≥ 13 years) was significantly associated with a diagnosis of preexisting obesity, hypertension, migraine, mental retardation, endocrine disorders, and substance abuse, whereas recurrent depressive episodes were associated with preexisting endocrine disorders and substance abuse. Preexisting ADHD, substance abuse, CNS disorders/epilepsy, cardiovascular disorders, obesity, and asthma were associated with higher overall medical and psychiatric outpatient and acute service use, but none of these comorbid disorders differentially made an impact on the course of illness or recovery in the BD cohort.

According to the authors, the current data indicate that while some neuropsychiatric and medical disorders temporally precede the diagnosis of early-onset BD in pediatric patients and are associated with discrete facets of illness presentation, they do not substantially alter the clinical course of BD over time. (52 References)
PSYCHIATRIC DISORDERS IN PRESCHOOL OFFSPRING OF PARENTS WITH BIPOLAR DISORDER: THE PITTSBURGH BIPOLAR OFFSPRING STUDY (BIOS)

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AM J PSYCHIATRY, 167:321-30, March 2010

The single largest risk factor for the development of bipolar disorder is a positive family history of the illness. Several risk studies of pediatric bipolar disorder have shown that offspring between the ages of 6 and 18 years whose parents are bipolar have an elevated risk of developing early-onset bipolar disorder as well as other psychiatric illnesses. In the present report, the authors evaluated the lifetime prevalence and specificity of DSM-IV psychiatric disorders and the severity of depressive and manic symptoms at intake in preschool offspring of parents with bipolar I and II disorders.

A total of 121 offspring (age range, 2 to 5 years) of 83 parents with bipolar disorder and 102 offspring of 65 demographically matched comparison parents (29 with non-bipolar psychiatric disorders and 36 without any lifetime psychopathology) were recruited for the study. The parents with bipolar disorder were recruited through advertisements and adult outpatient clinics; comparison parents were selected randomly from the community. The participants were evaluated by means of standardized instruments, and staff were blind to parental diagnoses. After adjusting for within-family correlations and both biological parents’ non-bipolar psychopathology, the researchers found that offspring of parents with bipolar disorder (particularly those older than age 4) showed an eight-fold greater lifetime prevalence of attention deficit hyperactivity disorder (ADHD) and significantly higher rates of having two or more psychiatric disorders relative to the offspring of the comparison parents. Only three offspring of bipolar parents had mood disorders. However, the offspring of parents with bipolar disorder (especially those with ADHD and oppositional defiant disorder) had significantly more severe current manic and depressive symptoms than the offspring of comparison parents.

According to the authors, the present findings indicate that preschool offspring of parents with bipolar disorder have an elevated risk for ADHD and have higher levels of subthreshold manic and depressive symptoms than offspring of parents with non-bipolar psychiatric disorders or without any lifetime psychopathology. (71 References) EAF
LONGITUDINAL COURSE OF BIPOLAR I DISORDER
Duration of Mood Episodes

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ARCH GEN PSYCHIATRY, 67:339-47, April 2010

Bipolar I disorder is usually characterized by recurrent mood episodes, with the risk of having additional episodes remaining relatively high for at least 40 years after illness onset. Because the phenomenology of bipolar I disorder affects treatment and prognosis, the authors of the present investigation attempted to describe the duration of bipolar I mood episodes and factors associated with recovery from these episodes by prospectively following 219 subjects with bipolar I disorder (97 males, 122 females) for up to 25 years.

The subjects (drawn from five academic medical centers (1) met Research Diagnostic Criteria for a major mood episode at the time of study enrollment, (2) were diagnosed at study intake or during follow-up as having either bipolar I disorder or schizoaffective disorder (mainly affective subtype), (3) recovered from the mood episode that was present at study intake, and (4) eventually had at least one recurrent mood episode. Level of psychopathology was assessed with the Longitudinal Interval Follow-up Evaluation every six months for the first five years of follow-up and annually thereafter. The probability of recovery over time from multiple successive mood episodes was examined by means of survival analytic techniques, including a mixed-effects grouped-time survival model. Of the 219 subjects, 196 (90%) were followed up for at least five years, 169 (77%) for at least 10 years, 144 (66%) for at least 15 years, and 122 (56%) for at least 20 years. A total of 1,208 mood episodes were observed during follow-up. The mean number of episodes per subject was 5.5. The probability of recovery was significantly less for those subjects whose mood episode had a severe onset (psychosis or severe psychosocial impairment in week 1 of the episode) and for subjects with greater cumulative morbidity (total number of years spent ill with any mood episode). Compared with the probability of recovery from a major depressive episode, there was a significantly greater probability of recovery from an episode of mania, hypomania, or minor depression, and conversely, a significantly reduced probability of recovery from a cycling episode (switching from one pole to the other without an intervening period of recovery).

The authors found that more than 75% of the subjects recovered from their mood episodes within one year of onset, with the median duration of bipolar I mood episodes being 13 weeks. (42 References)
ASSOCIATION OF SEASONALITY AND PREMENSTRUAL SYMPTOMS IN BIPOLAR I AND BIPOLAR II DISORDERS

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J AFFECT DISORD, 129:313-6, March 2011

Seasonal affective disorder (SAD) and premenstrual syndrome (PMS) are cyclic forms of clinical conditions in which characteristic mood symptoms recur and remit in a rhythmic pattern. Although SAD and PMS are frequently seen in patients with mood disorders (including bipolar disorder), it is not known whether general traits for seasonality and premenstrual distress are related to bipolar disorder independently of its affective episodes. In the present study, the authors attempted to identify the prevalence of seasonality and PMS, independently of mood episodes, in female patients with bipolar disorder and to clarify whether an association exists between these two conditions.

The sample was composed of 61 female patients who met DSM-IV diagnostic criteria for bipolar I (N=30) or bipolar II (N=31) disorder and 122 age-matched healthy women with no history of psychiatric illness (controls). Lifetime histories of seasonality and premenstrual distress were assessed by means of the following self-report rating scales: the Seasonal Pattern Assessment Questionnaire (SPAQ) and the Premenstrual Symptoms Screening Tool (PSST). The sum of individual item scores (5-point scale) on the SPAQ yielded a global seasonality score. All items were measured retrospectively on the basis of premorbid traits, regardless of the disease state. The data indicated that the bipolar patients showed higher global seasonality scores on the SPAQ than the normal controls. Furthermore, this patient-control difference was more prominent in patients with bipolar II disorder than in those with bipolar I disorder. Results from the PSST revealed that the prevalence of moderate to severe PMS was significantly greater in the patients with bipolar II disorder (51.6%) than in the healthy controls (19.7%). A significant association between seasonality and PMS was observed in both patient and control groups.

According to the authors, the findings of the current investigation suggest that female patients with bipolar disorder experience seasonal and premenstrual changes in mood and behavior that are independent of their affective episodes. The data also indicate that traits of seasonality and PMS are associated with each other. A biological mechanism held in common by these two cyclic conditions may be involved in the development of the cyclic nature of bipolar disorder. (30 References)
RACIAL/ETHNIC GROUP DIFFERENCES IN BIPOLAR SYMPTOMATOLOGY IN A COMMUNITY SAMPLE OF PERSONS WITH BIPOLAR I DISORDER

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Research has found systematic racial and ethnic variations in the expression of psychopathology. For example, compared with whites, African Americans with bipolar disorder tend to present with more severe psychotic symptoms, particularly auditory hallucinations, persecutory delusions, and delusions of inference. To date, few studies have examined the extent to which symptoms differ between racial groups or whether racial/ethnic bias in diagnosis may be explained by differential presentation of bipolar disorder symptoms. To better understand the problems associated with the diagnosis of bipolar disorder, especially those related to race and ethnicity, the present authors compared whites, African Americans, and Latinos with bipolar I disorder in terms of the presentation of manic symptoms, depressive episodes, functional impairments (as measured by the 12-item Short-Form Health Survey [SF-12]), and self-reports of a schizophrenia diagnosis.

Data for the study were derived from the 2001-2002 National Epidemiologic Survey on Alcohol and Related Disorders, which included a community-based representative sample of over 43,000 adults in the United States. Approximately 3.6% of those surveyed met lifetime criteria for bipolar I disorder, with rates being comparable across racial/ethnic groups. Compared with whites, African Americans and Latinos expressed similar rates in the presentation of 14 out of 16 manic symptoms, with the exception of grandiosity/self-esteem, a symptom that they were more likely to exhibit than were whites. Higher rates of depressive episodes were observed among whites, and these episodes occurred significantly earlier than they did in African Americans and Latinos. Latinos had slightly higher vitality scores on the SF-12 measures after adjustments were made for sociodemographic and clinical factors, but no other differences across the groups were found.

According to the authors, the results gleaned from the current community-based sample indicate that the expressions and functional impairments of bipolar I disorder appear to be very similar across different racial/ethnic groups. These findings also suggest that provider biases are more likely to explain problems in misdiagnosis than are fundamental differences in the presentation of bipolar disorder across racial/ethnic groups. (32 References) EAF
GENDER AND DEPRESSIVE SYMPTOMS IN 711 PATIENTS WITH BIPOLAR DISORDER EVALUATED PROSPECTIVELY IN THE STANLEY FOUNDATION BIPOLAR TREATMENT OUTCOME NETWORK

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While men and women are equally likely to develop bipolar disorder over the course of their lifetime, gender differences have been identified in certain aspects of the illness, including risk for rapid cycling, mixed states, and age at onset. However, few reports have systematically and prospectively followed patients with bipolar disorder to evaluate time spent in episodes of depression, mania, or euthymia as a function of gender. In the present study, the authors assessed gender differences in terms of the proportion of clinical visits spent depressed, manic, or euthymic in patients with bipolar disorder.

Data were gathered from 711 patients (406 women, 305 men) who met criteria for bipolar I (N=572) or bipolar II (N=139) disorder and who made visits during which they were not actively participating in a clinical trial. They were followed prospectively over a period of seven years (13,191 visits). The main outcome measures were the presence of symptoms of depression or of mania or hypomania. Assessment tools were the Inventory of Depressive Symptomatology and the Young Mania Rating Scale. In approximately half of the visits, the patients had depressive, manic or hypomanic symptoms. The likelihood of having depressive symptoms was significantly greater in women than in men. This could be accounted for by the women’s having higher rates of rapid cycling and anxiety disorders, each of which was associated with increased rates of depression. In the overall cohort, no gender differences were observed with regard to time spent in mania or hypomania. However, among patients with bipolar II disorder, men were significantly more likely than women to be hypomanic at any given visit. On average, the longer patients participated in the study, the less likely they were to be ill at a visit.

According to the authors, the current findings provide support for the notion that bipolar women spend a greater proportion of their time ill struggling with various degrees of depressive symptoms, whether they are in the depressive or manic phase of the disorder. The reasons for this, which may be biological (hormonal), psychosocial, or cultural, remain to be determined, the researchers conclude. (51 References)
CHARACTERISTICS OF PATIENTS WITH BIPOLAR DISORDER
MANAGED IN VA PRIMARY CARE OR SPECIALTY
MENTAL HEALTH CARE SETTINGS

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Bipolar disorders (types I and II) are chronic illnesses that are associated with substantial functional impairment and economic loss. In the Department of Veterans Affairs (VA), over 60,000 individuals were diagnosed with bipolar disorder in fiscal year (FY) 2000; by FY 2006 that number had increased by 25%. Little is known about the extent to which patients with bipolar disorder rely on general medical (primary) care as opposed to mental health care. In the present study, the authors compared clinical characteristics, use of guideline-concordant pharmacotherapy, and outcomes in two groups of patients with bipolar disorder: those who were seen exclusively in VA primary care settings and those who received any VA mental health services.

Data from the 1999 Large Health Survey of Veterans were linked with VA data from the National Psychosis Registry to identify patients diagnosed as having bipolar disorder (N=14,643). Multivariate analyses adjusted for sociodemographic characteristics and clinical and severity factors and determined whether exclusive primary care use versus any mental health care use was associated with poor clinical and services outcomes. Of the 14,643 individuals diagnosed with bipolar disorder, 7.6% (N=1,120) used primary care (general medical) services exclusively. Compared with persons who used specialty mental health care services (N=13,523), those who used primary care exclusively were more likely to be diagnosed with cardiovascular disease or hypertension, less likely to receive guideline-concordant pharmacotherapy, more likely to have an inpatient medical visit, and less likely to have an inpatient psychiatric visit. Results of the 36-Item Short-Form Health Survey indicated that individuals who received primary care exclusively were more likely to have poorer physical health and better mental health.

The findings of the current investigation showed that among patients with bipolar disorder, those who were treated in primary care settings were more likely to have comorbid general medical disorders than those who received some care in a mental health specialty setting. Optimal treatment settings for patients with bipolar disorder may require strategies that address gaps in both general medical and psychiatric care. (39 References)
TREATMENT DELAY AND EXCESSIVE SUBSTANCE USE IN BIPOLAR DISORDER

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Bipolar disorder (BD) is a severe mental illness that involves both significant personal suffering and functional loss. Despite this severity, however, a substantial proportion of persons with BD do not receive psychiatric treatment and of those who do, many experience long delays between illness onset and/or initiation of adequate treatment. There are some indications that the presence of substance abuse in BD patients may be associated with both shorter and longer treatment delays than in BD patients without a history of substance abuse. In the current study, the authors explored the ways in which differences in temporal sequencing of BD and substance abuse onsets may be related to delays in beginning adequate pharmacological treatment.

A total of 151 bipolar patients (91 with BD I and 60 with BD II) were recruited from inpatient and outpatient psychiatric units; 117 were categorized as having primary BD (no excessive substance use preceding the first affective episode) and 34, as having secondary BD (onset of first affective episode occurring after onset of excessive substance use). Logistic regression analyses were used to evaluate predictors of treatment delay in all patients as well as predictors of subsequent excessive substance use in patients with primary BD. The median treatment delay was two years; 79 patients had a short treatment delay (two years or less), and 72 had a long treatment delay (longer than two years). The risk of long treatment delays was increased in patients with BD II, in those with no lifetime history of psychosis, in those who were older at the time of first contact with specialized psychiatric services, in those with primary BD, and in those with excessive substance use. Among patients with primary BD, the risk of developing excessive substance use was increased in males, in those with lower levels of education, and in those with longer treatment delays. Patients with antecedent excessive substance use had a reduced risk for long treatment delays. The risk of developing excessive substance use after the onset of BD was found to increase with longer treatment delays.

According to the authors, the current data indicate that in BD, comorbid substance use is an important factor with regard to both diagnostic work and outcome prediction. (53 References)
COMPLEXITY OF PHARMACOLOGIC TREATMENT REQUIRED FOR SUSTAINED IMPROVEMENT IN OUTPATIENTS WITH BIPOLAR DISORDER

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Several recent studies have pointed out the need for complex pharmacologic regimens in a large proportion of inpatients and outpatients with bipolar illness; however, the details of which drugs and combinations are successful (or not) in achieving relative long-term stability in a prospectively followed cohort have rarely been delineated. In the present investigation, conducted from 1996 to 2002, the authors evaluated the types and clinical correlates of naturalistic treatments associated with sustained improvement/remission for at least six months in a cohort of outpatients with bipolar disorder.

The sample was composed of 525 outpatients with bipolar disorder. All gave informed consent, recorded all medications taken, and had their mood rated daily by means of the National Institute of Mental Health Life Chart Method for at least one year. Demographics and clinical characteristics of patients with a “sustained response” (ratings of “improved” or “very much improved” on the Clinical Global Impressions-Bipolar Version for at least six months) were compared with those of treatment nonresponders. Of the 525 patients, 96 were minimally impaired or essentially well at study entry and remained so for at least six months. Of the remaining 429 patients who were ill at study entry, 195 (45.5%) showed a sustained response, and 234 (54.5%) showed either an insufficient response or no response. A mean of 2.98 drugs was given at the time of improvement (beginning of sustained response), which occurred after a mean of 18 months of study participation. Lithium and valproate were the drugs most frequently prescribed at the time of improvement and were among those with the highest overall success rates. Equally complex drug regimens were employed in the nonresponders who did, however, have a more adverse clinical course prior to study entry. The nonresponders ultimately were exposed to more antidepressants and antipsychotics than the sustained responders.

The authors conclude that during naturalistic treatment of outpatients with bipolar disorder, a mean duration of one and a half years and, at times, highly complex medication regimens were required to achieve a sustained response for at least six months. (44 References)
Efficacy and Safety of Long-Term Fluoxetine Versus Lithium Monotherapy of Bipolar II Disorder: A Randomized, Double-Blind, Placebo-Substitution Study

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The long-term use of antidepressant therapy for individuals with bipolar disorder has received relatively little attention. Although some practice guidelines have recommended the cautious use of antidepressants in bipolar depression, these guidelines differ widely with regard to the optimum duration of antidepressant therapy. The authors of the present investigation examined the safety and efficacy of long-term fluoxetine monotherapy, lithium monotherapy, and placebo therapy in preventing the relapse and recurrence of bipolar type II major depressive episodes. They hypothesized that fluoxetine monotherapy would be superior to lithium monotherapy and would have a similar hypomanic mood conversion rate.

Patients who met DSM-IV-TR criteria for bipolar II disorder, who were at least 18 years of age, and who had recovered from a major depressive episode during and initial course of open-label fluoxetine monotherapy were randomly assigned to receive 50 weeks of double-blind monotherapy with fluoxetine (10-40 mg/day), lithium (300-1200 mg/day), or placebo. The primary outcome measure was time to relapse or recurrence. Secondary outcome measures included the proportion of patients who remained well and the frequency of hypomanic symptoms. There were no significant differences in clinical or demographic characteristics among the fluoxetine (N=28), lithium (N=26), and placebo (N=27) groups. The mean time to relapse was 249.9 days for the fluoxetine group, 156.4 days for the lithium group, and 186.9 days for the placebo group. The Cox proportional hazards ratio for relapse was significantly lower with fluoxetine than with lithium, and the estimated hazard of relapse with lithium was 2.5 times greater than with fluoxetine. There were no statistically significant or clinically meaningful differences in hypomanic symptoms among the treatment groups over time. One patient taking fluoxetine and one patient taking placebo discontinued treatment because of hypomania.

According to the authors, the findings of the current study suggest that, in patients who have recovered from a bipolar II major depressive episode, fluoxetine monotherapy may provide superior relapse-prevention benefits relative to lithium monotherapy and may do so without an increase in hypomanic mood conversion episodes. (40 References)
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SCHIZOPHRENIA AND BORDERLINE PERSONALITY DISORDER
Similarities and Differences in the Experience of Auditory Hallucinations, Paranoia, and Childhood Trauma

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Schizophrenia and borderline personality disorder (BPD) are frequently encountered in psychiatric practice. However, there appears to be very little research regarding comorbidity or the interface between these two conditions. In the present study, the authors investigated similarities and differences in the experience of auditory hallucinations, paranoia, and childhood trauma in individuals with schizophrenia, with BPD, or with both diagnoses.

Patients with clinical diagnoses of schizophrenia and/or BPD were interviewed by means of the Structured Clinical Interview for DSM-IV. Axes 1 and 2 and auditory hallucinations, paranoia, and childhood trauma (emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect) were assessed. A total of 111 patients (48 men, 63 women) participated in the study; 59 (40 men, 19 women) met criteria for schizophrenia only, 33 (three men, 30 women met criteria for BPD only, and 19 (five men, 14 women) were diagnosed with both disorders. The results indicated that the three groups were similar with regard to their experiences of voices (including perceived location), but they differed in frequency of paranoid delusions. Patients with a diagnosis of BPD, including those with comorbid schizophrenia, reported experiencing more childhood trauma, especially emotional abuse.

According to the authors, the similarities and differences found in the present study suggest that individuals who meet criteria for both schizophrenia and BPD (traumatic psychosis) resemble those with BPD in their experience of trauma, particularly with regard to emotional abuse. However, the nature of psychotic symptoms, such as hearing voices, appears to be similar in patients with BPD and schizophrenia, as well as in those with both diagnoses. Paranoia seems to occur frequently across all three diagnostic groups, although persecutory delusions appear to be more common in individuals with schizophrenia and in those with both BPD and schizophrenia. (27 References)
Little is known about the childhood and adolescent antecedents of adult borderline personality disorder (BPD), one of the most crippling and frequently lethal of all psychiatric illnesses. Characterized by poor impulse control, emotional dysregulation, unstable self-concept, and maladaptive behaviors such as suicide attempts and deliberate self-harm, BPD affects 2% of the general population and 20% of psychiatric inpatients. Despite its prevalence and high levels of morbidity and mortality, the precursors, risk factors, and developmental trajectories of BPD are only partially understood. To characterize precursors and trajectories in the development of BPD, the authors of the present study devised an anonymous 109-question Internet survey that was designed to elicit information from parents (respondents) about their offspring (probands) with and without BPD. The questions covered aspects of the probands’ lives from pregnancy through young adulthood, including clinical features, family history, and treatment history. Offspring with BPD were identified through both lifetime clinical diagnoses and diagnostic criteria embedded within the survey.

Data were gathered on 234 female offspring who met strict criteria for BPD and 87 non-BPD female siblings. Parents of daughters with BPD described affective symptomatology starting in infancy, with unusual moodiness being more frequently endorsed for probands with BPD than for their non-BPD siblings. These affective symptoms persisted beyond infancy and began to be coupled with interpersonal difficulties that manifested themselves in toddlerhood and childhood. By adolescence, difficulties with impulsivity, aggression, acting out and self-destructive behaviors had begun to predominate.

According to the authors, the current findings reveal important information about the prodromal symptoms and developmental trajectories of females with BPD. The data suggest that BPD-predictive features of moodiness may be identified as early as infancy. Thus, the researchers note, BPD may be viewed as a temperamental disturbance in affect, with moodiness that begins in infancy, with interpersonal problems that become evident in elementary school, and subsequently, with the emergence of high levels of impulsivity during the adolescent years. (38 References)
NEURAL PROCESSING OF EMOTIONAL OVERINVOLVEMENT IN BORDERLINE PERSONALITY DISORDER

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Patients with borderline personality disorder (BPD) seem to fare better clinically if their families are determined to have high levels of emotional overinvolvement (EOI), which is characterized by marked emotionality, anxious concern, and protective behavior toward the patient. The authors of the present study used both self-report methods and functional magnetic resonance imaging (fMRI) to examine the ways in which patients with BPD process EOI comments. The researchers tested the hypothesis that, unlike healthy control subjects or individuals with other psychiatric problems, people with BPD would process EOI as an approach-related stimulus.

The sample was composed of 34 right-handed female participants (mean age, 25 years; age range, 19 to 35 years); 13 met DSM-IV diagnostic criteria for BPD, 10 met diagnostic criteria for dysthymia, and 11 had no current or past history of psychopathology (healthy controls). While undergoing fMRI with a high field strength (3T) scanner, the participants listened to a standardized auditory stimulus that consisted of either four neutral or four EOI comments. The subjects also rated their mood before and after exposure to the comments. All the subjects reported an increase in negative mood after hearing EOI and rated the EOI comments as negative stimuli. However, after subtracting activation to neutral comments, the authors found that the participants with BPD showed higher activation in left prefrontal regions during EOI than the other two groups. Increased left prefrontal activation during EOI was also correlated with clinical measures indicative of borderline pathology. While the subjects with dysthymia showed increased amygdala activation during EOI, this was not evident in the healthy controls or the participants with BPD.

According to the authors, the findings of the present investigation indicate that in individuals with BPD, EOI may serve to activate neural circuitry that is implicated in the processing of approach-related stimuli. Increased left prefrontal activation to EOI may prove to be a vulnerability marker for BPD. Finally, the researchers note, the current data also may partially explain why patients with BPD appear to do better clinically in family environments that are characterized by high levels of EOI. (47 References)
DYSREGULATION OF REGIONAL ENDOGENOUS OPIOID FUNCTION IN BORDERLINE PERSONALITY DISORDER

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AM J PSYCHIATRY, 167:925-33, August 2010

Epidemiological data indicate that borderline personality disorder has a lifetime prevalence between 1% and 5%, with approximately 75% of clinical subjects being female. Borderline personality disorder is characterized by dysregulation of emotion processing, which is manifested as affective lability and impulsive behavior, including aggression and self-harm. This dysregulation is exemplified by short and often severe rapidly changing mood states that are highly reactive to environmental stimuli. In the present investigation, the authors used positron emission tomography and a selective -opioid receptor radiotracer to examine availability (nondisplaceable binding potential, or BP_{ND}) of these receptors under neutral (baseline) conditions and during induction of a sustained sadness state in 18 unmedicated, right-handed female patients with borderline personality disorder (mean age, 28 years) and 14 age-matched healthy female comparison subjects (mean age, 35 years).

The patients showed greater regional -opioid BP_{ND} than the comparison subjects at baseline (neutral state) bilaterally in the orbitofrontal cortex, caudate, and nucleus accumbens and in the left amygdala, but lower BP_{ND} in the posterior thalamus. Sadness induction was associated with greater reductions in BP_{ND} (endogenous opioid system activation) in the patient group than in the comparison group in the pregenual anterior cingulate, left orbitofrontal cortex, left ventral pallidum, left amygdala, and left inferior temporal cortex. Relative to comparison subjects, patients showed evidence of endogenous opioid system deactivation in the left nucleus accumbens, the hypothalamus, and the right hippocampus/parahippocampus. Correlations of baseline measures with the Dissociative Experiences Scale and endogenous opioid system activation with the Barratt Impulsiveness Scale did not remain significant after correction for multiple comparisons.

The authors conclude that differences exist between patients with borderline personality disorder and healthy comparison subjects in baseline in vivo -opioid receptor concentrations and in the endogenous opioid system response to a negative emotional challenge that can be related to some of the clinical characteristics of patients with borderline personality disorder. The regional network involved is implicated in the representation and regulation of emotion and stress responses. (53 References)
Borderline personality disorder (BPD) is a prevalent, chronic, and severe psychiatric disorder. Approximately 90% of persons with BPD improve or recover by the age of 50; however, most have multiple recurrences of suicidal behavior, and between 3% and 10% die by suicide. Variability in mood swings is a characteristic of BPD and is associated with suicidal behavior. The authors of the present investigation examined patterns of mood variability in individuals with BPD and attempted to determine whether such patterns could be predicted on the basis of demographic and suicide-related psychological risk factors.

The study sample was composed of 82 adults with BPD and histories of recurrent suicidal behavior, all of whom had been recruited from three outpatient psychiatric programs in Canada. The mean age of the patients was 33.5 years; most were female (82.9%), were not married (82.9%), and were highly educated (58.5% had university or college degrees) but unemployed (75.6%). Almost all (92.7%) reported previous psychiatric hospitalizations. Experience sampling methodology (ESM) was used to assess negative mood intensity ratings on a visual analog scale and was carried out at six randomized times every day for a period of 21 days. ESM is ecological, because experiences are measured in the participant’s natural environment. It is also considered to be momentary, because assessments capture information about the participant’s immediate or near-immediate experiences and require minimal retrospection. Three-level models estimated variability between times (52.8%), days (22.2%), and patients (25.1%) and supported a quadratic pattern of daily mood variability. Depression scores predicted variability between patients’ initial rating of the day. Average daily mood patterns depended on levels of hopelessness, suicide ideation, and sexual abuse history. Patients reporting moderate to severe sexual abuse and elevated suicide ideation were characterized by worsening moods from early morning up through evening, with little or no relief. Patients reporting mild sexual abuse and low levels of suicide ideation showed improved mood throughout the course of the day.

According to the authors, the current results, if replicated in larger ESM studies, could assist clinicians in determining which BPD patients require close monitoring. (32 References)
OLANZAPINE VERSUS HALOPERIDOL IN THE MANAGEMENT OF BORDERLINE PERSONALITY DISORDER
A Randomized Double-Blind Trial

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J CLIN PSYCHOPHARMACOL, 30:44-7, February 2010

Borderline personality disorder (BPD), a psychiatric problem that involves an enduring disturbance of personality and behavior, affects 2% of adults, most of whom are young women. Both psychotherapeutic and pharmacological approaches are currently being employed for the attenuation of BPD symptoms, with selective serotonin reuptake inhibitors, low-dose neuroleptics, lithium, and mood stabilizers all showing efficacy in reducing impulsive aggression in borderline patients. Because the newer atypical antipsychotics appear to be as effective as the older typical antipsychotics in controlling impulsivity and aggressiveness in BPD patients, the authors conducted the present study for the purpose of comparing the effectiveness of olanzapine with that of haloperidol in patients with BPD.

Twenty-eight female inpatients, all of whom met DSM-IV-TR criteria for BPD, were entered into one of two contemporaneous groups (14 in each group). After admission and a mandatory seven-day washout period, both groups entered an eight-week, parallel, double-blind trial and were randomly assigned to receive olanzapine or haloperidol in a one:one ratio. Primary outcome measurements were obtained by means of the Brief Psychiatric Rating Scale, the Clinical Global Impression-Severity Scale, and the Buss-Durkee Hostility Inventory. Baselines were created at the beginning of the trial through patient assessments, and final measures were obtained at the end of the study. Analysis of effect size, calculation of confidence intervals, and power analyses were also performed. All of the patients from both groups completed the eight-week study. Intra-group analysis at the eighth week revealed significant positive responses to both olanzapine and haloperidol when compared with baseline measures. However, between-group analysis at the end of the trial showed no significant differences among the patients. The analysis of specific Brief Psychiatric Rating Scale subscales revealed considerable and comparable improvement in both groups with regard to anxiety, tension, depressive mood, and hostility. Effect size analyses demonstrated substantial improvement in both groups.

According to the authors, the results of the current investigation indicate that there appear to be no significant differences between olanzapine and haloperidol with regard to the management of mental and behavioral symptoms in patients with BPD. (17 References)
A RANDOMIZED CONTROLLED TRIAL OF A DUTCH VERSION OF SYSTEMS TRAINING FOR EMOTIONAL PREDICTABILITY AND PROBLEM SOLVING FOR BORDERLINE PERSONALITY DISORDER

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J NERV MENT DIS, 198:299-304, April 2010

While several psychological treatments have been developed over the last decade for individuals with borderline personality disorder (BPD), for many, these programs remain out of reach, as they are rather lengthy, labor intensive, and not easy to implement in mental health care settings. In 2002, Blum et al. developed Systems Training for Emotional Predictability and Problem Solving (STEPPS), a group treatment program that is brief and relatively easy to implement. The purpose of the present investigation was to examine the efficacy of a Dutch version of this treatment. The program has three main components: (1) psychoeducation about BPD, (2) emotion management skills training, and (3) behavior management skills training. The Dutch version of the STEPPS group program involves 18 weekly sessions and a single follow-up session conducted three to six months after the program’s conclusion.

The study sample was composed of 79 outpatients who met DSM-IV criteria for BPD; 42 (35 females, seven males; mean age, 32.9 years) were randomly assigned to STEPPS plus adjunctive individual therapy, and 37 (33 females, four males; mean age, 31.8 years) were randomly allocated to treatment as usual (control condition). Assessments were carried out before and after the intervention, and at a six-month follow-up. STEPPS recipients showed a significantly greater reduction in general psychiatric and BPD-specific symptomatology than subjects who received treatment as usual; these differences remained significant at follow-up. The STEPPS program also led to greater improvement in quality of life, especially at follow-up. Effect sizes for the differences between the treatments ranged from moderate to large. In both conditions, the number of patients that could be labeled “recovered” after one year was small; however, more than two-thirds of the patients who received STEPPS plus individual therapy showed reliable improvement as compared with less than half of the patients in the treatment-as-usual condition. No differences between the two treatment conditions were found with regard to reducing impulsive and aggressive behaviors.

According to the authors, the current results suggest that the brief STEPPS program, in combination with limited individual therapy, can improve the treatment of BPD in a number of ways. (30 References) EAF
DYNAMIC DECONSTRUCTIVE PSYCHOTHERAPY VERSUS OPTIMIZED COMMUNITY CARE FOR BORDERLINE PERSONALITY DISORDER CO-OCCURRING WITH ALCOHOL USE DISORDERS
A 30-Month Follow-Up

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J NERV MENT DIS, 198:292-8, April 2010

Borderline personality disorder (BPD) is a serious psychiatric illness that often co-occurs with substance use disorders, particularly those involving alcohol. It has been determined that approximately 50% to 75% of BPD patients in mental health facilities also meet diagnostic criteria for alcohol use disorders (AUD). Although there is evidence that patients with co-occurring BPD and AUD represent a common but particularly severely ill and refractory subgroup, very few studies have examined the response of these patients to specific treatment modalities. While dynamic deconstructive psychotherapy (DDP), a time-limited, weekly, individual treatment, has been shown to be effective for those in the BPD/AUD subgroup, it is not known whether patients who receive DDP are likely to relapse to baseline levels of psychopathology and substance use after termination or whether improvement is sustained. The authors of the present investigation attempted to directly address this question.

The study participants were recruited from a sample of 30 patients who were enrolled in a 12-month randomized controlled trial in which treatment with DDT was compared with optimized community care (OCC). The subjects were between 18 and 45 years of age and were diagnosed as having BPD and active alcohol abuse (N=10) or dependence (N=20). Outcomes were assessed after an additional 18 months of naturalistic follow-up. The two treatment groups displayed an almost identical pattern of individual outpatient utilization, combining individual psychotherapy, alcohol counseling, case management, and separate medication management visits. During the follow-up period, 50% of both DDP and OCC participants were involved in some type of individual psychotherapy, and 75% of those in each group were receiving psychotropic medications. Over the course of 30 months, when compared with the patients receiving OCC, the DDP participants demonstrated large, sustained treatment effects over a broad range of outcomes and achieved significantly greater improvement in core BPD symptoms, depression, parasuicide, and recreational drug use.

According to the authors, the results of the current study suggest that DDP is a cost-effective treatment that can lead to broad and sustained improvement in patients dually diagnosed with BPD and AUD. (37 References)
TRANSFERENCE-FOCUSED PSYCHOTHERAPY V. TREATMENT BY COMMUNITY PSYCHOTHERAPISTS FOR BORDERLINE PERSONALITY DISORDER: RANDOMISED CONTROLLED TRIAL

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BR J PSYCHIATRY, 196:389-95, May 2010

Transference-focused psychotherapy, developed by Otto F. Kernberg, is a modified psychodynamic psychotherapy for people with borderline personality disorder. The treatment focuses on the integration of internalized experiences of dysfunctional early relationships; thus, the actual relationship between the individual and the therapist (“transference relationship”) is examined as much as possible. The authors of the present study conducted a randomized controlled trial in which the efficacy of transference-focused psychotherapy was compared with that of treatment by experienced community psychotherapists.

The sample was composed of 104 female outpatients (age range, 18 to 45 years) who met DSM-IV criteria for borderline personality disorder; 52 were randomly allocated to transference-focused psychotherapy, and 52 were randomly assigned to be treated by experienced psychotherapists in the community. The duration of treatment for both groups was one year. The primary outcome measures were drop-out rates and suicide attempts. Secondary outcome measures included DSM-IV diagnostic borderline criteria, psychosocial functioning, level of personality organization, and psychiatric inpatient admissions. There were significantly fewer drop-outs in the transference-focused psychotherapy group (38.5%) than in the group treated by community psychotherapists (67.3%). There were also significantly fewer suicide attempts among those treated with transference-focused psychotherapy. Transference-focused psychotherapy also proved to be significantly superior to treatment by community psychotherapists in the domains of borderline symptomatology, psychosocial functioning, personality organization, and psychiatric inpatient admissions. Both treatment groups improved significantly with regard to depression and anxiety, and the transference-focused psychotherapy group in general psychopathology, all without significant group differences. There were no changes in self-harm behavior in either group.

According to the authors, the findings of the current study indicate that transference-focused psychotherapy is more efficacious than treatment by experienced community psychotherapists for individuals with borderline personality disorder. (35 References)
TIME TO ATTAINMENT OF RECOVERY FROM BORDERLINE PERSONALITY DISORDER AND STABILITY OF RECOVERY: A 10-YEAR PROSPECTIVE FOLLOW-UP STUDY

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AM J PSYCHIATRY, 167:663-7, June 2010

Clinical experience suggests that some patients with borderline personality disorder exhibit only mild symptoms and function well psychosocially over time, while others remain quite symptomatic and may become increasingly impaired in terms of psychosocial functioning. In the present investigation, an extension of the McLean Study of Adult Development, the authors determined time to attainment of recovery from borderline personality disorder and also assessed the stability of recovery.

A total of 290 inpatients (233 females, 57 males; mean age, 26.9 years) who met both DSM-III-R and Revised Diagnostic Interview for Borderlines criteria for borderline personality disorder were assessed during their index admission by means of a series of semistructured interviews and self-report measures. The same instruments were readministered every two years for a period of 10 years. Attrition was relatively low; 275 patients were reinterviewed at two years, 269 at four years, 264 at six years, 255 at eight years, and 249 at 10 years. In all, 91.9% of surviving patients (249/271) were reinterviewed at all five follow-up waves. At 10 years, 93% of the patients had attained a symptomatic remission lasting at least two years and 86%, a sustained remission lasting at least four years. Only 50% attained recovery from borderline personality disorder, which was defined as having good social and vocational functioning as well as no longer meeting study criteria for borderline personality disorder during a two-year follow-up period. Approximately 34% of the patients who achieved recovery lost their recovery. About 30% of those who achieved a two-year remission of symptoms experienced a recurrence, and approximately 15% of those who attained a four-year sustained remission experienced a recurrence.

According to the authors of the current investigation, taken together, the results of the present prospective follow-up study suggest that recovery from borderline personality disorder (with both symptomatic remission and good psychosocial functioning) appears to be difficult for many patients to attain. The current data also indicate that once attained, such a recovery seems to be relatively stable over time. (23 References)
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APPLES TO ORANGES?: A DIRECT COMPARISON BETWEEN SUICIDE ATTEMPTERS AND SUICIDE COMPLETERS

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J AFFECT DISORD, 124:90-7, July 2010

Suicide attempters and suicide completers may represent different but overlapping groups of distressed individuals. Several psychiatric disorders are associated with an increased risk of both attempted and completed suicide. Although depression has been found to be related to an increased risk of suicide, the presence of a depressive disorder in itself may not distinguish suicide attempters from completers. In the current study, the authors sought to identify key differences between suicide attempters and suicide completers by comparing them in terms of symptoms of depression, the presence of suicide-related variables, and stressful life events.

The sample was composed of 50 suicide attempters (21 males, 29 females; mean age, 36.86 years) and 50 suicide completers (35 males, 15 females; mean age, 43.26 years). The attempters were identified through the inpatient unit of a private psychiatric hospital; the completers were identified through the county coroner’s office. All had been diagnosed with a major depressive disorder at the time of their suicidal act. The suicide attempters and family member informants of the suicide completers participated in a thorough psychosocial evaluation. To maximize comparisons with completers, attempters were subclassified on the basis of the lethality of their attempt, with 36 considered to be low-lethality attempters and 14 designated as high-lethality attempters. Suicide completers were significantly older than suicide attempters and were more likely to be male, whereas both groups of attempters were more likely to be female. Suicide attempters and completers were found to be similar on most measures of depressive symptoms. However, suicide completers were significantly more likely to use alcohol or drugs prior to their suicidal act, and they also were more likely to leave a suicide note. In addition, suicide completers were significantly more likely to have experienced substantial job stress and financial problems.

According to the authors, the present findings indicate that there appear to be both similarities and differences between individuals who attempt suicide and those who complete the suicidal act. Future research may help to clarify the key warning signs that reflect the risk of completed suicide in adults who have been diagnosed with a major depressive disorder. (45 References)
CHILDHOOD ADVERSITIES AS RISK FACTORS FOR ONSET AND PERSISTENCE OF SUICIDAL BEHAVIOUR

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BR J PSYCHIATRY, 197:20-7, July 2010

While suicide is one of the leading causes of death worldwide, the precise effects of childhood adversities as risk factors for the onset and persistence of suicidal behavior (suicide ideation, plans, and attempts) are not well understood. Using data from the World Mental Health Surveys, the authors of the present study examined the associations between childhood adversities and subsequent suicidal behavior. The World Mental Health Surveys were carried out in 21 different countries throughout Africa, the Americas, Asia and the Pacific, Europe, and the Middle East.

Respondents from nationally representative samples (N=55,299) were interviewed regarding childhood adversities that occurred before the age of 18 years and lifetime suicidal behavior. Childhood adversities included physical abuse, sexual abuse, neglect, parental death, parent divorce, other parental loss, family violence, physical illness, and financial adversity before the age of 18. Childhood adversities were found to be associated with an increased risk of suicide attempts and ideation in both bivariate and multivariate models (odds ratio range, 1.2-5.7) The risk increased with the number of adversities experienced, but at a decreasing rate. Sexual and physical abuse were consistently the strongest risk factors for both the onset and persistence of suicidal behavior, especially during adolescence. These associations remained similar after additional adjustments were made for the respondents’ lifetime mental disorder status.

According to the authors, the current data indicate that childhood adversities (especially intrusive or aggressive adversities) are powerful predictors of the onset and persistence of suicidal behavior. (36 References)
RISK AND PROTECTIVE FACTORS ASSOCIATED WITH SUICIDAL IDEATION IN VETERANS OF OPERATIONS ENDURING FREEDOM AND IRAQUI FREEDOM

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J AFFECT DISORD, 123:102-7, June 2010

A significant proportion of the veterans of Operations Enduring Freedom and Iraqi Freedom (OEF/OIF) are returning from their deployments with posttraumatic stress disorder (PTSD), depression, and other psychological problems that may increase the risk of suicide. However, the extent to which specific risk factors (e.g., PTSD) may increase the likelihood of suicidal ideation, or whether protective factors (e.g., social support, resilience) may buffer the negative effects of these conditions on suicidal ideation, has yet to be examined. In the present study, the authors’ purpose was to: (1) provide a descriptive analysis of demographic, risk, and protective correlates of suicidal ideation in OEF/OIF veterans; and (2) employ a multivariate approach to determine which risk and protective variables are most strongly associated with suicidal ideation.

The study participants were 272 OEF/OIF veterans who completed a survey containing measures of psychopathology, resilience, and social support. The surveys were completed an average of 27 months following return from last deployment (dates of service: 01/03 to 03/07). Thirty-four respondents (12.5%) reported contemplating suicide in the two-week period prior to completing the survey. The respondents who endorsed suicidal ideation were more likely to screen positive for PTSD, depression, and alcohol abuse; scored higher on measures of combat exposure, psychosocial difficulties, stigma, and barriers to care; and scored lower on measures of resilience, unit support, and postdeployment social support. In a multivariate model, positive screens for PTSD and depression, as well as increased psychosocial difficulties, emerged as positive predictors of suicidal ideation, while increased scores on measures of postdeployment accessibility of family and friends and sense of purpose and control emerged as protective factors.

The authors suggest that future research endeavor to: replicate the current findings in larger, more representative samples of OEF/OIF veterans as well as in other military and civilian populations; examine specific roles of protective variables in mediating the relationship between psychiatric conditions and suicidality; and develop and test the efficacy of suicide prevention programs in veteran populations. (33 References)
REWARD/PUNISHMENT REVERSAL LEARNING IN OLDER SUICIDE ATTEMPTERS

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Worldwide, suicide occurs more frequently among the elderly than in any other age group. Although cognitive decline is prevalent in old age and may contribute to the heightened suicide risk, little is known about the role of cognitive factors. However, since a suicide attempt may be viewed as an outcome of a nonoptimal decision process, it is possible that impaired decision making is a causal cognitive factor in suicidal behavior. The authors of the present study attempted to identify the components of decision making that are associated with attempted suicide in old age. They hypothesized that impairments in reward/punishment-based learning, a component of affective decision making, would be associated with attempted suicide in late-life depression.

Using a probabilistic reversal learning task, the researchers assessed reward/punishment-based learning in 65 individuals who were 60 years of age or older. The sample comprised 15 depressed suicide attempters, 12 depressed suicide ideators, 24 nonsuicidal depressed elderly subjects, and 14 nondepressed, nonsuicidal comparison subjects. A reinforcement learning computational model was used to decompose reward/punishment processing over time. The Stockings of Cambridge test served as a control measure of executive function. After controlling for the effects of education, global cognitive function, and substance use, the authors found that suicide attempters, but not suicide ideators, showed impaired probabilistic reversal learning when compared with both nonsuicidal depressed subjects and nondepressed, nonsuicidal subjects. Model-based analyses revealed that suicide attempters discounted previous history to a higher degree than comparison subjects, basing their choice largely on reward/punishment received on the last trial. The groups did not differ in their performance on the Stockings of Cambridge test.

According to the authors, the current data appear to indicate that older suicide attempters display impaired reward/punishment-based learning. They hypothesize that older suicide attempters may make overly present-focused decisions while ignoring past experiences. The researchers conclude that this “myopia for the past” may have therapeutic potential. (55 References)
GENDER DIFFERENCES IN RISK ASSESSMENT OF DEATH WISHES AND SUICIDAL IDEATION IN THE COMMUNITY
Results From the KORA Augsburg F3 Study With 3079 Men and Women, 35 to 84 Years of Age

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J NERV MENT DIS, 198:52-8, January 2010

Studies designed to improve evidence-based risk assessment of individuals at risk for suicide remains a major challenge of contemporary mental health research. Among risk factors for suicide that have been identified so far, engagement in death wishes and suicidal ideation (SID) has been found to be of paramount importance. In the present investigation, the authors assessed SID in a population-based sample and examined multiple sex- and age-adjusted affective and biobehavioral covariates. Data were drawn from the KORA F3 survey, which was conducted in 2004/2005 within the framework of the ongoing KORA project, a research platform for population-based health research.

The study sample was composed of 3,079 participants (age range, 35 to 84 years), all of whom underwent a standardized interview and an extensive medical examination. A total of 163 subjects (63 men, 100 women) reported experiencing some form of SID within the previous two weeks. In terms of sociodemographic factors, men with SID were substantially more likely to be unemployed, to have a low net income, and to live alone, whereas for women, only low net income was associated with SID. Anxiety and a high level of somatic complaints, particularly dyspnea, were found to contribute to the risk of SID. In both men and women, however, the clinical picture of subjects suffering from SID was dominated by a six-fold adjusted increased risk of a depressive syndrome, followed by impaired self-perceived health (three-fold adjusted relative risk).

According to the authors, the current results indicate that SID is associated with a number of sociodemographic, somatic, and psychological covariates, all of which may contribute to a better understanding of the complex and multiple interactive processes that lead an individual to consider his/her life as no longer worth living. These factors may not only open new insights into the multifaceted etiology of suicide but also offer new strategies for the early detection of those individuals at risk. (56 References)
SUICIDAL IDEATION AND BEHAVIOUR IN THE AFTERMATH OF MARITAL SEPARATION: GENDER DIFFERENCES

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While marital separation occurs frequently in Western countries and is thought to be a possible precipitant of suicidal behavior, there is a very limited body of research dedicated to the investigation of suicide risk factors within the context of marital separation. In the present study, the authors attempted to identify possible gender-specific social and psychological risk factors for suicidality by (1) comparing the risk of suicidal behavior during the separation process among recently separated males and females; and (2) analyzing differences in predictive factors of serious suicidal ideation during marital separation in males and females.

Separated males and females who had contacted relationship counseling services, help-line services, or a variety of support and self-help groups were asked to participate in the study. The participants were required to be 18 years of age or older and to have separated (but not yet divorced) from their married/de facto partner within the previous 18 months. Odds ratios (ORs) with 95% confidence intervals and adjusted ORs were calculated for categorical data and t-tests for continuing variables. Multinomial logistic regression was applied to estimate the independent contribution of the variables. A probability level of 0.05 was employed for all statistical tests. Compared with separated females (N=142), separated males (N=228) were found to be at an increased risk for developing suicidality during the separation process, even after the researchers adjusted for age, level of education, employment status, and having children with the separated partner. Psychosocial risk factors identified in the development of serious suicidal ideation were mental health problems (suffered during the previous year), history of previous suicide attempts, and feelings of internalized shame. For separated males, significant predictors of suicidality also included a lower level of education, separation-related shame, and stress from legal negotiations, especially those involving property/financial issues.

According to the authors, the findings of the current investigation serve to provide a better understanding of suicidal behaviors occurring in the aftermath of marital or de facto separation. This knowledge could prove to be useful in the implementation of future suicide prevention strategies in those individuals who are going through the process of a marital separation. (26 References) EAF
SUICIDE IN PATIENTS WITH STROKE: 
A POPULATION-BASED STUDY OF SUICIDE VICTIMS 
DURING THE YEARS 1988-2007 IN NORTHERN FINLAND

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J NEUROPSYCHIATRY CLIN NEUROSCI, 22:182-7, Spring 2010

While depression is the most common psychiatric complication to occur after stroke, it has also been found that depressed individuals are at increased risk for suffering a stroke. It is also well-known that depression is highly associated with suicide. The authors of the present study examined the prevalence of stroke among suicide victims and attempted to determine whether prestroke depression influenced the suicide process. They used a comprehensive database off all suicides (N=2,283) committed in Northern Finland over a period of 15 years, along with information on all hospital-treated somatic and psychiatric disorders. Data on age, gender, previous suicide attempts, suicide methods, and abuse of alcohol at the time of the suicide were based on death certificates issued after forensic medical-legal investigations. Diagnoses of subjects and hospital admissions of the suicide victims were obtained from the Finnish Hospital Discharge Register, which covers all treatment in general, private, mental, military, and prison hospitals, as well as inpatient wards of local health centers.

Of the total number of suicide victims, 75 (3.4%) had suffered a stroke at some point during their lifetime. The majority of the victims with stroke (80%) were not under the influence of alcohol at the time of suicide. Some 32% of the victims with stroke had been hospitalized due to depression. The age- and sex-adjusted hazard of suicide after stroke was increased 2.2-fold among victims who had suffered from prestroke depression as compared with those without any lifetime history of depression. The elevated hazard of suicide was not seen among victims with poststroke depression when compared with those with prestroke depression. Six of the stroke victims whose depression had been assessed before the stroke (55%) committed suicide within two years after having a stroke. Only three of the suicide victims with poststroke depression (23%) and 19 of those with no lifetime history of depression (37%) committed suicide within two years of suffering a stroke.

According to the authors’ knowledge, the current study appears to be the first investigation so far in which prestroke depression was found to increase the risk of accelerated suicide among stroke patients. (33 References)
SUICIDE IN HIV-INFECTED INDIVIDUALS AND THE GENERAL POPULATION IN SWITZERLAND, 1988-2008

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AM J PSYCHIATRY, 167:143-50, February 2010

Suicide is an important public health problem in Switzerland, with about 1,400 suicides being recorded annually. Swiss suicide rates are in the top third in Europe and in the top quintile worldwide. Rates of suicide have been found to be elevated in patients with chronic conditions such as HIV infection. While the introduction of highly active antiretroviral therapy (HAART) in 1996 has led to a substantial reduction in HIV-associated morbidity and mortality, it is unclear whether and to what extent HAART has affected suicide rates. The authors of the present study examined time trends and predictors of suicide in the pre-HAART (1988-1995) and HAART (1996-2008) eras in HIV-infected patients and in the general population in Switzerland.

The researchers analyzed data from the Swiss HIV Cohort Study and the Swiss National Cohort, a longitudinal study of the mortality in the Swiss general population. They calculated standardized mortality ratios comparing HIV-infected individuals with the general population and used Poisson regression to identify risk factors for suicide. From 1988 to 2008, 15,275 HIV-infected patients were followed in the Swiss HIV Cohort Study for a median duration of 4.7 years. Of these, 150 committed suicide (rate: 158.4 per 100,000 person-years). In men, standardized mortality ratios declined from 13.7 (95% Confidence Interval [CI]=11.0-17.0) in the pre-HAART era to 3.5 (95% CI=2.5-4.8) in the late HAART era. In women, the standardized mortality ratios declined from 11.6 (95% CI=6.4-20.9) to 5.7 (95% CI=3.2-10.3). In both time periods, suicide rates tended to be higher in older patients, in men, in injection drug users, and in patients with advanced clinical stages of HIV illness. An increase in CD4 cell counts was found to be associated with a reduced risk of suicide.

In the current study, the authors found that after the introduction of HAART, suicide rates declined substantially in HIV-infected men and women, with a somewhat steeper decline seen in men. Despite this decrease, however, suicide rates in HIV-infected individuals remained well above those observed in the general population. The researchers conclude that HIV-infected patients remain an important target group for suicide prevention. (41 References)
MENTAL HEALTH SERVICE USE AMONG SUICIDAL ADOLESCENTS:
FINDINGS FROM A U.S. NATIONAL COMMUNITY SURVEY

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PSYCHIATR SERV, 61:17-24, January 2010

In the United States, suicide is the third leading cause of death in children and adolescents between the ages of 10 and 19 years (Anderson, 2002). The authors of the present study assessed patterns of mental health service use among adolescents who had attempted suicide and examined factors associated with their service use at individual, family, and community levels.

Bivariate and multiple logistic regression analyses were conducted with data from 877 adolescents (age range, 12 to 17 years) who had attempted suicide in the past 12 months and who participated in the 2000 National Household Survey on Drug Abuse. Sixty-six percent (N=579) were white, 11% (N=96) were African American, 16% (N=140) were Hispanic, and 7% (N=64) were from other racial-ethnic groups. Seventy percent (N=614) were female, and 78% (N=684) were between the ages of 14 and 17 years. Of the 877 adolescents, only 45% (N=393) reported that they had used mental health services in the past 12 months. Of these, 22% (N=86) received inpatient services, 59% (N=234) used outpatient services but not inpatient services, and 19% (N=73) received only school-based services. Adolescents from racial-ethnic minority groups were found to be less likely than whites to receive inpatient or outpatient mental health treatment, even when the researchers controlled for other demographic, individual, and family and community characteristics. Poor self-perceived health and living in a single-parent family were associated with use of inpatient services. Female gender, higher family income, participation in extracurricular activities, and the presence of symptoms of anxiety or disruptive disorders were associated with use of outpatient services. Use of school-based mental health services was associated only with participation in extracurricular activities.

According to the authors, the mental health service needs of suicidal adolescents, especially those from racial-ethnic minority groups and from lower-income families, too frequently remain unmet. In the current investigation, larger racial-ethnic disparities were found in the use of inpatient and outpatient mental health services than the in use of school-based services. It appears that mental health services offered within school settings may reach suicidal adolescents who need such services but who may experience barriers to standard types of care. (50 References)
WHO SEEKS TREATMENT WHERE?
SUICIDAL BEHAVIORS AND HEALTH CARE
Evidence From a Community Survey

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J NERV MENT DIS, 198:412-9, June 2010

Occurring up to 23 times as often as fatal suicidal behavior, nonfatal suicidal behavior is a major contributor to the total burden of disease in the Australian population. However, the reason why some individuals seek help following a suicide attempt while others do not remains unclear. Using data collected in the community survey of the World Health Organization Suicide PREvention-Multisite Intervention Study on Suicidal Behavior (De Leo et al, 2005), the authors examined help-seeking behavior after a suicide attempt, including possible differences between persons who seek single or multiple treatments. The researchers also attempted to determine whether specific characteristics would be associated with choosing different care options (e.g., medical, psychological, or community support services).

In all, 399 subjects (age range, 18 to 83 years; mean age, 43 years) indicated that they had engaged in suicidal behaviors (suicide attempt only) during their lifetime. Within this group, 133 participants reported that they had sought treatment from one agency, 124 had sought treatment from two or more agencies, and 142 had not sought any treatment. Of the 257 subjects who had sought treatment following their suicide attempt, 163 had sought hospital treatment, 91 had visited a general practitioner, 117 had seen a mental health professional, and 37 had utilized telephone help lines. Compared with those who did not seek help (N=142), help-seekers (N=257) had significantly greater odds of overdosing with medication and communicating suicidal thoughts. They also were more likely to report a history of psychological problems, previous suicide attempts, and help-seeking behavior. Those who sought multiple services were more likely to be female and to suffer from some form of physical illness. Those who did not seek help were more frequently found to be males, with no history of having previously sought help or communicated suicidal intent. Non-help-seekers also appeared to be more likely to use more lethal methods (hanging) and less likely to express mental health concerns at the time of the attempt.

According to the authors, there appear to be clear differences between individuals who seek treatment after a suicide attempt and those who do not. The current findings emphasize the need to further understand the relationships between lethality of suicide attempt, severity of suicide intent, and help-seeking behavior. (45 References)
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INCREASED MORTALITY IN BULIMIA NERVOSA AND OTHER EATING DISORDERS

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AM J PSYCHIATRY, 166:1342-6, December 2009

The mortality from eating disorders is known to be elevated, with this being the case for both all-cause mortality and suicide. While anorexia nervosa has been consistently associated with increased mortality, it is unclear whether this is true for other types of eating disorders. In the present study, the authors attempted to describe mortality associated with anorexia nervosa, bulimia nervosa, and eating disorder not otherwise specified in a large sample followed up after an extended period of time through death records.

Using computerized record linkage to the National Death Index, the researchers conducted a longitudinal assessment of mortality over a period of eight to 25 years in 1,885 individuals (93 males and 1,792 females) who had presented for treatment at a specialized eating disorders clinic located in an academic medical center. Of these patients, all of whom had been evaluated between 1979 and 1997, 177 (five males and 172 females) received a diagnosis of anorexia nervosa; 906 (39 males and 867 females), a diagnosis of bulimia nervosa; and 802 (49 males and 753 females), a diagnosis of eating disorder not otherwise specified. Diagnoses were generated on the basis of algorithms that were formulated through use of patient self-report data from the Eating Disorders Questionnaire. Crude mortality rates were found to be 4.0% for anorexia nervosa, 3.9% for bulimia nervosa, and 5.2% for eating disorder not otherwise specified. The all-cause standardized mortality ratios were significantly elevated for bulimia nervosa and for eating disorder not otherwise specified. The suicide standardized mortality ratios were found to be elevated both for bulimia nervosa and for eating disorder not otherwise specified.

In the present study, the authors state, individuals diagnosed with eating disorder not otherwise specified, which is sometimes viewed as a “less severe” type of eating disorder, had elevated mortality risks that were similar to those found in patients suffering from anorexia nervosa. In addition, the researchers note, the current data also revealed an increased risk of suicide across all eating disorder diagnoses. (26 References)
EMPIRICAL IDENTIFICATION AND VALIDATION OF EATING DISORDER PHENOTYPES IN A MULTISITE CLINICAL SAMPLE

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The system by which psychopathology is described and classified is critical in guiding research and practice. Identified problems with the classification system of eating disorders (EDs), including its imperfect application to clinical samples, challenge its validity and limit its utility. The authors of the present study attempted to empirically identify and validate ED phenotypes in a multisite clinical sample through the application of latent profile analysis (LPA). LPA was used to identify underlying (or latent) groups of like individuals on the basis of their patterned responses across a set of ED features.

ED symptom data collected from 687 individuals seeking treatment for EDs (48 men, 639 women; mean age, 29.5 years) were included in LPA. Identified latent profiles (LPs) were compared with regard to clinical validators. The following five LPs were identified: LP1 (N=178), objective bingeing and multiple purging methods; LP2 (N=172), objective bingeing without purging; LP3 (N=130), objective bingeing and vomiting; LP4 (N=108), low/normal weight and excessive exercise; and LP5 (N=99), low/normal weight and absence of ED symptoms. Validation analyses showed the most extreme psychopathology/medical morbidity in LP1 and the least in LP5. Individuals in LP1 and LP3 were the most likely to report medication treatment for EDs. Identified LPs imperfectly resembled EDs as classified in DSM-IV-TR. Multiple purging methods and the absence of ED cognitions marked differences in severity across groups, but low weight did not. Clinical differences in psychopathology, medical morbidity, and treatment utilization validated groups.

According to the authors, the results of the current investigation suggest that within a multisite clinical sample of individuals with EDs, meaningful ED phenotypes can be identified through the application of LPA. However, they state, continued classification research is needed to determine possible revisions to be included in the forthcoming diagnostic and statistical manual of mental disorders (DSM-V). Future studies should examine the longitudinal stability of empirically-derived phenotypes and the incremental validity of alternative classification schema. (68 References)
IMPULSIVITY AND PERSONALITY VARIABLES IN ADOLESCENTS WITH EATING DISORDERS

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J NERV MENT DIS, 197:251-9, April 2009

Impulsivity is a multidimensional construct that has been variably defined as acting without thinking (Smith, 1952), acting without adequate forethought or conscious judgment (Hinslie and Shatzky, 1940), inability to delay gratification (L'Abate, 1993), and tendency to act without regard for potential risks (Eysenck, 1993). While impulsivity in individuals with eating disorders (EDs) has been found to be associated with severe comorbidities and poor treatment outcomes, only limited research has focused on investigating the construct of impulsivity in persons with EDs. The objectives of the present study were to characterize multiple dimensions of impulsivity in adolescents with EDs; to determine whether differences in impulsivity would be associated with ED diagnosis and/or broader personality traits; and to explore the relationship between impulsivity and etiologically significant variables.

Experienced clinicians from a practice-research network were administered a battery of questionnaires and provided data on ED symptoms, impulsive characteristics, DSM comorbidity, and family and developmental history for 120 adolescent patients with EDs. One patient was excluded from further analysis because of insufficient data, and the remaining 119 were diagnosed as follows: anorexia nervosa (N=18), bulimia nervosa (N=44), and eating disorder not otherwise specified (N=57). The patients had been seen by the responding clinicians for an average of 8.3 months, with the length of treatment ranging from one to 26 months. Principal components analysis yielded three distinct types of impulsivity: general, acting out, and aggressive/destructive. These impulsivity types were found to have specific relationships with ED diagnosis, broader personality factors, individual histories of adverse (traumatic) events, and family histories of externalizing disorders.

The authors recommend that future investigations of ED pathology include a more comprehensive assessment of impulsivity and encompass client reports, independent observations, and behavioral measures as well as information provided by clinicians. Given the interest in delineating the relationship between impulsivity and eating pathology, the researchers note, it is important that these variables be assessed prospectively throughout the course of ED treatment and recovery. (64 References)

EAF
RISK FACTORS FOR FULL- AND PARTIAL-SYNDROME
EARLY ADOLESCENT EATING DISORDERS:
A POPULATION-BASED PREGNANCY COHORT STUDY

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 48:800-9, August 2009

Eating disorders affect a significant proportion of young adolescent women, as well as some young adolescent men, and are a source of considerable psychosocial and physiological morbidity in this age group. Despite a considerable body of research, the etiology of eating disorders remains poorly understood. Using previously collected antenatal, biomedical, familial, demographic, and psychosocial data, the authors of the present study attempted to identify prospective predictors of eating disorders in a population-based sample of 14-year-old boys and girls.

The participants (N=1,597) were drawn from the Western Australian Pregnancy Cohort (Raine) Study. Data were collected during the mother's pregnancy, at birth, and when the child was one, two, five, eight, 10, and 14 years of age. An adapted version of the Eating Disorder Examination Questionnaire was used to assess eating disorder symptoms when the adolescents were 14 years old. Logistic regression was used to identify prospective predictors of eating disorder caseness, relative to general control and psychiatric control groups. At age 14 years, 2.8% (N=44) of the sample met full self-report criteria for a DSM-IV eating disorder; 3.2% (N=51) met partial criteria for an eating disorder; and 3.3% (N=53) were classified as being at risk for developing an eating disorder. Being female and being perceived as overweight by one’s parent were the strongest predictors of eating disorder caseness in the final multivariate models, relative to both the general control (N=1,324) and the psychiatric control (N=125) cases. Maternal body mass index, social problems, low social-related self-efficacy, and neurocognitive difficulties were also predictive of eating disorder caseness (relative to the general control group only).

According to the authors, the current results suggest that a parent’s perception of the child’s weight are more powerful than the objective body weight of the child in predicting the development of eating disorders. A parent’s perception of the child as being overweight appears to be a specific risk factor for developing an eating disorder, whereas elevated maternal weight and childhood psychosocial difficulties seem to be associated more generally with an increased risk for psychiatric disturbances. (50 References)
CHILDHOOD RISK FACTORS FOR LIFETIME ANOREXIA NERVOSA
BY AGE 30 YEARS IN A NATIONAL BIRTH COHORT

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 48:791-9, August 2009

Identification of childhood risk factors for eating disorders (EDs) is important in understanding etiology and developing prevention strategies. However, most studies that explore childhood risk factors for EDs are limited by retrospective or cross-sectional designs and/or small sample sizes. In the present investigation, the authors attempted to determine whether previously identified childhood risk factors for anorexia nervosa (AN) would predict self-reported lifetime AN by age 30 years in a prospective, nationally representative birth cohort. The British national birth cohorts collect data prospectively from large samples, are population-based, and allow examination of risk factors across the life course.

The researchers examined data from the 1970 British Cohort Study, a continuing longitudinal study of infants born between April 5 and April 11, 1970, in England, Scotland, Wales, and Northern Ireland. Using information gleaned at birth and at ages five, 10, and 30 years, the authors explored the associations between suggested childhood risk factors and self-reported lifetime AN at 30 years while adjusting for sex and socioeconomic factors. Data on a lifetime history of EDs were available for 11,211 subjects at age 30 years. Of 406 participants who reported an eating difficulty, 101 reported a lifetime history of AN at age 30. This AN group and those with no eating disorders formed the core sample for analyses (N=10,906). AN was independently predicted by female sex (odds ratio [OR], 22.1), infant feeding problems (OR, 2.6), maternal depressive symptoms (OR, 1.8), and a history of undereating (OR, 2.7). High self-esteem (OR, 0.3) and higher maternal body mass index (OR, 0.91) were found to be protective factors.

According to the authors, they did not find evidence in support of a role for many of the childhood risk factors for AN that had been previously suggested by earlier retrospective or case-control studies. Of 22 suggested risk factors for the development of AN, only four were confirmed in the current prospective investigation. No role was found for such previously identified risk factors as perinatal events or gestational age/birth weight, separations from mother, childhood emotional disorder, parenting style, sleep problems, somatic symptoms, academic ability, childhood body mass index, or early puberty. (37 References)
Individuals with eating disorders (EDs) frequently are first diagnosed during adolescence. While a few descriptive studies of community-dwelling adolescents with EDs have been published, treatment data for this age group are generally lacking. The current study was intended as a preliminary, naturalistic investigation of the treatment of adolescents with EDs in the community, using clinicians as informants. More specifically, the authors attempted to provide preliminary data concerning the following: (1) the characteristics of clinicians who treat adolescent patients with EDs in the community; (2) the characteristics of patients with EDs who receive treatment in the community; (3) the treatment interventions commonly employed by clinicians; and (4) the predictors of clinician-reported treatment response.

Experienced clinicians from a practice-research network provided information on ED symptoms, global functioning, comorbidity, therapy, and outcome for 120 adolescents currently in treatment for an ED. All the patients were female and between the ages of 15 and 18 years. Some 15% (N=18) were diagnosed with anorexia nervosa; 36.7% (N=44), with bulimia nervosa; and 47.5% (N=57), with eating disorder not otherwise specified. One patient was excluded from further analyses because of insufficient data. After an average of eight months of treatment, clinician reports indicated that almost 70% of the patients were showing significant improvement; 30% were considered to have recovered from their ED, with those with anorexia nervosa showing the most improvement. The clinicians utilized a wide range of treatment interventions, including cognitive behavioral therapy (CBT), family intervention, dynamic therapy, emotion regulation, trauma therapy, and conjoint therapy. In addition, two thirds of the patients received adjunctive psychoactive medication. Although CBT showed the strongest association with outcome in a subsample characterized by poor relational/personality functioning, dynamic therapy was associated with better global outcome in the sample as a whole.

These findings highlight the need for further research on the dissemination of manual-based treatment in adolescent ED populations and its utility in the community. New treatments for adolescents with EDs might incorporate elements of both dynamic therapy and CBT and allow for treatment tailored to the patient’s level of psychological maturity. (69 References)
THE IMPACT OF NARCISSISM ON DROP-OUT FROM COGNITIVE-BEHAVIORAL THERAPY FOR THE EATING DISORDERS
A Pilot Study

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J NERV MENT DIS, 197:278-81, April 2009

Despite evidence that cognitive-behavioral therapy (CBT) is an effective intervention in the treatment of many patients with eating disorders, there are substantial numbers of individuals with eating disorders who do not benefit from this or any other form of psychological intervention. Patient retention in therapy is key to giving patients the opportunity to benefit from CBT, but many of them drop out of treatment, and the reasons for such attrition are not well understood. In the present study, the authors examined the relationship between narcissism and drop-out from the early stage of CBT in an eating-disordered population. Narcissism was defined in terms of both its core elements (grandiosity, entitlement) and the narcissistic defense styles that are used to maintain self-esteem (“narcissistically abused personality” or the “poor me” defense; “poisonous pedagogy” or the “bad you” defense).

The study participants were 41 adults (39 women, two men; mean age, 27.1 years) who were referred to a specialist eating disorder service and who were offered outpatient CBT. Eleven patients had a diagnosis of anorexia nervosa, 18 received a diagnosis of bulimia nervosa, and 12 had a diagnosis of eating disorder not otherwise specified. Each completed measures of narcissism and eating disorder psychopathology. Those patients who ceased attending therapy during the first 10 treatment sessions offered to them were classified as drop-outs (N=10), and the other 31 patients were designated as remaining in treatment. When the researchers controlled for age and body mass index, they found no significant difference in the likelihood of dropping out of treatment as a result of a patient’s level of eating disorder psychopathology. However, the drop-outs had higher levels of the narcissistically abused defensive personality style, seeing other individuals as hostile and over-demanding and presenting themselves as “martyred.”

According to the authors, the current findings suggest that patients with eating disorders and with higher levels of the “martyred” form of narcissism have a greater likelihood of prematurely terminating CBT, thereby reducing their access to evidence-based care. (33 References)
COMPETITIVE MEMORY TRAINING (COMET) FOR TREATING LOW SELF-ESTEEM IN PATIENTS WITH EATING DISORDERS: A RANDOMIZED CLINICAL TRIAL

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In addition to the overevaluation of eating, body shape, and weight, low self-esteem is considered to be an important aspect of the clinical presentation of the various eating disorders. In the current study, the authors evaluated a short (eight sessions), manualized, stepwise cognitive-behavioral intervention for the treatment of low self-esteem in patients with eating disorders. Competitive memory training (COMET) for low self-esteem is based on insights and findings from the field of experimental psychology. It is conducted with small groups of between six and eight patients. Sessions are held once a week, with each one lasting for one and a half hours. The COMET protocol encompasses four main steps: (1) identifying the patient's negative self-image; (2) identifying a credible positive self-image that is incompatible with the negative self-image; (3) strengthening the positive self-image through such means as imagery, posture and facial expressions, self-verbalization, and music; and (4) forming new associations between risk cues and positive self-image through the use of counterconditioning.

The study sample was composed of 52 female patients with eating disorders and low self-esteem, all of whom were treated at a routine outpatient mental health center. After a minimum of two months of their regular treatment (therapy as usual [TAU]), the patients were randomly assigned to receive eight weeks of COMET + TAU (N=26) or eight weeks of TAU only (N=26). All were assessed at the beginning of the trial and again eight weeks later. Differential effects in favor of COMET + TAU were found for two indexes of self-esteem and for one index of depressive mood. Of those patients who completed the COMET + TAU protocol, 27% were considered to have experienced a clinically significant change between pre- and post-treatment. In the TAU-only group, no patient realized a clinically significant change.

According to the authors, COMET appears to be an effective additional intervention for patients with eating disorders and low self-esteem. The promising results of the current study warrant further investigation of this treatment among individuals with eating disorders as well as with other psychiatric populations. (26 References)
TRANSDIAGNOSTIC COGNITIVE-BEHAVIORAL THERAPY FOR PATIENTS WITH EATING DISORDERS: A TWO-SITE TRIAL WITH 60-WEEK FOLLOW-UP

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AM J PSYCHIATRY, 166:311-9, March 2009

DSM-IV recognizes two specific eating disorders (anorexia nervosa and bulimia nervosa), as well as a residual diagnostic category termed “eating disorder not otherwise specified.” The aim of the present study was to compare two forms of “enhanced” cognitive-behavioral therapy (CBT-E) for the treatment of outpatients with eating disorders. One is a focused form (CBT-Ef) that exclusively targets eating disorder psychopathology, while the other is a more complex broad form (CBT-Eb) that also addresses mood intolerance, clinical perfectionism, low self-esteem, and interpersonal difficulties.

A total of 154 patients who had a DSM-IV eating disorder but were not markedly underweight (body mass index over 17.5) were enrolled in a two-site, randomized controlled trial involving 20 weeks of treatment and a 60-week closed period of follow-up. The control condition was an eight-week waiting list period preceding treatment. Outcomes were measured by independent assessors who were blind to treatment conditions. Of the 154 patients, 53 were assigned to immediate CBT-Ef, 50 to immediate CBT-Eb, and 51 to the waiting list control condition, after which they received either CBT-Ef (N=25) or CBT-Eb (N=26). Patients in the waiting list control condition exhibited little change in symptom severity, whereas those in the two treatment conditions showed substantial and equivalent change, which was well maintained during follow-up. At the 60-week follow-up assessment, 51.3% of the sample had a level of eating disorder features less than one standard deviation above the community mean. Treatment outcome did not depend on eating disorder diagnosis. Patients with marked mood intolerance, clinical perfectionism, low self-esteem, or interpersonal difficulties appeared to respond better to the more complex treatment, with the reverse pattern evident among the remaining patients.

The authors conclude that CBT-Ef and CBT-Eb appear to be suitable transdiagnostic therapies for the majority of patients with an eating disorder. The simpler treatment may best be viewed as the default version, with the more complex version being reserved for patients with marked additional psychopathology of the type targeted by the treatment. (26 References) EAF
THE EFFICACY OF SELF-HELP GROUP TREATMENT AND THERAPIST-LED GROUP TREATMENT FOR BINGE EATING DISORDER

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AM J PSYCHIATRY, 166:1347-54, December 2009

Binge eating disorder is characterized by binge eating episodes, frequent comorbid obesity with associated medical problems, high rates of co-occurring psychiatric disorders, and psychosocial impairment. Several psychological treatments have been found to be helpful in treating this condition, including cognitive-behavioral therapy (CBT), interpersonal therapy, dialectical behavior therapy, and behavioral weight loss. The aims of the present study were to compare therapist-led and self-help group CBT for the treatment of binge eating and associated symptoms, as well as to examine the viability and potential efficacy of therapist-assisted and partial self-help group treatment.

The study sample was composed of 259 adults (227 women, 32 men; age range, 19 to 65 years; mean age, 47.1 years) who were diagnosed with binge eating disorder. They were randomly assigned to 20 weeks of the following: therapist-led group treatment (N=60), therapist-assisted group treatment (N=63), self-help group treatment (N=67), or a waiting list condition (N=69). Binge eating as measured by the Eating Disorder Examination was assessed at baseline, at end of treatment, and at six and 12 months. Outcome was evaluated through the use of logistic regression and analysis of covariance (intent to treat). At end of treatment, patients in the therapist-led (51.7%) and therapist-assisted (33.3%) groups had higher binge eating abstinence rates than those in the self-help (17.9%) and waiting list (10.1%) conditions. However, no between-group differences in abstinence rates were observed at either of the follow-up assessments. The therapist-led condition also resulted in more reductions in binge eating at end of treatment and follow-up assessments when compared with the self-help condition. Treatment or waiting list completion rates were higher in the therapist-led (88.3%) and waiting list (81.2%) conditions than in the therapist-assisted (68.3%) and self-help (59.7%) conditions.

According to the authors, the current results indicate that psychoeducational and cognitive-behavioral techniques can be implemented in therapist-led, therapist-assisted, and structured self-help group formats for the treatment of patients with binge eating disorder. While therapist delivery of group treatment appears to be associated with better short-term outcome and less attrition than self-help therapy, self-help group treatment may still serve as a viable alternative to therapist-led interventions. (28 References)
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WIDESPREAD CORTICAL THINNING IS A ROBUST ANATOMICALLY MARKER FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 48:1014-22, October 2009

Although prior brain imaging studies have indicated that significant neuroanatomical differences exist between populations with and without attention-deficit/hyperactivity disorder (ADHD), the extent, timing, and regional specificity of morphometric changes remain less certain. In the current cross-sectional investigation, the authors attempted to confirm the presence and regional profile of previously reported changes in laminar cortical thickness in children and adolescents with ADHD when compared with that of typically developing control subjects. Cortical thickness represents the number, size, density, and arrangement of cells (neurons, neuroglia, and nerve fibers) within the cortical mantle.

High-resolution magnetic resonance images were obtained from 22 children and adolescents with ADHD (19 males, three females; age range, 7.2-16 years; mean age, 11.7 years) and 22 age- and sex-matched controls. Brain tissue volumes were estimated for each subject. Cortical pattern matching methods were used to sample measures of laminar thickness at high spatial frequency across homologous regions of the cortex. Volume and thickness measures were compared across diagnostic groups both with and without controlling for general intelligence. False discovery rate correction confirmed regional results. Compared with the controls, the subjects with ADHD exhibited significant reductions in overall brain volume, gray matter volume, and mean cortical thickness. However, white matter volumes were found to be significantly increased in those with ADHD. Highly significant cortical thinning (false discovery rate-corrected \( p < .0006 \)) was observed over large areas of the frontal, temporal, parietal, and occipital association cortices and aspects of motor cortex but not within the primary sensory regions.

According to the authors, the current data indicate that cortical thickness reductions present a robust neuroanatomical marker for child and adolescent ADHD. Observations of widespread cortical thinning expand on earlier cross-sectional findings and provide further support for the theory that the neurobiological underpinnings of ADHD extend beyond prefrontal and subcortical circuits. (58 References)
ARE ADHD SYMPTOMS ASSOCIATED WITH DELAY AVERSION OR CHOICE IMPULSIVITY? A GENERAL POPULATION STUDY

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 48:837-46, August 2009

Delay aversion theory has been influential in attention-deficit/hyperactivity disorder (ADHD) research, rekindling interest in motivational processes as explanatory factors for symptoms of inattention and hyperactivity-impulsivity. The term delay aversion has been used both to describe a behavioral tendency of greater preference for smaller-immediate over larger-delayed rewards (choice impulsivity) and to refer to an acquired motivational tendency postulated by delay aversion theory as an explanatory construct contributing to choice impulsivity. The authors of the present study examined the association between ADHD symptoms and choice impulsivity; they also tested the specific hypothesis derived from delay aversion theory.

A total of 1,062 children (age range, 7.9 to 10.9 years; mean age, 8.8 years; 49% females) made a fixed number of repeated choices between a smaller reward delivered immediately and a larger reward delivered after a delay (choice-delay task), under two conditions (including and excluding a postreward delay). The children’s IQs ranged from 70 to 158 (mean, 109.74). While controlling for age (or age and IQ), the researchers assessed the unique contribution of each ADHD symptom dimension to the prediction of choice impulsivity and delay aversion. Sex effects were also examined. The results showed that inattention ratings uniquely predicted preference for smaller-immediate rewards under both task conditions in both girls and boys. An index of delay aversion was associated with inattention only in boys; the effect size was small but significant. Hyperactivity-impulsivity ratings were negatively associated with choice impulsivity in girls in the postreward delay condition, whereas no significant association with hyperactivity-impulsivity ratings was seen in boys. Categorical analyses that used groups with high ADHD symptoms yielded similar results.

According to the authors, the current study is the first to report a unique association between symptoms of inattention and behavioral measures of choice impulsivity and delay aversion. These findings emphasize the importance of the primary constitutional processes that underlie choice impulsivity and their potential role in behavioral inattention. (58 References)
PERSONALITY TRAITS AMONG ADHD ADULTS: IMPLICATIONS OF LATE-ONSET AND SUBTHRESHOLD DIAGNOSES

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PSYCHOL MED, 39:685-93, April 2009

Diagnosing attention deficit hyperactivity disorder (ADHD) in adults is difficult when diagnosticians cannot establish onset prior to the DSM-IV criterion of age 7 or when the number of symptoms does not achieve the DSM threshold for diagnosis. Previous studies have assessed the validity of such diagnoses on the basis of psychiatric comorbidity, family history, and neuropsychological functioning, but none of these reports have used personality as a validation criterion. In the present study, the authors attempted to further assess the validity of late-onset and subthreshold ADHD by evaluating personality traits.

Personality profiles were examined and compared in the following four groups of adult probands: (1) 127 full ADHD subjects who met all DSM-IV criteria for childhood-onset ADHD; (2) 79 late-onset subjects who met all DSM-IV criteria for ADHD except for age at onset; (3) 41 subthreshold subjects who did not meet the full symptom criteria for ADHD, but who reported a chronic history of three or more inattentive symptoms or three or more hyperactive-impulsive symptoms; and (4) 123 non-ADHD subjects who did not meet any of the criteria for the disorder. Diagnoses were made by means of the Structured Clinical Interview for DSM-IV. The Temperament and Character Inventory (TCI) was used to assess personality traits. The results revealed that subjects with full ADHD and those with late-onset ADHD exhibited similar personality profiles; both of these groups had TCI scores that were significantly different from those of non-ADHD subjects on every dimension except reward dependence and self-transcendence. There were no significant differences between subthreshold probands and non-ADHD subjects on the TCI dimensions of harm avoidance, reward dependence, persistence, cooperativeness, and self-transcendence. The probands with subthreshold ADHD only showed deviations on the TCI dimensions of novelty-seeking and self-directiveness.

According to the authors, the current data further the theory of the similarities between late-onset ADHD and full ADHD and call into question the stringent age-at-onset criteria for adults when making retrospective diagnoses of ADHD. In addition, they note that subthreshold ADHD appears to be a milder form of the disorder that is consistent with dimensional views of ADHD. (56 References)
IS ADULT ATTENTION DEFICIT HYPERACTIVITY DISORDER
A VALID DIAGNOSIS IN THE PRESENCE OF HIGH IQ?

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PSYCHOL MED, 39:1325-35, August 2009

Initially characterized as a childhood disorder, attention deficit hyperactivity disorder (ADHD) often persists into adulthood. While some symptoms tend to decline with age, inattentive symptoms appear to be the most persistent. Because the diagnosis of ADHD in higher education settings is rapidly becoming a contentious issue, particularly among patients with high IQs, the authors of the present investigation attempted to evaluate the validity of diagnosing ADHD in high-IQ adults and to characterize the clinical features associated with their ADHD. For the purposes of this study, the researchers operationalized high IQ as being ≥120.

The sample was composed of 64 adults who had a high IQ and met diagnostic criteria for ADHD as well as 53 adults who had a high IQ but did not have ADHD (controls). The two groups did not differ in terms of estimated IQ, socioeconomic status, or gender. However, the mean age of the ADHD group was significantly greater than that of the control group (33.4 years vs. 27.9 years, respectively). This difference was taken into account in all subsequent analyses. Compared with the controls, the high-IQ adults with ADHD reported a lower quality of life, exhibited poorer familial and occupational functioning, and had more functional impairments, including more speeding tickets, accidents, and arrests. In addition, major depressive disorder, obsessive-compulsive disorder, and generalized anxiety disorder were found to occur more frequently in the high-IQ adults with ADHD. The occurrence of all other psychiatric comorbidities, including antisocial personality disorder and substance abuse, did not differ between the two high-IQ groups. ADHD was found to be more prevalent in the first-degree relatives of the adults with ADHD than in those of the controls.

According to the authors, the current data suggest that adults with ADHD and a high IQ display patterns of functional impairment, familiality, and psychiatric comorbidity that parallel those found in the adult ADHD population with average IQs. In light of the growing debate over ADHD diagnoses in post-secondary educational settings, the researchers recommend that future studies continue to assess the extent to which ADHD is a valid diagnosis in the high-IQ population. (69 References)
BIPOLAR SYMPTOMS IN ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A CROSS-SECTIONAL STUDY OF 510 CLINICALLY DIAGNOSED PATIENTS AND 417 POPULATION-BASED CONTROLS

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J CLIN PSYCHIATRY, 71:48-57, January 2010

Attention-deficit/hyperactivity disorder (ADHD) is a commonly occurring condition during childhood, adolescence, and adulthood, with recent worldwide preference estimates ranging from 2% to 12% in children and 3% to 4% in adults. Bipolar spectrum disorders (BSD) have several symptoms and features in common with ADHD, with both disorders being characterized by symptoms involving dysregulation of energy, activity, affect, and impulsivity. The aims of the current study were to: (1) investigate the prevalence of BSD in clinically diagnosed adults with ADHD; (2) explore the relationship between symptoms of ADHD and symptoms of BSD in the same patients; and (3) examine the clinical characteristics of ADHD patients who had co-occurring symptoms of BPD.

In all, 510 Norwegian adults (269 men, 241 women) diagnosed with DSM-IV ADHD between 1997 and 2007 and 417 controls (176 men, 241 women) randomly selected from the general population were recruited and responded to 85 questions rating symptoms of ADHD, lifetime symptoms of mood disorders, other comorbid conditions, and sociodemographic data. According to the Mood Disorder Questionnaire (MDQ), 50.6% of the ADHD patients screened positive for BSD, as compared with 8.3% of the controls. The prevalence of BSD (according to DSM-IV criteria) in a subsample of interviewed patients (N=50) was 32%. In the study sample as a whole (N=927), an ADHD diagnosis was the strongest predictor for screening positive on the MDQ (Odds Ratio=5.0, P<.001), but the correlation between dimensional symptom levels of ADHD and of BSD was strongest in the control group. Patients who screened positive on the MDQ had significantly more drug problems, higher ADHD symptom scores, and lower educational and occupational levels.

The findings of the current study illustrate the close relationship between some symptoms of BSD and ADHD in adults. The authors suggest that in clinical and research settings, patients who screen positive for BPD should be assessed for the presence of a possible underlying or coexisting ADHD condition and vice versa. (68 References)
THE MTA AT 8 YEARS: PROSPECTIVE FOLLOW-UP OF CHILDREN TREATED FOR COMBINED-TYPE ADHD IN A MULTISITE STUDY

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The objectives of the present multisite study were as follows: (1) to examine any long-term effects (six and eight years after childhood enrollment) of four randomly assigned 14-month treatment strategies (medication management, multicomponent behavior therapy, their combination, or usual community care) in the NIMH Collaborative Multimodal Treatment Study of Children with Attention-Deficit/Hyperactivity Disorder (MTA, N=436); (2) to determine whether attention-deficit/hyperactivity disorder (ADHD) symptom trajectory through three years would predict outcome in subsequent years; and (3) to evaluate the functioning level of the MTA adolescents relative to their non-ADHD peers (local normative comparison group, N=261). At baseline (pretreatment), the MTA participants ranged in age from 7 to 9.9 years; at six and eight years after random assignment, there were between 13 and 18 years old.

Mixed-effects regression models with planned contrasts at six- and eight-year follow-ups tested a wide range of symptom and impairment variables that were assessed by means of parent, teacher, and youth reports. In nearly every analysis, the originally randomized treatment groups did not differ significantly on repeated measures or newly analyzed variables (e.g., grades earned in school, arrests, psychiatric hospitalizations, other clinically relevant outcomes). Medication use decreased by 62% after the 14-month controlled trial, but adjusting for this factor did not alter the results. ADHD symptom trajectory in the first three years predicted 55% of the outcomes. The MTA sample did more poorly than the local normal comparison group on 91% of the variables tested.

The authors conclude that the type or intensity of 14 months of treatment for ADHD in childhood does not predict functioning six to eight years later. Instead, early ADHD symptom trajectory, regardless of treatment type, is prognostic. This implies that children with behavioral and sociodemographic advantages and with the best response to any treatment will have the best long-term prognosis. However, despite initial symptom improvement during treatment that is largely maintained after treatment, as a group, children with combined-type ADHD still exhibit significant impairment in adolescence. (49 References)
A MAGNETIC RESONANCE IMAGING STUDY OF THE CEREBELLAR VERMIS IN CHRONICALLY TREATED AND TREATMENT-NAÏVE CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER COMBINED TYPE

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BIOL PSYCHIATRY, 65:620-4, April 1, 2009

Attention-deficit/hyperactivity disorder (ADHD) is thought to affect approximately 5% to 10% of all school-age children; cardinal symptoms include inattention, impulsivity, and hyperactivity. While the cause of ADHD is unknown, current theories suggest that impairments in frontostriatal neurocircuitry are at the core of ADHD symptomatology. Numerous magnetic resonance imaging (MRI) studies have found abnormalities in the cerebellum in children with ADHD. Stimulant medication is often prescribed for children with ADHD, because of its effects on the frontostriatal dopaminergic system. While some reports appear to suggest that certain brain structures are affected by chronically administered stimulant medication, it remains unclear whether the cerebellum is also affected. In the current MRI study, the authors attempted to determine whether cerebellar morphology observed in treatment-naïve ADHD children was different from that seen in chronically treated children with ADHD.

The sample was composed of 47 right-handed children (32 boys, 15 girls) with a mean age of 11.34 years. They were grouped as follows: children with ADHD-combined type (ADHD-C) and no history of stimulant medication treatment (N=14); ADHD-C children chronically treated with stimulant medication (N=18); and typically developing control children (N=15). The chronically treated children with ADHD-C had taken medication for at least one year (range, 2.3 to 5 years). The treatment-naïve ADHD-C children had never received medication for any psychiatric illness, including ADHD. The results showed that the treatment-naïve children with ADHD had significantly smaller area in the posterior inferior vermis (lobules VIII-X) than both the chronically treated children with ADHD (p=.004) and the typically developing control children (p=.001). No differences were seen between the chronically treated children with ADHD and the typically developing control children.

According to the authors, the current data suggest that a reduction in the posterior inferior vermis may be a structural abnormality specific to ADHD children who do not have a history of treatment with stimulant medication. In addition, it appears that chronic treatment with stimulant medication may normalize the development of important areas of the cerebellar vermis in children with ADHD. (35 References)
ADJUNCTIVE DIVALPROEX VERSUS PLACEBO FOR CHILDREN WITH ADHD AND AGGRESSION REFRACTORY TO STIMULANT MONOTHERAPY

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AM J PSYCHIATRY, 166:1392-1401, December 2009

Preadolescents who exhibit chronic aggressive behavior most often fulfill diagnostic criteria for a disruptive disorder (e.g., oppositional defiant disorder, conduct disorder) and for attention deficit hyperactivity disorder (ADHD). While guidelines for the pharmacotherapy of aggressive children with ADHD suggest that initial drug therapy adhere to strategies recommended for ADHD, a substantial proportion of children with ADHD do not experience satisfactory reductions in aggressive behavior with stimulant treatment. The purpose of the present study was to evaluate the efficacy of the antimanic/anticonvulsant drug divalproex in reducing aggressive behavior among children who had ADHD and a disruptive disorder and whose chronic aggression was refractory to monotherapy with a psychostimulant.

Boys and girls between the ages of six and 13 years participated in the current trial. Over an average lead-in phase of five weeks, the children received open stimulant treatment. Agent and dose were assessed weekly and modified to optimize response. Children whose aggressive behavior persisted at the conclusion of the lead-in phase were randomly assigned to receive double-blind, flexibly dosed divalproex or a placebo in addition to their stimulant medication for a period of eight weeks. Families received weekly behavioral therapy throughout the course of the study. The primary outcome measure was the proportion of children whose aggressive behavior remitted, as defined by post-trial ratings of negligible or absent aggression. The Retrospective-Modified Overt Aggression Scale was used to gauge the severity of aggressive behavior. The children’s parents reported the frequency of 16 aggressive behaviors that were grouped into four areas: verbal aggression; physical aggression toward others; aggression toward one’s self; and damage to, or hostile misuse of, property. The proportion of children fulfilling criteria for remission of aggressive behavior at the end of the controlled trial was significantly higher within the group randomly assigned to divalproex (eight of 14 [57%]) than within the group randomly assigned to placebo (two of 13 [57%]). Divalproex was generally well tolerated.

The authors conclude that in ADHD children whose chronic aggressive behavior is refractory to optimized stimulant treatment, the addition of divalproex increases the likelihood that aggression will remit. However, larger trials are needed to determine more exactly how large a benefit adjunctive divalproex provides. (44 References)

EAF
GUANFACINE EXTENDED RELEASE IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A PLACEBO-CONTROLLED TRIAL

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 48:155-65, February 2009

Attention-deficit/hyperactivity disorder (ADHD) affects up to 10% of children in the United States. Although psychostimulants are still the mainstay of ADHD therapy, many patients cannot tolerate or do not respond to treatment with this class of drugs. The α2-adrenoceptor agonist guanfacine has been used off label as an alternative therapy for ADHD. However, immediate-release guanfacine has a short duration of action and requires multiple daily doses. Peak plasma concentration is achieved rapidly and declines precipitously, with considerable interindividual variability. In the present double-blind, dose-ranging, parallel-design, multicenter study, the authors compared the efficacy of guanfacine extended release (GXR) with that of placebo in children and adolescents (age range, six to 17 years) with ADHD.

The trial lasted for a period of nine weeks, with subjects being randomly assigned to receive once-daily oral doses of GXR (1-, 2-, 3-, or 4-mg) or placebo. The primary outcome measure was change in total ADHD Rating Scale-IV score between baseline and endpoint. Secondary outcomes included changes in scores on hyperactive/impulsive and inattentive subscales; clinician and parent ratings; duration of clinical effect; and safety measures. The safety population, which included all subjects who had received at least one dose of study drug, consisted of 233 males and 89 females. Statistically significant reductions in ADHD Rating Scale-IV scores were observed from baseline to endpoint at all doses of GXR, with effect sizes ranging from 0.43 to 0.62. In subjects receiving GXR, mean heart rate and systolic and diastolic blood pressure decreased as the dose of GXR increased and returned toward baseline levels during the dose-maintenance and dose-tapering phases of the trial. The most frequent treatment-emergent adverse events were somnolence, headache, fatigue, sedation, dizziness, irritability, upper abdominal pain, and nausea. Somnolence, sedation, and fatigue emerged within the first two weeks of treatment and generally resolved by the end of the trial.

The authors conclude that guanfacine extended release appeared to be effective in reducing symptoms in children and adolescents with ADHD. Adverse events were mild to moderate, did not interfere with improvements in attention, and rarely led to discontinuation of the drug. (35 References) EAF
ATTENTION-DEFICIT HYPERACTIVITY DISORDER: TREATMENT DISCONTINUATION IN ADOLESCENTS AND YOUNG ADULTS

Suzanne McCarthy; Philip Asherson; David Cog hill; Chris Hollis; Macey Murray; Laura Potts; Kapil Sayal; Ruwan de Soysa; Eric Taylor; Tim Williams; and Ian C. K. Wong (Institute of Child Health, University College London, 29/39 Brunswick Square, London WC1N 1AX, UK; e-mail: ian.wong@pharmacy.ac.uk);
BR J PSYCHIATRY, 194:273-7, March 2009

While attention-deficit hyperactivity disorder (ADHD) was once considered to be a condition confined to childhood, there is increasing evidence to suggest that the core symptoms persist into adulthood and are associated with continued clinical and psychosocial impairments. There are now guidelines in the United Kingdom (UK) on how ADHD should be treated in older adolescents and young adults, including a revised recommendation from the National Institute for Health and Clinical Excellence on the use of stimulant medication in adults with a diagnosis of ADHD. The aims of the present descriptive cohort study were to determine the prevalence of methylphenidate, dexamfetamine, and atomoxetine prescribing and to investigate treatment discontinuation patterns in adolescents and young adults with ADHD. Data were drawn from the General Practice Research Database.

The sample was composed of patients who were between 15 and 21 years of age from 1999 to 2006 and who had received at least one prescription for methylphenidate (immediate and modified-release preparations), dexamfetamine, or atomoxetine. Between 1999 and 2006, 22,013 prescriptions were issued to 1,636 patients (1,452 males and 184 females). The prevalence of prescribing averaged across all ages increased 6.23-fold during the study period. However, logistic regression indicated that increasing age significantly decreased treatment prevalence. In 2006, prescription prevalence in males dropped 95% from 12.77 per 1000 in 15-year-olds to 0.64 per 1000 in 21-year-olds. A longitudinal analysis of a cohort of 44 patients who were 15 years old in 1999 showed that no patient received treatment after the age of 21 years.

Since 1999, the prevalence of drug prescribing by general practitioners in the UK for adolescents and young adults with ADHD has increased rapidly, but the rise in prevalence is lower as the patients become older. A marked pattern of drug discontinuation occurs between 15 and 21 years of age, with almost all patients having discontinued treatment by early adulthood. The current study raises the possibility that therapy may be discontinued prematurely by or for some adolescents and young adults with ADHD and that in general the relative decline in treatment prevalence may be out of step with the number of people who still require treatment as young adults. (29 References)

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POSTTRAUMATIC STRESS AMONG HOSPITALIZED AND NONHOSPITALIZED SURVIVORS OF SERIOUS CAR CRASHES: A POPULATION-BASED STUDY

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Recent reviews have emphasized the increasing global burden of road traffic injuries while acknowledging methodological problems in estimating the incidence of disabling nonfatal sequelae related to these injuries. The primary aim of the present population-based, prospective cohort study was to investigate the prevalence of posttraumatic stress among survivors of serious, injury-producing car crashes in Auckland, New Zealand. The authors recruited all hospitalized car occupants (passengers and drivers) as well as nonhospitalized drivers involved in crashes that resulted in the hospitalization of at least one vehicle occupant.

Of 299 drivers and 96 passengers who met study eligibility criteria, 209 drivers (70%) and 59 hospitalized passengers (61%) completed interviews either by telephone or in person at both five months and 18 months after the crash. The Impact of Event Scale was used to assess symptoms of posttraumatic stress. Levels of posttraumatic stress indicative of posttraumatic stress disorder (PTSD) were reported by 64 participants (25%) at five months and by 33 participants (13%) at 18 months. At the five-month follow-up, 28% of hospitalized passengers, 24% of hospitalized drivers, and 24% of nonhospitalized drivers reported symptoms consistent with PTSD. At 18 months after the crash, 23% of hospitalized passengers, 11% of hospitalized drivers, and 7% of nonhospitalized drivers reported significant levels of stress. In general, female crash survivors were significantly more likely than male survivors to report significant levels of posttraumatic stress at the 18-month follow-up. A third of accident survivors who had significant levels of posttraumatic stress also reported symptoms suggestive of depression and an appreciable deterioration in their overall health since the car crash.

According to the authors, the findings of the present investigation indicate that strategies designed to prevent disabling psychological sequelae of car crashes must address the needs of both hospitalized and nonhospitalized survivors. (14 References)
A STUDY OF THE PROTECTIVE FUNCTION OF ACUTE MORPHINE ADMINISTRATION ON SUBSEQUENT POSTTRAUMATIC STRESS DISORDER

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BIOL PSYCHIATRY, 65:438-40, March 1, 2009

Fear conditioning models of posttraumatic stress disorder (PTSD) posit that noradrenergic release at the time of trauma leads to excessive conditioning of trauma memories and that attenuation of noradrenergic activation in the immediate aftermath of exposure to trauma may limit fear conditioning and the development of PTSD (Pitman, 1989). The present study examines the effect of morphine administration on adults who were hospitalized after traumatic injury. The authors hypothesized that acute administration of morphine would limit fear conditioning and result in less severe subsequent PTSD.

One hundred fifty-five patients (101 men, 54 women; mean age, 37 years) admitted to hospital after experiencing a traumatic injury were assessed with regard to current psychiatric disorder, pain, and morphine dose in the initial week after injury. Seventy-eight of the patients suffered a mild traumatic brain injury. Mechanisms of injury included transport accidents (N=102), traumatic falls (N=31), assaults (N=7), work-related accidents (N=8), and other injuries (N=7). Patients spent an average of 11 days in the hospital. At the three-month follow-up assessment, 35 patients could not be contacted or declined to participate; the remaining 120 were interviewed by telephone and reassessed for the presence of PTSD and other psychiatric disorders. At three months post-injury, 17 patients (14%) met diagnostic criteria for PTSD, 22 participants (18%) had a major depressive disorder, and 32 (27%) had a non-PTSD-related anxiety disorder. Patients who met criteria for PTSD received significantly less morphine than those who did not develop PTSD; there was no difference in morphine levels in those who did and did not develop major depressive disorder or another anxiety disorder. When injury severity, gender, age, and type of injury were controlled, hierarchical regression analysis indicated that PTSD severity at three months was significantly predicted by acute pain, mild traumatic brain injury, and elevated morphine dose in the initial 48 hours after trauma.

According to the authors, the current findings indicate that acute administration of morphine may limit fear conditioning in the aftermath of traumatic injury and may serve as a secondary prevention strategy to reduce the development of PTSD. (18 References)
AMBULATORY CARDIOVASCULAR ACTIVITY AND HOSTILITY RATINGS IN WOMEN WITH CHRONIC POSTTRAUMATIC STRESS DISORDER

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BIOL PSYCHIATRY, 65:268-72, February 1, 2009

Posttraumatic stress disorder (PTSD) affects approximately between 6% and 8% of the adult population and occurs twice as often in women as in men. Several studies have found that individuals with PTSD report increased somatic complaints, use of the health care system, functional impairment, and morbidity due to problems with their physical health. PTSD has also been linked to cardiovascular health problems such as hypertension, an increased incidence of cardiac events, and sudden death from cardiac-related problems. Evidence also suggests that individuals with PTSD display increased hostility, a construct that has been linked to poor cardiovascular outcomes. The objective of the current investigation was to evaluate the relationship between hostility and ambulatory cardiovascular activity in women with and without PTSD.

One hundred and one women completed 24 hours of ambulatory monitoring as well as standardized diagnostic and hostility measures, including the Clinician Administered PTSD Scale, the Structured Clinical Interview for DSM-IV, the Cook-Medley Hostility Scale, the Buss-Durkee Hostility Inventory, and the Spielberger Anger Expression Scale. Generalized estimating equations analysis was used to examine the effects of group (PTSD subjects vs non-PTSD subjects) and hostility factor scores (hostile beliefs, overt hostility, and covert hostility) on ambulatory heart rate (AHR), and ambulatory systolic (ASBP) and diastolic (ADBP) blood pressure. After controlling for covariates, the authors found an interaction between PTSD and hostile beliefs and overt hostility with regard to AHR. Increases in hostility were associated with greater increases in heart rate among the women with PTSD as compared with those who did not have PTSD. A similar interaction was found between hostile beliefs and group with regard to ADBP; increases in hostile beliefs were associated with a greater increase in ADBP in women with PTSD as compared with non-PTSD subjects.

The authors of the current study found evidence linking PTSD, hostility, and cardiovascular functioning. In general, women with PTSD appear to demonstrate significantly higher heart rate readings over time than women without PTSD. The present findings suggest that PTSD may, in part, moderate the relationship between hostility and cardiovascular outcomes. (38 References)
Approximately 25% to 30% of individuals who have experienced traumatic life events develop symptoms of posttraumatic stress disorder (PTSD). The lifetime prevalence of PTSD in the general population is approximately 8%, with the disorder occurring twice as frequently in women as in men. Several studies have shown that PTSD tends to exacerbate chronicity and disability in chronic pain patients, while the treatment of PTSD has been found to lessen both pain and disability. In the present investigation, the authors evaluated the relative frequency of PTSD in episodic migraine (EM) and chronic daily headache (CDH) sufferers and examined the impact of PTSD on headache-related disability.

A prospective, cross-sectional survey was conducted at six headache centers. PTSD was assessed by means of the Life Events Checklist and the Posttraumatic Stress Disorder Checklist–Civilian Version. The Patient Healthcare Questionnaire-9 was used to assess depression, and the Headache Impact Test-6 was utilized to measure disability. Of the 767 individuals who completed the survey, 593 fulfilled criteria for EM (N=398) or CDH (N=195) and served as the subjects of this study; the mean age of the sample was 42.2 years, and 92% were women. The relative frequency of PTSD found in the total group of all headache participants (25%), as well as in the EM and CDH groups individually, was significantly greater than that reported in previous general population studies (8%). The relative frequency of PTSD was significantly greater in CDH participants (30.3%) than in EM sufferers (22.4%); however, this finding did not remain significant after the authors adjusted for age, sex, marital status, income, body mass index, and depression. Participants with PTSD and major depression were more likely to suffer from CDH than EM (24.6% vs. 15.79%, respectively). Headache-related disability was significantly greater in headache sufferers with PTSD than in migraineurs without PTSD; this held true even after adjustments were made for demographic variables, body mass index, and depression.

According to the authors, the association between migraine and PTSD is complex and probably multifactorial. Taken together, the current findings suggest that the identification and treatment of PTSD in migraine sufferers is an important and potentially modifiable part of their care that may reduce migraine-related disability and progression to CDH. (37 References)
THE LONGITUDINAL COURSE OF POSTTRAUMATIC STRESS DISORDER SYMPTOM CLUSTERS AMONG WAR VETERANS

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J CLIN PSYCHIATRY, 70:837-43, June 2009

Despite substantial research on the phenomenology of posttraumatic stress disorder (PTSD) symptomatology, significant gaps remain in the current comprehension of the psychological sequelae of traumatic events. The natural course of symptom formation and the dynamic interplay of symptoms over time are not yet fully understood. While PTSD is commonly thought of as a monolithic entity consisting of several symptom clusters, it remains unclear whether changes in the different clusters occur in the same manner and direction over time or whether different clusters follow different routes. In the present investigation, the authors examined the long-term trajectories and interrelationships of PTSD symptom clusters (intrusion, avoidance, and hyperarousal) in clinical and nonclinical groups of war veterans.

The study sample was composed of 675 male Israeli veterans who had fought in the 1982 Lebanon War. The clinical group consisted of 369 veterans who had been identified by military mental health personnel during the war as having acute combat stress reaction (CSR). The nonclinical group consisted of 306 veterans who had served in the same combat units as the clinical group but who had no history of CSR. The two groups were matched in terms of age, education, military rank, and assignment. They were prospectively evaluated one, two, and 20 years after the war had ended. The data indicated that the clinical group endorsed a higher number of PTSD symptoms than the nonclinical group, both cross-sectionally and across time. In both the clinical and nonclinical groups, the PTSD symptom clusters of intrusion, avoidance, and hyperarousal were interrelated at any given point in time and across the 20-year span. In both groups, avoidance was found to be a particularly stable symptom cluster over time. Hyperarousal levels recorded one year after the war were found to play an important role in both the clinical and nonclinical groups, as they predicted the future occurrence of avoidance and intrusion symptoms.

According to the authors, the results of the current investigation suggest that PTSD is not a monolithic disorder; symptom clusters differ in several important aspects, and the course and severity of PTSD symptoms differ between clinical and nonclinical groups. The researchers recommend that practitioners focus on the identification and treatment of early hyperarousal, since it appears to play a prominent role in the development of other PTSD symptoms. (24 References)
COMPREHENSION OF AFFECTIVE PROSODY IN VETERANS WITH CHRONIC POSTTRAUMATIC STRESS DISORDER

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J NEUROPSYCHIATRY CLIN NEUROSCI, 21:52-8, Winter 2009

In order to meet diagnostic criteria for chronic posttraumatic stress disorder (PTSD), traumatized individuals must report significant problems with reexperiencing, avoidance, and arousal symptoms. PTSD is one of the few psychiatric conditions in which a subjective decrease in emotional range serves as a diagnostic criterion. While not absolutely necessary for the diagnosis, a restricted range of affect is a common complaint among veteran patients with chronic PTSD, and it is frequently encountered in combination with feelings of detachment from others and diminished interest in significant activities. To date, few studies have attempted to determine whether overall emotional perception is objectively impaired in patients with chronic PTSD. In order to examine affective processing in persons with chronic PTSD, the authors of the present investigation used the Aprosodia Battery to assess these patients’ ability to comprehend and discriminate the affective aspects of language and communication. The Aprosodia Battery is designed to specifically distinguish between profiles of affective prosodic deficits caused by focal left brain damage versus those caused by focal right brain damage (Ross et al., 1997).

The Aprosodia Battery was administered to 11 male veterans with Vietnam-era, combat-related chronic PTSD; 12 healthy comparison subjects; nine subjects with right hemisphere brain damage; and seven subjects with left hemisphere brain damage. All of the patients with left and right brain damage had focal ischemic infarctions that predominantly involved cortex and adjacent white matter as seen on magnetic resonance imaging scans. All of the patients with chronic PTSD were receiving service-connected disability for their condition. The patients with PTSD displayed significant deficiencies in the comprehensive and discriminative components of affective speech on the Aprosodia Battery; their performance was similar to that of the patients with focal right hemisphere brain damage.

According to the authors, further research should be directed not only at determining more about overall affective processing, both pre- and postmorbidly, in individuals with combat-related PTSD, but also at exploring potentially important relationships between affective prosodic deficits, self-reports of alexithymia, and overall affective processing. (40 References)
A 6-MONTH FOLLOW-UP STUDY OF POSTTRAUMATIC STRESS AND ANXIETY/DEPRESSIVE SYMPTOMS IN KOREAN CHILDREN AFTER DIRECT OR INDIRECT EXPOSURE TO A SINGLE INCIDENT OF TRAUMA

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J CLIN PSYCHIATRY, 70:1148-54, August 2009

The aims of the current study were to examine the symptoms of posttraumatic stress and anxiety/depression in Korean children after direct or indirect exposure to a single traumatic event that occurred during a fire escape drill and to assess the incidence of psychiatric disorders in this population.

On May 17, 2007, two mothers of school children fell to their deaths when a basket attached to a fire engine ladder they were riding on abruptly malfunctioned. A total of 1,394 students who attended the elementary school at which the traumatic event took place were evaluated by means of self-administered questionnaires and structured diagnostic interviews. The assessments took place two days (time point 1), two months (time point 2), and six months (time point 3) after the incident. The 335 students who witnessed the accident were defined as the direct-exposure group; the remaining 1,059 comprised the indirect-exposure group. At time point 1, the prevalence of severe posttraumatic stress disorder (PTSD), anxiety symptoms, and depressive symptoms was 18.2%, 5.5%, and 3.4%, respectively. The prevalence of severe PTSD symptoms, as measured by the Child Posttraumatic Stress Disorder-Reaction Index, was significantly higher in the direct-exposure group (36.6%) than in the indirect-exposure group (12.7%). At time point 2, the prevalence of severe PTSD symptoms was 7.4% (14%, direct-exposure group; 4.9%, indirect-exposure group). At time point 3, 38 of the 58 subjects from the direct-exposure group who had been evaluated with the Diagnostic Interview for Children, Version IV had one or more of the seven anxiety/depressive disorders assessed, including subthreshold diagnoses. Of the diagnoses meeting full DSM-IV criteria, agoraphobia was the most prevalent (22.4%), followed by generalized anxiety disorder (13.8%), separation anxiety disorder (6.9%), PTSD (5.2%), and social phobia (5.2%). When subthreshold diagnoses were included, separation anxiety was the most common (41.4%), followed by agoraphobia (34.5%), obsessive-compulsive disorder (22.4%), PTSD (20.7%), and social phobia (20.7%).

The authors conclude that, in addition to PTSD, various anxiety and/or depressive disorders may occur after direct or indirect exposure to trauma. (29 References)
TRAUMA AND POSTTRAUMATIC STRESS DISORDER
IN SOUTH AFRICAN ADOLESCENTS
A Case-Control Study of Cognitive Deficits

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Posttraumatic stress disorder (PTSD) is associated with significant impairments in social, work, and relational functioning as well as long-term disability. The lifetime prevalence of PTSD is estimated to be between 1% and 3% in adolescents, but in South Africa the prevalence may be as high as 12% to 22%, with as many as 97% of South African teenagers being exposed to some form of violent trauma. Previous studies have indicated that traumatized adults suffering from PTSD exhibit neuropsychological deficits in memory, attention, and learning. Like adults, traumatized adolescents display a range of psychological, behavioral, and cognitive difficulties following exposure to trauma. However, very little research has been done on cognitive impairments in severely traumatized adolescents. The present authors conducted a cross-sectional, case-control study in order to assess the impact of PTSD on various neurocognitive functions in South African adolescents.

The study sample consisted of 40 severely traumatized adolescents (21 boys, 19 girls; age range, 12 to 18 years; mean age, 15.2 years) who were evaluated for the presence of PTSD and then referred for neuropsychological assessment with a standardized neuropsychological test battery. Twenty of the adolescents were suffering from PTSD and 20 were not (controls). The PTSD-positive adolescents were similar to the controls on all demographic variables, including ethnicity, gender, language, level of education, religion, type of trauma exposure, and primary caretaker. In the sample as a whole, PTSD symptoms correlated significantly with depression, community violence exposure, stressful life events, and early trauma. Compared with the controls without PTSD, the traumatized adolescents with current PTSD demonstrated significantly more impairments in cognitive functions related to attention, verbal recognition, and visuo-spatial memory, as well as frontal lobe functions involved in sequencing and organizational skills.

The current findings indicate that the presence of PTSD itself (especially active symptoms), rather than trauma exposure per se, may lead to cognitive deficiencies. Awareness of the association between trauma exposure, PTSD, and cognition in adolescents is crucial, given the potential implications for referral, diagnosis, treatment and prognosis. (55 References)
The diagnosis of posttraumatic stress disorder (PTSD) has been revised in successive versions of the Diagnostic and Statistical Manual of Mental Disorders (DSM), beginning with the third edition (1980) and continuing with the most recent edition (DSM-IV-TR). In the present study, the authors evaluated a revision of PTSD symptom criteria that was aimed at increasing the parsimony and efficiency of the PTSD diagnosis through the application of a briefer symptom set designed to reduce overlap with other anxiety disorders or with depressive disorders. While this revised symptom set has been tested in adults, in the current investigation, its use was extended to a representative community sample of adolescents. The researchers hypothesized that a 2-factor PTSD model that deletes symptoms potentially overlapping with depression or other anxiety disorders would have comparable PTSD prevalence estimates, greater structural validity, and reduced comorbidity rates when compared with 3- and 4-factor DSM-IV models that retain depressive and anxiety disorder symptoms.

Cross-sectional data from the National Survey of Adolescents, a 1995 household probability sample of 4,023 adolescents (age range, 12 to 17 years), were examined. DSM-IV PTSD symptoms were assessed with a modification of the National Women’s Study PTSD module. Comorbidity was assessed through the use of DSM-IV criteria for major depressive episodes and substance use disorders. The results revealed that PTSD prevalence estimates varied across models (5.2%-8.8%, lifetime; 3.2%-5.7%, within the past six months). When the 2-factor model was used with a proportionate symptom threshold, lifetime PTSD prevalence was comparable to that found with the 3-factor DSM-IV model, and major depressive comorbidity was reduced by 9%-14%. Comorbidity with substance use disorders was comparable across models. Structural validity, tested with confirmatory factor analyses, showed that the 2-factor model and the 4-factor DSM-IV model were superior to the DSM-IV 3-factor model.

According to the authors, the current findings suggest that the prevalence of PTSD in adolescents is not primarily an artifact of comorbidity with depression or substance use disorders, and that a briefer symptom set that deletes DSM-IV PTSD symptoms overlapping with depression and anxiety disorders warrants testing with adolescent clinical samples.
COMPLEX PTSD, INTERPERSONAL TRAUMA AND RELATIONAL CONSEQUENCES: FINDINGS FROM A TREATMENT-RECEIVING NORTHERN IRISH SAMPLE

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J AFFECT DISORD, 112:71-80, January 2009

The phenomenology of individuals who experience a single traumatic incident differs considerably from that of persons who are exposed to chronic, repeated, relational trauma. The concept of “complex posttraumatic stress disorder (PTSD)” has been proposed to describe the complicated clinical presentation of persons who experience recurring trauma, particularly that of an interpersonal nature (e.g., physical abuse, sexual abuse). Compared with individuals with “simple” PTSD, those with complex PTSD have a more severe and complicated symptom profile, experience alterations in their character, and demonstrate more vulnerability with regard to self-directed harm and revictimization from others. In the DSM-IV field trial, complex PTSD was studied under Disorders of Extreme Stress Not Otherwise Specified (DESNOS). It is not clear whether DESNOS is a severe or more “complex” form of PTSD, and the relationship between PTSD and complex PTSD remains uncertain. The authors of the present study attempted to determine the degree to which DESNOS (complex PTSD) was related to interpersonal trauma and had relational consequences.

The study participants were 81 individuals (60 males, 21 females; age range, 19 to 73 years; mean age, 40.5 years) who were in treatment at a center in Belfast that served those with Troubles-related trauma histories (i.e., those referred as a direct result of exposure to the political violence in Northern Ireland known as the “Troubles”). The subjects were assessed with regard to various forms of interpersonal trauma, including exposure to the Troubles, as well as on measures of interpersonal and community connectedness. DESNOS symptom severity was found to be related to childhood sexual abuse and perceived psychological impact of Troubles-related exposure. A lifetime diagnosis of DESNOS was related to childhood Troubles-related experiences, while a current diagnosis of DESNOS was associated with childhood emotional neglect. PTSD avoidance predicted current DESNOS diagnosis and severity. Feeling emotionally disconnected from family and friends was related to all three indices of DESNOS (i.e., lifetime diagnosis, current diagnosis, and symptom severity).

The authors conclude that complex PTSD appears to be associated with PTSD but when present, it should be considered a superordinate diagnosis. (45 References)
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OBSESSIVE COMPULSIVE SYMPTOMS IN THE PSYCHOSIS PRODROME: CORRELATES OF CLINICAL AND FUNCTIONAL OUTCOME

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SCHIZOPHR RES, 108:170-5, March 2009

The link between obsessive-compulsive symptomatology (OCS) and psychosis has been noted since the early years of the 20th century. Obsessive-compulsive disorder (OCD) is a common comorbid condition in schizophrenia, with prevalence rates as high as 30% being reported in schizophrenia populations. Despite these findings, the prevalence of OCS and its relationship to outcome has not been evaluated in adolescents considered to be at ultra high-risk for psychosis (UHR). To explore the potential role of OCS in the developmental period preceding onset of psychosis, the authors of the present study investigated the presentation and effects of OCS on clinical course in young people who were putatively prodromal for psychosis.

The sample was composed of 64 UHR youth and 26 non-prodromal comparison (NPC) youth, all of whom were between the ages of 12 and 22 years and were enrolled in an ongoing investigation of adolescents at high clinical risk for developing psychosis. The subjects were ascertained by means of the Structured Interview for Prodromal Syndromes. The participants completed diagnostic interviews as well as the Padua Inventory (Sanavio, 1988), a 60-item self-report questionnaire designed to assess common obsessions and compulsions in different areas of routine daily functioning. Compared with NPC youth, UHR youth reported significantly higher rates of OCS on the Padua Inventory. A clinical diagnosis of OCD (20% of the sample) was associated with a lower risk of conversion to psychosis over an average 11-month follow-up period but was unrelated to clinical severity or psychosocial functioning. However, dimensional ratings of OCS were significantly associated with positive symptom severity, self-reported depression, and a trend toward increased suicidal ideation within the UHR group.

According to the authors, the findings of the present investigation indicate that OCS rates in UHR youth are well above estimated prevalence rates found in normal populations and are commensurate with rates of comorbidity observed in schizophrenic individuals. While the presence of OCS was not found to be associated with diagnostic outcome in UHR youth, obsessive-compulsive symptoms do appear to contribute significantly to the severe psychological distress sometimes experienced by these young people. (29 References) EAF
Obsessive-compulsive disorder (OCD) is a chronically debilitating, heritable neuropsychiatric disorder that hypothetically is underpinned by disconnectivity of large-scale brain systems. The extent of white matter abnormalities in OCD is unknown, and its genetic basis is complex, polygenic, and poorly understood. The authors of the present investigation performed diffusion tensor imaging in OCD patients, their unaffected first-degree relatives, and unrelated healthy comparison subjects in order to confirm whether white matter abnormalities exist in OCD patients and to determine whether such abnormalities also occur in first-degree relatives, indicating that they are markers of increased genetic risk for OCD. Diffusion tensor imaging is a magnetic resonance imaging technique that allows investigation of brain tissue microstructure through quantification of water diffusion (Le Bihan et al, 2001).

Fractional anisotropy of white matter was measured in 30 OCD patients, 30 unaffected first-degree relatives, and 30 healthy comparison subjects. The three groups were well matched in terms of age, gender, verbal IQ, and handedness. Regions of significantly abnormal fractional anisotropy in patients relative to comparison subjects were identified through permutation tests, and it was determined whether these abnormalities were also evident in the first-degree relatives. A secondary region-of-interest analysis was undertaken to assess the extent of replication between the current data and previous relevant literature. Patients with OCD demonstrated significantly reduced fractional anisotropy in a large region of right inferior parietal white matter and significantly increased fractional anisotropy in a right medial frontal region. First-degree relatives also exhibited significant abnormalities of fractional anisotropy in these regions.

According to the authors, the current findings indicate that OCD is associated with white matter abnormalities in parietal and frontal regions of the brain. Similar abnormalities observed in unaffected first-degree relatives suggest that these may be white matter endophenotypes representing an increased genetic risk for OCD. (48 References)
GRAY MATTER STRUCTURAL ALTERATIONS IN PSYCHOTROPIC DRUG-NAÏVE PEDIATRIC OBSESSIVE-COMPULSIVE DISORDER: AN OPTIMIZED VOXEL-BASED MORPHOMETRY STUDY

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AM J PSYCHIATRY, 165:1299-1307, October 2008

Obsessive-compulsive disorder (OCD) is a seriously debilitating neuropsychiatric disorder with a lifetime prevalence between 2% and 3% in the general population. Abnormal feedback loops within cortical-striatal-thalamic-cortical circuits have been hypothesized to play a key role in the pathophysiology of OCD. Although several magnetic resonance imaging (MRI) studies have been conducted with adults with OCD, few researchers have used voxel-based morphometry to examine brain structure, especially in psychotropic drug-naïve pediatric patients. In the present study, MRI examinations of 37 psychotropic drug-naïve pediatric OCD outpatients (14 males, 23 females; mean age, 13 years) and 26 age- and sex-matched healthy volunteers (nine males, 17 females; mean age, 13 years) were acquired on a 1.5 T MRI system, normalized to a customized template, and segmented with optimized voxel-based morphometry. The results indicated that the pediatric OCD patients had significantly more gray matter in regions predicted to differ a priori between groups, including the right and left putamen and orbital frontal cortex. Among the OCD patients, more gray matter in the left putamen and right lateral orbital frontal cortex correlated significantly with greater OCD symptom severity, but not with anxiety or depression. Manual region-of-interest measurements confirmed more gray matter in the orbital frontal cortex and putamen in OCD patients relative to healthy volunteers. More anterior cingulate gray matter was evident in the patients than in the healthy volunteers with regional volumetry but not with voxel-based morphometry. Regions of significantly less gray matter in OCD patients were confined to the occipital cortex and were not predicted a priori.

According to the authors, the current data suggest that OCD is characterized by more gray matter in brain regions comprising cortical-striatal-thalamic-cortical circuits. The present findings are consistent with functional neuroimaging studies reporting hypermetabolism and increased regional cerebral blood flow in striatal, anterior cingulate, and orbital frontal regions among OCD patients while in a resting state. (43 References)
STRUCTURE OF OBSESSIVE-COMPULSIVE SYMPTOMS IN PEDIATRIC OCD

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 47:773-8, July 2008

Obsessive-compulsive disorder (OCD) may represent a heterogeneous group of multiple, overlapping syndromes rather than a unitary disorder. Multiple factor and cluster-analytical studies have identified at least four relatively independent symptom dimensions, often termed contamination/cleaning, obsessions/checking, symmetry/ordering, and hoarding. However, it not clear whether the structure of OCD symptoms reported in adults is also seen in pediatric samples. In the study presented here, 238 children and adolescents who had been referred to a specialty pediatric OCD clinic were administered the Children’s Yale-Brown Obsessive Compulsive Scale Symptom Checklist, and its 13 major symptom categories were subjected to exploratory principal components analysis. The sample was predominantly male (63%) and ranged in age from eight to 18 years (mean, 13.8 years). The mean age at onset of OCD was 10 years. Thirty-seven of the patients had comorbid Tourette syndrome; 26 had other chronic tics, and 23 had a positive family history of OCD.

The principal components analysis identified four symptom dimensions that explained 55% of the total variance and broadly corresponded to those seen in adult samples. The first factor (hoarding/checking) explained 14% of the variance; the second factor (obsessions) explained 13.7%; the third factor (contamination/cleaning), 13.6%; and the fourth (symmetry/ordering), 13.3%. Multiple regression analyses revealed that none of the symptom dimensions was particularly associated with age at assessment, age at illness onset, or duration of illness, with the exception of the hoarding/checking dimension, which tended to be (nonsignificantly) associated with a longer illness duration, even after the researchers controlled for age at assessment and overall symptom severity. Boys were more likely than girls to display sexual obsessions (34% vs. 18%), while girls were more likely than boys to endorse hoarding compulsions (53% vs. 36%). High scores on the hoarding dimension were associated with increased levels of pervasive slowness, responsibility, indecisiveness, pathological doubt, depression, and a variety of emotional difficulties, both self- and parent-rated.

The authors conclude that the structure of OCD symptoms is broadly comparable across the lifespan. Hoarding symptoms appear to be highly prevalent in pediatric OCD, especially among girls, and are associated with greater levels of disability. (23 References)
DECREASED FAMILY ACCOMMODATION ASSOCIATED WITH IMPROVED THERAPY OUTCOME IN PEDIATRIC OBSESSIVE-COMPULSIVE DISORDER

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Pediatric obsessive-compulsive disorder (OCD) is a chronic, disabling condition that affects both patients and their families. Despite the identification of efficacious treatments such as cognitive-behavioral therapy (CBT) and selective serotonin reuptake inhibitor medications, not all patients respond fully. Studies examining family accommodation (FA) in both adult and pediatric OCD samples have reported that family members often participate in and maintain OCD symptoms. While parents may believe that family functioning is facilitated by accommodating a child’s OCD behaviors, accommodation unfortunately may maintain or exacerbate symptoms by providing short-term relief, which in turn negatively reinforces the behaviors and prevents habituation. Providing accommodation also directly contradicts the goals of CBT. In the current study, the authors attempted to determine whether the amount of FA provided to pediatric OCD patients would be associated with treatment outcome and whether decreases in FA would be related to improved outcome.

The sample was composed of 49 youths (age range, six to 18 years; mean, 12.8 years) who participated in 14 sessions of family-based CBT for OCD, and their parents. Assessment measures were administered at pretreatment and posttreatment. In all, 88% of parents reported at least mild FA. FA was significantly correlated with clinician-rated symptom severity and parent-rated impairment at pretreatment and posttreatment. Levels of FA decreased from pretreatment to posttreatment, and the change in FA from baseline to posttreatment was significantly associated with parent- and clinician-rated symptom severity at posttreatment, even when the researchers controlled for pretreatment symptom severity/impairment.

According to the authors, the current results indicate that participation in family-based CBT is associated with a significant decrease in FA and that this decrease is associated with positive treatment outcome. Given that the primary goals of CBT for pediatric OCD are to expose the child to anxiety-provoking situations and to prevent ritual engagement, it seems clear that FA contradicts the goals of treatment. Clinical experience suggests that targeting FA can lead to decreases in symptom severity and functional impairment, even if the patient is unwilling to participate fully in treatment. (20 References)
QUETIAPINE AUGMENTS THE EFFECT OF CITALOPRAM IN NON-REFRACTORY OBSESSIVE-COMPULSIVE DISORDER: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF 76 PATIENTS

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To date, several studies have reported on the usefulness of atypical antipsychotic drugs in augmenting the response to selective serotonin reuptake inhibitors (SSRIs) in patients with refractory obsessive-compulsive disorder (OCD). The purpose of the present investigation was to evaluate the usefulness of combining an atypical antipsychotic (quetiapine) with an SSRI (citalopram) in OCD patients who had never received appropriate treatment for their condition.

In a 10-week, double-blind trial, 76 patients who met DSM-IV criteria for OCD and who were drug-free or drug-naïve at study entry were randomly assigned to receive either citalopram (60 mg/day) with quetiapine (300-450 mg/day) or citalopram with placebo. Of the 76 patients, 66 completed the trial (31 in the quetiapine group and 35 in the placebo group). The change from baseline to endpoint on the total Yale-Brown Obsessive Compulsive Scale (YBOCS) and the response to treatment were the primary outcome measures. Response was defined as a 35% or greater reduction on the YBOCS and a Clinical Global Impressions-Improvement (CGI-I) scale score at endpoint of 1 or 2. As measured by the mean reduction in YBOCS scores following an intent-to-treat, last-observation-carried-forward analysis, the addition of quetiapine was found to be significantly superior to that of placebo, with a mean decrease of 11.9 and 7.8, respectively. Quetiapine addition was also found to be significantly superior to placebo addition as measured by the CGI-I scale, with mean scores of 2.1 and 1.4, respectively, at endpoint. Twenty-two patients (69%) in the quetiapine group and 15 (41%) in the placebo group were classified as treatment responders; this difference was significant. While quetiapine was generally well tolerated, more patients in the quetiapine group (N=8) than in the placebo group (N=2) discontinued treatment because of adverse events.

In the current study, the combination of quetiapine and citalopram proved to be more effective than citalopram alone in reducing OCD symptoms in treatment-naïve or medication-free OCD patients. According to the authors, the present results should be duplicated in larger, randomized, controlled trials of longer duration. (50 References)
QUETIAPINE ADDITION TO SEROTONIN REUPTAKE INHIBITORS IN PATIENTS WITH SEVERE OBSESSIVE-COMPULSIVE DISORDER
A Double-Blind, Randomized, Placebo-Controlled Study

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J CLIN PSYCHOPHARMACOL, 28:550-4, October 2008

Obsessive-compulsive disorder (OCD) is a neuropsychiatric disorder characterized by either obsessions or compulsions that cause significant distress to the afflicted individual. Although serotonin reuptake inhibitors (SRIs) are considered to be the most effective and well-established pharmacotherapeutic agents for the treatment of OCD, it is estimated that between 40% and 60% of OCD patients do not respond adequately to SRI therapy, and an even greater proportion fail to experience complete remission of their symptoms. The primary objective of the present study was to evaluate the efficacy of quetiapine when used in combination with SRIs for the treatment of OCD in severely ill adults.

Forty patients (21 men, 19 women; age range, 18 to 65 years) with a primary DSM-IV diagnosis of OCD participated in a 12-week, double-blind, placebo-controlled trial. They were randomly assigned to receive quetiapine titrated up to 400 mg/day (N=20) or placebo (N=20) in addition to their current SRI treatment. During the continuation phase (weeks 6 to 12), the patients were administered doses between 400 and 600 mg/day on the basis of their clinical response. At study entry, all subjects had been unresponsive to at least one 12-week course of treatment with SRIs at defined doses. For the current trial, the total Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) score was the primary efficacy parameter. Intention-to-treat, last-observation-carried-forward analysis showed a mean decrease in Y-BOCS scores of 5.2 (22%) in the quetiapine group and 3.9 (15%) in the placebo group after 12 weeks of treatment. Analysis of treatment effects revealed no significant difference between the two groups. No significant between-group differences emerged in any other variables, including self-rating scales and clinician-administered rating scales.

The authors conclude that on the basis of the current results, quetiapine augmentation cannot be recommended as a first-line strategy in OCD patients with at least one insufficient SRI treatment response. Evidence regarding the efficacy of quetiapine augmentation in treatment-resistant OCD remains inconclusive, they note. (20 References)
A LONG-TERM TRIAL OF THE EFFECTIVENESS AND SAFETY OF ATYPICAL ANTIPSYCHOTIC AGENTS IN AUGMENTING SSRI-REFRACTORY OBSESSIVE-COMPULSIVE DISORDER

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J CLIN PSYCHIATRY, 70:863-8, June 2009

Although atypical antipsychotic agents have been found to be effective in the augmentation of serotonin reuptake inhibitors (SRIs) for treatment-resistant obsessive-compulsive disorder (OCD) in short-term trials, there are few studies that address the effectiveness and safety of these agents when used in clinical settings over the long term. In the present investigation, the authors examined the response of selective SRI (SSRI)-refractory patients to augmentation with atypical antipsychotics; they compared adverse events in these treatment-refractory patients with those in a control group of SSRI responders.

After an initial 12-week SSRI trial, study subjects (outpatients who met DSM-IV criteria for OCD) were divided into two groups. Those who responded to SSRIs (N=46) were continued on SSRI monotherapy and also received cognitive-behavioral therapy (CBT) for a period of one year. Those who failed to respond to SSRIs (N=44) were randomly assigned to receive one of three atypical antipsychotics (olanzapine, quetiapine, or risperidone) and were subsequently treated with an SSRI plus an antipsychotic in combination with CBT for one year. For both groups, one-year treatment response was evaluated by measuring change in total score on the Yale-Brown Obsessive-Compulsive Scale (YBOCS). Although the SSRI-refractory patients responded to augmentation with atypical antipsychotics, they had higher YBOCS scores both before and after treatment than did the patients who showed good responses to SSRI monotherapy. In addition, although the patients who received SSRIs plus atypical antipsychotics were highly adherent to their antipsychotic regimen, they demonstrated significant increases in body mass index.

According to the authors, the current findings do not sufficiently support the long-term effectiveness of atypical antipsychotics in the augmentation of SSRIs for treatment-resistant patients with OCD. Even though this approach may be useful for some types of OCD patients, such as those with symmetry/ordering and/or hoarding symptoms, the present data emphasize the limitations of the current pharmacotherapeutic options in treatment-refractory OCD, and their chronic use raises several safety concerns. (45 References)
Obstructive-compulsive disorder (OCD), an often debilitating condition, is characterized by recurrent anxiety-laden thoughts, images, or impulses (obsessions) and accompanying behavioral or mental rituals (compulsions) meant to neutralize the anxiety. Data from the fields of genetics and neuroimaging, along with animal studies, case reports, and small clinical trials, point to a risk for glutamatergic dysfunction in the pathophysiology of OCD. The authors of the present open-label, augmentation study attempted to determine whether the administration of memantine, a noncompetitive glutamate antagonist, would result in a clinically meaningful reduction of OCD symptoms in adults with treatment-resistant OCD.

The sample was composed of 15 recruited adults who met DSM-IV criteria for OCD; who had baseline Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) scores of 18 or higher; and who had failed to respond to at least 12 weeks of treatment with an adequate and stable dose of a serotonin reuptake inhibitor (SRI). Memantine was added to the subjects’ therapeutic regimen for a period of 12 weeks, with the dose gradually being increased to a target of 20 mg/day. Response was defined as a 25% or greater reduction in Y-BOCS score at study end and a Clinical Global Impression-Improvement scale rating of “much” or “very much” improved. Data from 14 subjects were available for analysis (last observation carried forward, intent-to-treat). The mean baseline Y-BOCS score was 27.4. The subjects had failed an average of 2.8 SRI trials, and six had failed to respond to augmentation with atypical antipsychotics. At the end of the memantine trial, six subjects (42.9%) were deemed to be responders, with response being achieved by the end of week 4. Compared with nonresponders, responders had significantly lower Y-BOCS scores at baseline and had failed fewer SRI trials. Overall, memantine was well tolerated, and no subject withdrew from the study because of adverse side effects.

In the present open-label, augmentation trial of memantine in treatment-resistant OCD, almost half the subjects experienced a meaningful improvement in their symptoms. However, the authors note, this study was limited by small sample size, presence of comorbidities, and lack of controls. They recommend that large double-blind, placebo-controlled trials be carried out to further test the current findings. (34 References)
LONG-TERM FOLLOW-UP STUDY OF PATIENTS WITH REFRACTORY OBSESSIVE-COMPULSIVE DISORDER

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J NEUROPSYCHIATRY CLIN NEUROSCI, 20:450-7, Fall 2008

Although long-term follow-up studies indicate that obsessive-compulsive disorder (OCD) is often a chronic condition with a fluctuating course, very little research has been devoted to the highly disabled subgroup of OCD patients who appear to be treatment-refractory. It is estimated that between 10% and 30% of patients with OCD fail to respond to standard psychopharmacological and cognitive-behavioral interventions. To examine the long-term outcome of patients identified as having treatment-refractory OCD, the authors conducted a follow-up study of patients treated with intravenous clomipramine at the New York State Psychiatric Institute.

Between 1988 and 1995, 56 patients with a DSM-III-R diagnosis of OCD and a history of inadequate response to oral clomipramine received a total of 14 infusions of intravenous clomipramine. The range of the follow-up period was four to 11 years posttreatment. Forty-four patients (23 men, 21 women; age range, 27 to 62 years; mean age, 41.2 years) were available for follow-up interviews. At follow-up, eight patients were working full-time, nine were working part-time, and 27 were either unemployed or on disability. Fourteen patients were living with a significant other, 16 were living alone or with a roommate, 10 were living with parents or other relatives, and four were residing in group homes. In terms of current treatment, 41 of the 44 patients were receiving medication with or without some form of psychotherapy, and three were not receiving any form of therapy. At the time of the follow-up interview, 31 patients (70.5%) met full DSM-IV criteria for OCD, and 13 (29.5%) had subthreshold OCD. Almost half (N=20) reported feeling much improved or very much improved on the patient-rated Clinical Global Impressions-Improvement scale, as compared with their state prior to treatment with intravenous clomipramine. However, none reported full remission of symptoms.

According to the authors, the current results suggest that a substantial percentage of patients with “treatment-refractory” OCD improve symptomatically with time. In the present study, it is unclear whether the patients’ improvement was gradual and sustained or one that fluctuated over time. It is also not known whether the improvement was in fact due to the intravenous clomipramine treatment or whether it could be attributed to some other therapeutic intervention over the course of follow-up. (15 References)
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STRESSFUL LIFE EVENTS, CHRONIC DIFFICULTIES, AND
THE SYMPTOMS OF CLINICAL DEPRESSION

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J NERV MENT DIS, 197:154-60, March 2009

Major depressive disorder (MDD) is a serious psychiatric condition that
afflicts millions of people each year and is the leading cause of disability in North
America. It is estimated to produce an economic disease burden exceeding 83
billion dollars per year in the United States alone and is associated with a
significantly elevated risk for several serious medical conditions. While major life
events and chronic difficulties have been found to be associated with the onset
of depression, few studies have examined the association between life stress and
the clinical characteristics of depression. The present authors addressed these
issues by investigating the ways in which exposure to severe major life events
and chronic difficulties relate to two key clinical features of MDD: symptom
severity and level of global functioning.

The study participants were 100 adults (74 women, 26 men; age range, 18 to
58 years; mean age, 35 years) who had been diagnosed with MDD. An interview-
based measure (Life Events and Difficulties Schedule) was used to assess life
stress from one year before the onset of depression up to the day of the
interview. The Beck Depression Inventory (BDI) was used to measure the
severity of depression, while the Global Assessment of Functioning (GAF) scale
was administered to examine the current level of global functioning. Participants
with (N=19) and without (N=81) a preonset severe acute life event and subjects
with (N=15) and without (N=85) a preonset severe chronic difficulty were
compared with regard to BDI and GAF scores. The results indicated that
participants who experienced a preonset severe life event exhibited greater
overall levels of depression severity, endorsed more cognitive and somatic
symptoms of depression, and functioned at lower levels than did their
counterparts without preonset severe life events. On the other hand, exposure to
a preonset severe chronic difficulty was found to be unrelated to participants’
severity of depression, cognitive and somatic symptoms, or level of global
functioning.

Although both acute and chronic stressors often precede the onset of
depression, in the current study only acute stress was found to be associated
with the clinical characteristics of this disorder. These findings, the authors
note, highlight the potential specificity with which stress influences key clinical
features of depression. (48 References)
CIGARETTE SMOKING, STAGES OF CHANGE, AND MAJOR DEPRESSION IN THE CANADIAN POPULATION

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CAN J PSYCHIATRY, 54:204-8, March 2009

Numerous studies have explored the association between depression and smoking cessation. While many hypotheses have been proposed with regard to the influence of depression on smoking cessation, abstinence, and relapse, few population-based studies have been reported. In the current investigation, the authors describe the 12-month prevalence of major depression in relation to smoking status, nicotine dependence levels, commitment to quit smoking, attempts to quit, and maintenance of smoking cessation among members of the Canadian general population.

Data for the study were drawn from the Public Use Microdata File of the Canadian Community Health Survey: Health and Well-Being. The Composite International Diagnostic Interview–Short Form (CIDI-SF) for major depression was used to assess depressive disorder status. The survey also included a smoking module. Nicotine dependence levels were measured by administration of the Fagerstrom Tolerance Questionnaire to a subset of current smokers. A total of 49,249 respondents were assessed by means of the CIDI-SF (46,271 nondepressed and 2,978 depressed); 10,236 of these respondents were administered the smoking module. The prevalence of major depression was found to be highest in current smokers, followed by ever smokers and former smokers, with prevalence being lowest in those who had never smoked. This pattern persisted after stratification for age and sex. With regard to smoking cessation, the prevalence of major depression was determined to be highest among people who tried to quit, followed by those who considered quitting and those who quit in the past year, with the lowest prevalence being found among those who maintained their smoking cessation status for longer than one year. The prevalence of depression among people with a high nicotine dependence level was approximately twice that of those with a low nicotine dependence level.

Because an appreciable number of people (in the general population) who are trying to quit smoking are depressed, the authors conclude, smoking cessation programs should have the capacity to deal with this clinical reality. This is further reinforced by the possibility that attempts to quit smoking may increase the risk of major depressive episodes. (26 References)
DELINEATION OF TWO GENETIC PATHWAYS TO MAJOR DEPRESSION

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BIOL PSYCHIATRY, 65:808-11, May 1, 2009

Major depression (MD) is a familial and moderately heritable multifactorial disorder that is generally believed to result from a wide range of genetic and environmental risk factors. Studies have shown that the risk for MD is substantially increased in individuals with relatives who have MD and that most, if not all, of this risk is genetically transmitted. There is also evidence to suggest that persons with an early age at onset (AAO) of MD are particularly likely to have a strong family history of depression. The authors of the present investigation hypothesized that two sets of familial/genetic risk factors for MD could be identified: (1) high familial loading for MD, which would be most prominent in cases of MD with an early AAO; and (2) high familial loading for vascular disease (VD), which would be strongest in cases of MD with a late AAO.

The study sample consisted of 4,785 twin pairs drawn from the Swedish Twin Registry and assessed at a mean age of 54 years. Both members of each pair were evaluated by means of interview, and at least one member reported a lifetime history of modified DSM-IV MD. Risk for VD was assessed through examination of hospital discharge information and death certificates. Using Cox proportional hazard models and controlling for zygosity, age, and sex, the researchers found that early AAO in depressed twins predicted risk for MD in their cotwins, whereas late AAO predicted cotwin risk for VD. Application of piecewise regression revealed that the hazard ratio (HR) relating AAO per decade to risk for MD in the cotwin was much stronger for AAO between 13 and 23 years (HR=0.62) than for AAO between 24 and 65 years (HR=0.94). The HR relating AAO of MD in twin and risk for VD in cotwin was twice as strong for AAO between 47 and 65 years (HR=1.17) than for AAO between 13 and 46 years (HR=1.08).

The findings support the commonly held view that MD is etiologically and genetically heterogeneous; they also indicate that this familial/genetic heterogeneity can, with some power, be indexed by AAO, with possible interaction being seen between various molecular variants in predicting risk for MD. This interaction would be negative if the variant reflected familial risk for MD and positive if it reflected familial risk for VD. (34 References)
Several researchers have investigated the effects of brief psychotherapies in the treatment of individuals suffering from unipolar depression. A number of treatment modalities have been found to be generally effective with regard to major depressive disorder, and some recent studies have found evidence to support the long-term efficacy of cognitive-behavioral therapies. However, there has been little or no evaluation of the long-term effects of experiential therapies. In the present investigation, the authors examined the maintenance of gains in depression over an 18-month period following short-term treatment with client-centered therapy (CC) or emotion-focused therapy (EFT). Both of these experiential approaches place the therapeutic focus on the empathic relationship, the deepening of exploration, and the facilitation of the moment-by-moment emotional experience of the client.

The sample was composed of 43 adults (18 men, 25 women) who had been randomly assigned, and had responded, to short-term CC (N=21) or EFT (N=22) for the treatment of major depression. The long-term effects of these short-term therapies were evaluated by means of relapse rates, number of asymptomatic or minimally symptomatic weeks, survival time across the 18-month follow-up, and group comparisons on self-report measures at six- and 18-month follow-up among those clients who had responded to the acute treatment phase. By the end of the 18-month follow-up period, approximately 52% (11/21) of CC clients but only 23% (5/22) of EFT clients had experienced depressive relapse. EFT also showed superior effects over the 18 months in terms of greater numbers of asymptomatic or minimally symptomatic weeks, and the probability of maintaining treatment gains was significantly more likely in the EFT group than in the CC group. The results of follow-up self-reports showed significantly greater effects for EFT clients with regard to reduction of depression and improvement of self-esteem, and there were trends favoring EFT over CC in terms of reduction of general symptom distress and interpersonal problems.

According to the authors, maintenance of treatment gains following an empathic relational therapy for depression appears to be enhanced by the addition of specific experiential and gestalt-derived, emotion-focused interventions. (50 References)
CONTINUATION-PHASE COGNITIVE THERAPY’S EFFECTS 
ON REMISSION AND RECOVERY FROM DEPRESSION

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J CONSULT CLIN PSYCHOL, 77:367-71, April 2009

Major depressive disorder (MDD) is a commonly occurring mental disease that produces significant disability but can be treated effectively with cognitive therapy (CT). In an attempt to expand the CT evidence base and shift from the traditional emphasis on acute symptom reduction and prevention of relapse and recurrence, the present authors focused on an examination of extended periods of minimal or absent MDD symptoms in patients who had responded to acute-phase CT (A-CT). They examined the effects of continuation-phase CT (C-CT) on remission and recovery from recurrent MDD, with remission and recovery being defined as minimal or absent depressive symptoms maintained continuously for at least six weeks and eight months (35 weeks), respectively.

Responders to A-CT were randomly assigned to receive eight months of C-CT (N=41) or assessment control (N=43) and then were followed for an additional 16 months. The C-CT protocol consisted of 10 sessions (60-90 minutes each) provided by the patient’s A-CT therapist. The control condition consisted of 10 evaluation visits conducted on the same schedule as C-CT. Independent evaluators completed the Longitudinal Interval Follow-Up Evaluation at four, eight, 12, 16, 20, and 24 months post-A-CT (with each assessment covering the preceding four months); at study exit; and when patients, therapists, or follow-up evaluators suspected major depressive relapse or recurrence. A numerically larger proportion of patients in the C-CT group than in the control group achieved remission (97% vs. 88%), but the effect was not significant. However, the C-CT condition produced significantly more recovery than the control condition (84% vs. 62%). All of the patients who failed to achieve remission and recovery later relapsed, while most who remitted (60%) and who recovered (75%) did not experience later relapse or recurrence.

According to the authors, the present findings clarify the importance of treating patients through to remission and recovery and discovering how long to treat with which therapies. Although many A-CT responders will remit and recover, the addition of C-CT appears to increase the chance of recovery. The current data suggest that absence of remission and recovery portends relapse among patients with recurrent MDD and reinforces calls for persistence and flexibility in treatment in order to achieve periods of minimal or absent depressive symptoms. (26 References)
REMISSION AND RECOVERY IN THE TREATMENT FOR ADOLESCENTS WITH DEPRESSION STUDY (TADS): ACUTE AND LONG-TERM OUTCOMES

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 48:186-95, February 2009

While understanding of acute treatment outcomes in pediatric depression has increased in recent years, much less is known about the long-term outcomes of acute-phase therapy. As part of the Treatment for Adolescents with Depression Study, a multisite clinical trial, the authors examined remission rate probabilities, recovery rates, and residual symptoms in adolescents with major depressive disorder (MDD) over a period of 36 weeks.

The study sample was composed of 439 adolescents who met DSM-IV criteria for MDD and who were randomly assigned to 12 weeks of treatment with fluoxetine (N=109), cognitive-behavioral therapy (N=111), a combination of the two aforementioned treatments (N=107), or pill placebo (N=112). Those in the pill placebo group were treated openly after week 12 of the study and were not included in subsequent analyses. Treatment differences in remission rates and probabilities of remission over time were compared. Recovery rates in remitters at week 12 (acute-phase remitters) and week 18 (continuation-phase remitters) were examined. It was also determined whether the presence of residual symptoms at the end of 12 weeks of acute treatment predicted later remission. At week 36, the estimated remission rates for intention-to-treat cases were as follows: combination, 60%; fluoxetine, 55%; cognitive-behavioral therapy, 64%; and overall, 60%. Paired comparisons revealed that at week 24, all active treatment groups converged on remission outcome. The recovery rate at week 36 was 65% for acute-phase remitters and 71% for continuation-phase remitters, with no significant between-treatment differences in recovery rates. Residual symptoms present at the end of acute treatment predicted failure to achieve remission at weeks 18 and 36.

The authors conclude that, despite early low remission rates, most depressed adolescents go on to achieve remission after nine months of treatment. Methods of achieving higher and/or more rapid remission rates are still needed. A better understanding of which remitted patients will fail to maintain their recovery and how to better assist them is also necessary. (41 References)
EARLY PREDICTION OF ACUTE ANTIDEPRESSANT TREATMENT RESPONSE AND REMISSION IN PEDIATRIC MAJOR DEPRESSIVE DISORDER

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 48:71-8, January 2009

Over the past 10 years, research on the treatment of pediatric major depressive disorder (MDD), particularly the acute phase of therapy, has increased significantly. Although most clinical trials use treatment response as the primary outcome, remission (i.e., minimal or no depressive symptoms) is the goal of acute-phase treatment. However, less than 50% of children and adolescents achieve remission after acute antidepressant treatment. In the prospective, open-label fluoxetine study presented here, the authors examined indicators of acute treatment response and remission.

In all, 168 children and adolescents who were between the ages of 7 and 18 years and who had a primary diagnosis of MDD received 12 weeks of fluoxetine therapy. Information on demographic and baseline clinical features were collected, including data on age, sex, ethnicity, MDD episodes, number of concurrent psychiatric comorbidities, length of illness, current episode length, baseline depression severity, global functioning of the child and his/her family, suicidal behaviors, and family history of depression among first-degree relatives. The youths were evaluated by means of the Kiddie Schedule for Affective Disorders and Schizophrenia. Outcome measures included the Children’s Depression Rating Scale-Revised. More than 80% of the 168 participants completed the entire 12 weeks of acute-phase treatment. A positive first-degree family history of depression was the only demographic or baseline clinical characteristic that predicted a favorable treatment response. However, the rate of symptom reduction early in treatment identified remission status (discriminated remitters from nonremitters) by the end of acute treatment. As early as week 1, patients who eventually achieved remission showed significantly greater symptom improvement than patients who did not. Improvement in depression severity by week 4 was as effective in discriminating remitters from nonremitters as was improvement by week 6 or week 8.

According to the authors, the current findings indicate that both children and adolescents with MDD need to demonstrate sufficient improvement (above 50%) by week 4 of acute treatment in order to have a strong likelihood of achieving remission by week 12. (28 References)
EVIDENCE FOR EFFICACY AND TOLERABILITY OF VILAZODONE IN THE TREATMENT OF MAJOR DEPRESSIVE DISORDER: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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J CLIN PSYCHIATRY, 70:326-33, March 2009

Major depressive disorder (MDD) is a chronic, often debilitating illness that contributes to functional impairment and increases morbidity and mortality. Despite the burden of MDD, many patients remain untreated or are inadequately treated after diagnosis. Little evidence is available to guide the initial choice of therapy, and discontinuation and switching of medications are common. In the present study, the efficacy and tolerability of vilazodone, a combined selective serotonin reuptake inhibitor and partial 5-hydroxytryptamine-1A receptor agonist, were evaluated in a sample of adult patients with MDD.

Between February 2006 and May 2007, 410 patients (age range, 18 to 65 years) who met DSM-IV criteria for MDD and who had a baseline 17-item Hamilton Rating Scale for Depression (HAM-D-17) score of 22 or higher were randomly assigned to receive vilazodone (N=205) or placebo (N=205) for eight weeks. Vilazodone was titrated from 10 mg daily to 40 mg daily over a period of two weeks. Efficacy was assessed in terms of mean change from baseline to week 8 on the Montgomery-Asberg Depression Rating Scale (MADRS), the HAM-D-17, and the Hamilton Rating Scale for Anxiety. Response rates were determined at week 8 for the MADRS, the HAM-D-17, and the Clinical Global Impressions (CGI) Severity of Illness and Improvement (CGI-I) scales. Data were analyzed by using a last-observation-carried-forward method in the intention-to-treat (ITT) sample. The Arizona Sexual Experience Scale (ASEX) was also measured at baseline and at week 8. Of the 410 randomly assigned patients, 198 receiving vilazodone and 199 receiving placebo were included in the ITT population. Mean changes in MADRS and HAM-D-17 total scores from baseline to week 8 were significantly greater with vilazodone than with placebo. Significant improvements in MADRS and HAM-D-17 were seen at week 1, the earliest time point measured. Response rates were significantly higher with vilazodone than with placebo on the MADRS, the HAM-D-17, and the CGI-I. Treatment-emergent adverse events with vilazodone included diarrhea, nausea, and somnolence; however, most adverse events were of mild or moderate intensity. There were no clinically significant differences for either gender in ASEX scores at the end of treatment.

The authors conclude that vilazodone is an effective and well-tolerated treatment for adults with MDD. (48 References) EAF
LOW DOSES OF CONTROLLED-RELEASE PAROXETINE IN THE TREATMENT OF LATE-LIFE DEPRESSION: A RANDOMIZED, PLACEBO-CONTROLLED TRIAL

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J CLIN PSYCHIATRY, 70:46-57, January 2009

While depression in the elderly is a significant public health concern, late-life depression remains underdiagnosed and undertreated. Even when appropriately diagnosed, patients with late-life depression pose unique challenges, such as the physiologic changes that accompany aging, the presence of concurrent medical illnesses, and the increased risk of drug-drug interactions. The purpose of the present study was to evaluate the efficacy and tolerability of low daily doses of controlled-release (CR) paroxetine in patients with late-life depression.

In a 10-week, multicenter, placebo-controlled, double-blind, fixed-dose trial, patients 60 years of age or older were randomly assigned to receive daily doses of paroxetine CR 12.5 mg (N=168), paroxetine CR 25 mg (N=177) or placebo (N=180). All patients met DSM-IV criteria for major depressive disorder and had 17-item Hamilton Rating Scale for Depression (HAM-D) total scores of 18 or higher. The primary efficacy variable was the change from baseline to endpoint in total HAM-D scores. All analyses were based on a modified intent-to-treat population (N=516), which consisted of all patients who were randomly assigned, received at least one dose of double-blind study medication, and had at least one postbaseline efficacy assessment. The drug/placebo difference in HAM-D change from baseline at study endpoint was −1.8 for paroxetine CR 12.5 mg and −3.3 for paroxetine CR 25 mg. A significantly larger percentage of patients achieved remission (HAM-D total score of 7 or lower at endpoint) with paroxetine CR 25 mg (41%), but not with paroxetine CR 12.5 mg (31%), than with placebo (28%). Compared with placebo, both doses of paroxetine CR achieved statistical significance with regard to the Clinical Global Impressions-Severity of Illness scale and the patient-rated measures of depression severity and quality of life. Both active treatments were generally well tolerated; adverse event withdrawal rates were 6% for paroxetine CR 12.5 mg, 8% for paroxetine CR 25 mg, and 7% for placebo.

According to the authors, the current findings demonstrate that paroxetine CR administered in daily doses of 12.5 mg or 25 mg is efficacious and well tolerated in the treatment of major depressive disorder in patients who are 60 years of age or older. (41 References)
EIGHTEEN MONTHS OF DRUG TREATMENT FOR DEPRESSION: PREDICTING RELAPSE AND RECOVERY

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J AFFECT DISORD, 114:263-70, April 2009

For the most part, depression is a chronic, recurring illness with a range of possible outcomes. The clinically relevant outcomes in treating depression are persistent recovery, relapse, and treatment resistance. As part of the Christchurch Outcome of Depression study, 175 outpatients who had been treated with antidepressant medications for six months were assessed for the presence of major depression. Those who had recovered were monitored prospectively for one year to determine rates of relapse (at least two weeks of major depression). Those who were depressed at the six-month assessment were monitored for rates of recovery (at least eight weeks with no major depression).

At 18 months, 165 of the 175 patients assessed at six months were reassessed (94% of the sample). Of the 123 patients who were not depressed at their six-month assessment, 57 (46%) relapsed over the next 12 months. The patients who relapsed were more likely to have a history of recurrent depression, to have residual depressive symptoms, to have a less sustained response to initial treatment, and to have avoidant personality disorder symptoms, schizotypal personality disorder symptoms, higher harm avoidance scores, and lower self-directedness scores. Of the 38 patients who were depressed at the six-month assessment, 13 (34%) recovered over the next 12 months. No particular patient characteristics were found to be associated with recovery. Over the course of 18 months, 84% of the patients experienced recovery, but nearly half (42%) of these individuals also relapsed. Eight percent had a remission but no recovery or had persistent depressive symptoms, and the other 8% suffered from depression throughout the 18 months. Only 37% of the patients had recovered and remained well at the 18-month assessment.

According to the authors, the results of the current investigation indicate that most patients with depression will recover, but many will become unwell again within 12 months. Possible predictors of relapse include variables that are associated with patients’ early treatment response as well as personality factors. The writers conclude that there is an increased need to conceptualize depression as a long-term, recurring disorder and to develop management and research strategies accordingly. (33 References)
DIGEST of NEUROLOGY and PSYCHIATRY

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- **BOOKS RECEIVED FOR REVIEW**
SCHIZOPHRENIA AND OFFSPRING’S RISK FOR ADVERSE PREGNANCY OUTCOMES AND INFANT DEATH

Emma Nilsson, PhD (Centre for Epidemiology, National Board of Health and Welfare, SE-106 30 Stockholm, Sweden; e-mail: Emma.Nilsson@Socialstyrelsen.se); Christina M. Hultman, PsyD; Sven Cnattingius, MD, PhD; Petra Otterblad Olausson, PhD; Camilla Björk, MSc; and Paul Lichtenstein, PhD
BR J PSYCHIATRY, 193:311-5, October 2008

Several studies have shown that women with schizophrenia are at increased risk for adverse pregnancy outcomes. However, it is not known whether offspring born to schizophrenic fathers also have such an increased risk. In the present investigation, the authors examined the association between schizophrenia in mothers and fathers and the risk for four adverse pregnancy outcomes: infant death (death within the first year of life), low birth weight, pre-term delivery, and small-for-gestational-age birth. A record linkage that included two million births was made through the use of Swedish population-based registers. The risk for adverse pregnancy outcomes was evaluated by means of logistic regression.

Compared with men and women without schizophrenia, parents with schizophrenia tended to be older, less educated, and more likely to be having their first child. Schizophrenic women were less likely to cohabit with the infant’s father, and schizophrenic fathers were less likely to cohabit with their pregnant spouse. Schizophrenic women were also more likely to smoke during pregnancy. Offspring with a schizophrenic mother or a schizophrenic father faced a doubled risk of infant mortality, which could not be explained by maternal behavior alone during pregnancy. Excess infant death risk was largely attributable to post-neonatal death. Schizophrenic mothers had a significantly increased risk of giving birth to a low-birth-weight infant. The risk was also significantly increased for partners of schizophrenic fathers. Compared with mothers without schizophrenia, mothers with schizophrenia had a significantly increased risk for pre-term delivery; the corresponding risk among offspring of schizophrenic fathers was minor. Both mothers and fathers with schizophrenia had an increased risk for having a small-for-gestational-age infant.

The results of the current study indicate that there is an increased risk for adverse pregnancy outcomes among offspring of schizophrenic fathers as well as schizophrenic mothers. With the exception of that for infant death, this increased risk can be primarily explained by factors in the pregnant woman’s psychosocial situation, such as smoking and single motherhood. According to the authors, the risks to offspring with schizophrenic fathers suggest that, in addition to maternal risk behaviors, non-optimal social and/or parenting circumstances need to be considered. (23 References)
GLOBAL AND TEMPORAL CORTICAL FOLDING IN PATIENTS WITH EARLY-ONSET SCHIZOPHRENIA

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 47:1125-32, October 2008

Adult-onset schizophrenia has repeatedly been associated with disturbances in the temporal lobes and alterations in cortical folding, which are thought to reflect neurodevelopmental impairment. Early-onset schizophrenia (EOS; onset before the age of 18 years) is considered to involve even more pronounced neurodevelopmental deviance across a wide range of structural brain measures. The authors of the present study hypothesized that overall alteration of cortical folding also applies to EOS and that EOS involves prominent structural aberrations in temporal regions that mature late in adolescence (i.e., in superior temporal and collateral sulci).

Magnetic resonance T1 images of 51 patients with EOS and 59 healthy subjects were evaluated. The patients met DSM-IV criteria for schizophrenia, and all had experienced disease onset after the age of 12 years and before the age of 18 years. The patients and healthy participants were carefully matched in terms of age, sex ratio, and handedness. A fully automated method was applied to the magnetic resonance images in order to extract, label, and measure the sulcus area in the whole cortex. Cortical folding was assessed by computing global sulcal indices (the ratio between total sulcal area and total outer cortex area) for each hemisphere and local sulcal indices (the ratio between the area of labeled sulcus and total outer area cortex in the corresponding hemisphere) for superior temporal and collateral sulci. The researchers found that, as compared with the healthy study participants, the patients with EOS had significantly lower global sulcal indices in both hemispheres and a lower local sulcal index in the left collateral sulcus.

According to the authors, the results of the current investigation extend earlier findings of altered cortical folding in adult-onset schizophrenia to patients with EOS and suggest that reduced hemispheric sulcation is a feature of schizophrenia that is already manifesting itself during the early years of the illness. Structural deviation in the left collateral sulcus, which borders the fusiform and lingual lobules and the circumvolution of hippocampus, may be related to the neurobiological substrates of EOS. (71 References)
SELF AND OTHER IN SCHIZOPHRENIA:
A COGNITIVE NEUROSCIENCE PERSPECTIVE

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AM J PSYCHIATRY, 165:1465-72, November 2008

Deficits in social cognitive abilities and interpersonal functioning, which have
been described and interpreted for over 150 years, are among the most dramatic
features of schizophrenia and are key determinants of functional outcome.
However, the component processes that contribute to social cognitive
impairments in schizophrenia are not fully understood. Recent data indicate
that in healthy individuals, self-referential processing and social cognition rely
on common neural substrates. The authors of the present investigation assessed
self-referential source memory and social cognition in schizophrenic individuals
and healthy comparison subjects in order to compare how these critical
processes were associated in the two groups.

The study sample was composed of 91 schizophrenic outpatients (68 men, 23
women; mean age, 39.9 years) and 30 healthy comparison subjects (20 men, 10
women; mean age, 39.7 years). All were assessed on measures of basic social
cognition and source memory for previously learned word items (self-generated,
externally presented, and new). Partial correlations and multiple regression
analyses were used to test the association between social cognition measures
and source memory performance and the contribution of source memory and
general cognitive abilities to a social cognition composite score. Schizophrenic
patients demonstrated significantly lower source memory for self-generated
items (self-referential source memory) relative to comparison subjects but
showed intact external source memory. In both groups, self-referential source
memory and social cognition were strongly correlated. When the effects of
general cognitive abilities were controlled, these correlations were attenuated in
the schizophrenic group. Regression analysis revealed discrepancies between
groups in the cognitive functions contributing to social cognition performance.

These data suggest that individuals with schizophrenia are impaired in their
ability to recognize that their “self” was the source of an earlier mental event. In
healthy subjects, this specific ability to recognize “self as source” is strongly and
uniquely related to their ability to identify facial and vocal emotion and to
recognize faces, probably because they normally process social stimuli (the
“other”) partly by activating internal representations of their own sense of “self.”
Schizophrenics are impaired in this process, possibly because of disturbances in
the neurocognitive systems that normally facilitate the accurate processing of
both self-referential and social information. (43 References)
INEFFICIENT FACE DETECTION IN SCHIZOPHRENIA

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SCHIZOPHR BULL, 34:367-74, March 2008

While recognizing a face appears to be a natural and usually effortless process, deficiencies in this behavioral capacity can have profound consequences in everyday life. Facial processing comprises multiple functional components, namely, visual processing, analysis of facial identity, and recognition of facial expression. While earlier studies have shown that the higher levels of facial processing, such as recognition of the individuality and emotional expression of faces, are abnormal in persons with schizophrenia, it is not known whether the visual detection of a face as face is also impaired in these individuals. The focus of the present investigation was to examine the process involved in analyzing the visual information fundamental to perceiving a face as such (face detection) in schizophrenia patients.

Twenty-nine schizophrenia patients (12 men, 17 women; mean age, 41.2 years) and 28 normal controls (nine men, 19 women; mean age, 38.7 years) participated in the study. The researchers examined their performance with regard to locating a line-drawn face on the left or the right side of a larger line drawing. To prevent the normal formulation of general facial impressions, stimulus presentations were brief (13-104 ms). The face stimuli were either displayed upright or inverted in order to evaluate the face inversion effect, i.e., the specific effect of stimulus inversion on face processing. The results indicated that compared with normal controls, the schizophrenia patients demonstrated a significantly reduced face inversion effect, resulting primarily from a significantly lower accuracy in detecting upright faces. In tree detection, a comparison task that was also administered, the stimulus inversion effect was similarly small in both the schizophrenia patients and the normal controls.

By isolating face detection from cognitive, emotional aspects of face recognition, the authors of the present study found that the first stage of facial information processing is inefficient in schizophrenic individuals, as was demonstrated by low accuracy, a reduced stimulus inversion effect, and long reaction times. This inefficient face detection suggests that, unlike normal controls, patients with schizophrenia have difficulty in accessing the normally highly efficient, face-specific brain system. Like many other cognitive and emotional deficits, facial recognition impairment in schizophrenia actually has its specific sensory counterparts. (39 References)
SYMPTOM REMISSION IN FIRST EPISODE PATIENTS

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SCHIZOPHRENIA RES, 106:281-5, December 2008

Recently, new remission criteria for schizophrenia have been proposed that are based on a low symptom severity of specifically selected core symptoms (the severity criteria), which must be sustained over a minimum period of six months (the time criteria). These proposed criteria are considered to be conceptually viable and can be easily implemented in clinical trials and clinical practice. They appear to have clinical validity and in previous studies have been found to be associated with insight, global assessment of functioning, quality of life, and social functioning. The purpose of the present investigation was to examine, in a secondary analysis, these symptom remission criteria in a cohort of first-episode patients from the Calgary Early Psychosis Program, a comprehensive multi-element program in which all patients from a defined catchment area were offered three years of comprehensive treatment.

The sample was composed of 240 individuals who were experiencing their first episode of psychosis. All met DSM-IV criteria for a schizophrenia spectrum disorder or other psychotic disorder. Assessments were conducted at baseline, six months, 12 months, 24 months, and 36 months; mean follow-up was 26.4 months. All 240 subjects completed the six-month assessment; 196, the one-year assessment; 163, the two-year assessment; and 147, the three-year assessment. Eighty-eight subjects (36.7%) met both the severity criteria and time criteria for remission (in-remission group); 47 (19.6%) met only the severity criteria at their most recent assessment (severity only group); 49 (20.4%) had met severity criteria at one or more assessments but did not meet severity criteria or severity and time criteria at their most recent assessment (fluctuating group); and 56 (23.3%) did not meet remission criteria (non-remission group). Subjects who achieved remission had lower levels of symptoms and higher levels of functioning at baseline and at the final follow-up assessment. Those individuals who achieved remission were also characterized by improved premorbid functioning, shorter duration of untreated psychosis, and increased changes in symptoms over time.

Compared with the findings of previous studies, the rates of symptomatic remission found in the current investigation are good. However, the authors note, they confined themselves only to three dimensions of psychopathology (positive symptoms, negative symptoms, and disorganization). Future research should consider additional domains in order to move to a more sophisticated concept of remission and recovery. (24 References)
SYMPTOMS VERSUS NEUROCOGNITION AS PREDICTORS OF CHANGE IN LIFE SKILLS IN SCHIZOPHRENIA AFTER OUTPATIENT REHABILITATION

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SCHIZOPHR RES, 102:303-11, July 2008

Schizophrenia is a chronic and profoundly disabling psychiatric disorder. A growing body of literature has shown that neurocognitive deficits in schizophrenia account for between 20% and 60% of the variance in measures of outcome, and many studies suggest that neurocognitive deficits are more closely linked to functional outcome than are psychiatric symptoms. Few longitudinal studies have investigated the degree to which neurocognition and symptoms predict the ability to benefit from outpatient rehabilitation, and none have utilized performance-based measures of everyday life skills. The current study was designed to investigate the degree to which five measures of neurocognitive function (crystallized verbal ability, visual vigilance, verbal learning and memory, problem-solving, and processing speed), measured upon entry to a rehabilitation program, would be linked to change in functional status as measured by a laboratory-administered, functional capacity measure that assessed key tasks relevant to everyday life skills after a one-year course of outpatient cognitive and psychosocial rehabilitation. The degree to which positive and negative symptoms related to change in functional status was also evaluated.

The study sample was composed of 46 outpatients who met DSM-IV criteria for schizophrenia or schizoaffective disorder. The results showed that neurocognitive skills predicted change in functional status after one year of cognitive and psychosocial rehabilitation, even when the variance attributable to symptoms, baseline life skill scores, and type of computerized cognitive rehabilitation (cognitive remediation versus pre-vocational computer-skills training) was controlled. Analysis of individual neurocognitive measures indicated that verbal learning predicted change in functional status after the rehabilitation trial, even when other neurocognitive and symptom variables were taken into account. Measures of positive and negative symptoms, crystallized verbal ability, sustained visual vigilance, problem-solving, and processing speed were not related to change in functional status after outpatient rehabilitation.

According to the authors, the current findings emphasize the importance of verbal learning as a predictor of the acquisition of everyday life skills for schizophrenia patients who are enrolled in outpatient psychosocial and cognitive rehabilitation programs. (41 References)
COMPARING THE EFFICACY OF INTERVENTIONS THAT USE ENVIRONMENTAL SUPPORTS TO IMPROVE OUTCOMES IN PATIENTS WITH SCHIZOPHRENIA

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SCHIZOPHR RES, 102:312-9, July 2008

While environmental supports such as signs, checklists, alarms, and the organization of belongings have been used to bypass cognitive impairments in individuals with head injuries and mental retardation for many years and have been found to improve medication adherence in persons with psychoses, the comprehensive utilization of environmental supports has only recently been applied in a systematic manner in the rehabilitation of those with schizophrenia. The present authors studied two different treatments that use environmental supports and examined their efficacy in terms of improving functional outcome in individuals with schizophrenia.

In all, 120 participants who met DSM-IV criteria for schizophrenia or schizoaffective disorder were randomly assigned to one of the following three treatment groups: 1) Cognitive Adaptation Training (CAT), whereby supports are customized to individual cognitive impairments and behaviors and are maintained on weekly home visits; 2) Generic Environmental Supports (GES), whereby a generic set of supports is given to patients at a routine clinic visit and replaced on a monthly basis; and 3) treatment as usual (TAU). Functional outcomes, positive symptoms, and motivation were assessed at baseline and at three, six, nine, 18, and 24 months. After nine months of intensive CAT treatment, home visits were decreased from weekly to monthly to determine whether any treatment gains would be maintained. Of the 120 original participants, 113 (36, CAT; 38, GES; 39, TAU) had a baseline and at least one follow-up assessment and were considered as the intent-to-treat sample for purposes of data analysis. Results of a mixed effects regression model with repeated measures indicated a significant main effect of group (CAT>GES>TAU), with nonsignificant time and group by time interactions. Post-hoc analyses indicated that while those in CAT remained significantly better than those in TAU when treatment frequency was reduced, gains in CAT decreased to the level of those seen in GES. While group differences for positive symptoms were not significant, motivation improved in CAT and GES relative to TAU.

The authors conclude that the highest intensity treatment produced the best functional outcomes. However, some improvements were seen with a relatively inexpensive, clinic-based treatment using GES. (25 References)
COMPARISON OF ANTIPSYCHOTIC MEDICATION EFFECTS ON REDUCING VIOLENCE IN PEOPLE WITH SCHIZOPHRENIAS

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Violence is an uncommon but significant problem associated with schizophrenia. Drawing from the National Institute of Mental Health Clinical Antipsychotic Trials of Intervention Effectiveness project, the aims of the present study were as follows: (1) to examine violence risk reduction in schizophrenic patients after six months of treatment with one of four second-generation antipsychotics (olanzapine, risperidone, quetiapine, or ziprasidone) or a representative first-generation antipsychotic (perphenazine); (2) to identify significant clinical and nonclinical predictors of violent behavior; and (3) to evaluate the impact of medication adherence on violence reduction.

The trial participants were randomly assigned to treatment with perphenazine or one of the four second-generation antipsychotics and then followed for up to 18 months in a double-blind study. The present analyses focused on 1,445 patients for whom baseline violence data were available (the intention-to-treat sample) and on a subset of 653 patients who completed six months of treatment with their initially assigned medication (the retained sample). The estimated rate of violence declined from 19% to 14% in the intention-to-treat sample, whereas the observed rate of violence declined from 16% to 9% in the retained sample. The proportional magnitude of decline in violence was substantially greater in the retained sample (43%) than in the intention-to-treat sample (27%). No difference by medication group was found, except for the fact that in the retained sample only, those on perphenazine showed greater violence reduction than those on quetiapine. Medication adherence reduced violence, but not in patients with a history of childhood antisocial conduct. Prospective predictors of violence included childhood conduct problems, substance use, victimization, economic deprivation, and living situation. The presence of negative psychotic symptoms predicted lower rates of violence.

In the present investigation, newer second-generation antipsychotics did not reduce violence more than perphenazine, a representative first-generation antipsychotic. Effective antipsychotics are needed, but may not reduce violence that is unrelated to acute psychopathology. (43 References) EAF
A MULTIPLE-CENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF ORAL ARIPIPRAZOLE FOR TREATMENT OF ADOLESCENTS WITH SCHIZOPHRENIA

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AM J PSYCHIATRY, 165:1432-41, November 2008

Aripiprazole is a dopamine partial agonist that has been approved for use in adults for the short- and long-term treatment of schizophrenia and bipolar disorder. The current six-week, randomized, double-blind, placebo-controlled clinical trial assessed the efficacy, safety, and tolerability of aripiprazole in the acute treatment of adolescents with schizophrenia.

The study sample consisted of 302 subjects who were between 13 and 17 years of age, met DSM-IV criteria for a diagnosis of schizophrenia, and had a Positive and Negative Syndrome Scale (PANSS) total score of 70 or higher. They were randomized in a 1:1:1 ratio to receive placebo (N=100), 10 mg/day of aripiprazole (N=100), or 30 mg/day of aripiprazole (N=102). The primary endpoint was mean change from baseline to endpoint (last observation carried forward) in PANSS total score. Assessments of safety and tolerability included spontaneously reported adverse events, extrapyramidal symptom scores, serum prolactin concentration, body weight, and metabolic measures. Of the 302 originally enrolled patients, 258 (85%) completed the six-week study. The mean baseline PANSS score was 94.1. Between baseline and the end of treatment, both doses of aripiprazole resulted in significantly greater improvement than placebo on the PANSS total score. At week 6, the rate of remission was 54% for the group taking 10 mg/day of aripiprazole, 58% for those taking 30 mg/day, and 36% for those on placebo. The most common adverse events associated with aripiprazole (more than 5% in either aripiprazole group and a combined incidence at least twice that for placebo) were extrapyramidal disorder, somnolence, and tremor. Patients in the placebo group lost an average of 0.8 kg during the trial, while the aripiprazole-treated patients either had no overall change in weight (10-mg group) or gained an average of 0.2 kg (30-mg group). All groups showed mean decreases in serum prolactin after six weeks, with both active treatment groups showing significantly greater reductions than the placebo group.

The authors conclude that both 10- and 30-mg/day doses of aripiprazole were superior to placebo in the acute treatment of adolescents with schizophrenia and were generally well tolerated. (39 References)
OLANZAPINE VERSUS PLACEBO IN ADOLESCENTS WITH SCHIZOPHRENIA: A 6-WEEK, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 48:60-70, January 2009

Schizophrenia in adolescents is similar to the disorder in adults. While olanzapine has been shown to be effective in treating the symptoms of schizophrenia, its efficacy and safety have not been established in controlled trials with adolescents. The purpose of the present randomized (2:1), international, multisite, industry-sponsored trial was to assess the efficacy and tolerability of olanzapine in adolescents with schizophrenia.

A total of 107 adolescent patients were randomly assigned to receive olanzapine (N=72, mean age, 16.1 years) or placebo (N=35, mean age, 16.3 years) for a period of up to six weeks. All patients met DSM-IV-TR criteria for schizophrenia. Olanzapine was administered in flexible doses ranging from 2.5 mg to 20 mg per day. The researchers assessed last-observation-carried-forward mean changes from baseline to endpoint on the anchored version of the Brief Psychiatric Rating Scale for Children, the Clinical Global Impression Scale-Severity of Illness, and the Positive and Negative Syndrome Scale (PANSS). More olanzapine-treated than placebo-treated patients completed the trial (68.1% versus 42.9%). Compared with placebo-treated patients, olanzapine-treated adolescents showed significantly greater improvement on the Brief Psychiatric Rating Scale for Children, the Clinical Global Impressions Scale-Severity of Illness, and the PANSS total and positive scores. Olanzapine-treated patients gained significantly more baseline-to-endpoint weight (4.3 kg versus 0.1 kg). Significantly more olanzapine-treated than placebo-treated patients gained 7% or more of their body weight at any time during treatment (45.8% versus 14.7%). Mean baseline-to-endpoint changes in prolactin and triglyceride levels were significantly higher in the olanzapine group than in the placebo group. While the incidence of treatment-emergent significant changes in fasting glucose, cholesterol, and triglycerides did not differ between the groups at endpoint, significantly more olanzapine-treated patients exhibited high triglycerides at any time during treatment.

While olanzapine-treated adolescents with schizophrenia experienced significant symptom improvement, the authors note, substantial increases in weight, uric acid, prolactin, triglycerides, and most liver function tests were seen during treatment with this drug. (43 References)
BOOKS RECEIVED FOR REVIEW

*Brain-Based Therapy with Adults: Evidence-Based Treatment for Everyday Practice*, by John B. Arden and Lloyd Linford. John Wiley & Sons, 2009. 323 pages, $40.00 (paperback).

Abstracts and Reviews of Selected Literature in Psychiatry, Neurology, and their Allied Fields

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POSITIVE SCREENING FOR AUTISM IN EX-PRETERM INFANTS: PREVALENCE AND RISK FACTORS

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PEDIATRICS, 121:758-65, April 2008

Due to advances in neonatal intensive care, the survival of very low birth weight infants has increased markedly in recent years. Despite this decrease in mortality, however, the prevalence of significant and lifelong motor, cognitive, and behavioral dysfunction has remained a major problem confronting these children. The authors of the present study performed screening tests for early autistic features in children with a history of very low birth weight and attempted to identify risk factors associated with a positive screening result.

The sample was composed of 91 ex-preterm infants whose gestational age at birth ranged from 23 to 30 weeks and whose birth weight ranged from 460 to 1490 g. Sixty-five percent were delivered by cesarean section, and 88% required ventilatory resuscitation at birth. The subjects underwent conventional magnetic resonance imaging (MRI) at preterm and/or term-adjusted age. The researchers collected pertinent demographic, prenatal, intrapartum, acute postnatal, and short-term outcome data for all infants. Follow-up evaluations were performed at a mean age (corrected for prematurity) of 21.9 months. Assessment tools included the Modified Checklist for Autism in Toddlers (M-CHAT), the Vineland Adaptive Behavior Scale, and the Child Behavior Checklist. Of the 91 children, 23 (25%) had positive results on the autism screening tool (M-CHAT). Abnormal scores on the M-CHAT correlated highly with internalizing behavioral problems on the Child Behavior Checklist and socialization and communication deficits on the Vineland Adaptive Behavior Scale. Lower birth weight, gestational age, male gender, chorioamnionitis, acute intrapartum hemorrhage, illness severity on admission, and abnormal MRI studies were significantly associated with an abnormal autism screening score.

According to the authors, the present results suggest that the unusual social and behavioral profile observed by many clinicians in the follow-up of high-risk preterm infants may represent the early signs of an autism spectrum disorder. The current data indicate that early screening for signs of autism may be warranted in ex-preterm infants, with definitive autism testing to follow in those with positive screening results. (68 References)
PREVALENCE OF AUTISM AMONG ADOLESCENTS WITH INTELLECTUAL DISABILITIES

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General population studies of the prevalence of autism have consistently found that autism commonly co-occurs with intellectual disabilities (ID). Among individuals who meet formal diagnostic criteria for autistic disorder, up to 75% are estimated to be intellectually disabled, whether defined in terms of IQ and/or level of adaptive skills. The present authors attempt to extend previous research by providing contemporary, population-based data on the prevalence of autism in individuals with ID. Their study was conducted within the context of a Canadian population survey of adolescents with ID.

The prevalence of autism was examined through use of the Autism Diagnostic Interview–Revised (ADI-R), with appropriate care taken in assessing lower functioning individuals and those with additional physical and sensory impairments. Individual assessment during psychological evaluation and consensus classification of complex cases, involving clinicians experienced in the assessment of autism, contributed to the identification of autism. Among those adolescents with ID who agreed to participate in the study, 171 had a composite IQ of 75 or below. ADI-R data were not available in 11 cases and were indeterminate in an additional six cases, thus reducing the ID population to 154. Of these, 27.9% (30 males, 13 females) met ADI-R criteria for autism. Males predominated, with a ratio of 2.3 males to 1 female; this was particularly true for those with mild ID (2.8 males to 1 female, as compared with a ratio of 2 males to 1 female for those with severe ID). Among the entire participant population with ID (N=171), 48 subjects (28.2%) were estimated to have autism. Placed in the context of the larger general population from which the ID population was ascertained, 7.2/1,000 were identified with ID, of which 2.0 were estimated to have autism. Autism rates among those with mild ID (24.1%) and severe ID (32%) were not significantly different. Socioeconomic status did not differentiate the groups with and without autism. Less than one half of the adolescents who met diagnostic criteria for autism had been previously diagnosed as such.

The authors conclude that their overall prevalence estimate for autism lies in the higher range of estimates reported in previous studies (particularly for mild ID). This could be a reflection of the changes in diagnostic criteria for autism that have subsequently occurred. (54 References)
EVIDENCE FOR OVERLAPPING GENETIC INFLUENCES ON AUTISTIC AND ADHD BEHAVIOURS IN A COMMUNITY TWIN SAMPLE

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High levels of clinical comorbidity between autistic spectrum disorders (ASD) and attention deficit hyperactivity disorder (ADHD) have been reported, although their core diagnostic symptoms do not explicitly overlap. In the present investigation, the authors utilized the twin design in order to explore the extent to which genetic and environmental influences might explain the association between autistic traits and ADHD behaviors as seen throughout normal variation, at the impaired extreme, and in cases that appear to meet criteria for an ASD or ADHD diagnosis.

The Twins Early Development Study focuses on a community sample of twins born in England and Wales. Families with twins born between 1994 and 1996 were invited to join; 6,771 families participated in the study when the twins were eight years old. Parents completed the Childhood Asperger Syndrome Test and the Conners’ DSM-IV subscales. Teacher data were also collected on a subsample. High scores on the Conners’ subscales were used to identify possible ADHD cases. The Development and Well-Being Assessment interview was used to identify potential ASD cases. The researchers employed multivariate structural equation model-fitting, as well as DeFries Fulker extremes analysis and liability threshold model-fitting. Significant positive phenotypic correlations were found between autistic and ADHD traits in the general population (.54 for parent data, .51 for teacher data). In the bivariate models, all genetic correlations were greater than .50, indicating a moderate degree of overlap in genetic influences on autistic and ADHD traits, both throughout the general population and at the quantitative extreme. This phenotypic and genetic overlap still held when sex, IQ, and conduct problems were controlled (for both parent and teacher data). There was also substantial overlap in suspected cases; 41% of children who met criteria for an ASD had suspected ADHD, and 22% with suspected ADHD met criteria for an ASD.

According to the authors, the findings of the current study suggest that ASD and ADHD, whether considered as quantitative traits or at the quantitative extreme, are both highly heritable, with a moderate degree of genetic influences that are common across both sets of behaviors, as well as some genetic influences that are specific to each. (42 References)
EVIDENCE FOR THREE SUBTYPES OF REPETITIVE BEHAVIOR IN AUTISM THAT DIFFER IN FAMILIALITY AND ASSOCIATION WITH OTHER SYMPTOMS

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J CHILD PSYCHOL PSYCHIATRY, 49:1193-1200, November 2008

Autism is a pervasive developmental disorder that is characterized by social impairments, deficits in verbal and nonverbal communication, and repetitive interests and behaviors. While each of these core features must be present in order for a diagnosis of autism to be made, the severity and clinical presentation of autism has proven to be extremely heterogeneous. Recent work has suggested that restricted repetitive behaviors (RRBs) may be used to reveal homogeneous subgroups within the autism spectrum. RRBs consist of a variety of behaviors that range from repetitive body movements to more cognitively mediated symptoms, such as intense interests or hobbies. Once considered to be a single unitary domain of behavior, there is a growing body of evidence that points to the existence of considerable structure within RRBs. In the present investigation, the authors used relevant items from the Autism Diagnostic Interview-Revised to examine the structure of RRBs.

The study sample was composed of 316 individuals with autistic disorder (age range, 20 months to 29 years; mean age, 9.02 years); 82.5% were male, and 85% were Caucasian. Through the use of exploratory factor analysis, the researchers identified the following three distinct factors: Repetitive Motor Behaviors (RMB), Insistence on Sameness (IS), and Circumscribed Interests (CI). The RMB factor was found to be associated with a variety of subject characteristics, including IQ, age, social/communication impairments, and the presence of regression. IS was determined to be associated with social and communication impairments, but CI appeared to be independent of subject characteristics. On the basis of sib-pair correlations, IS and CI (but not RMB) appeared to be familial. Analysis of the data at the case level indicated that the presence of multiple forms of RRBs in an individual was associated with greater impairment in the social and communication domains, which in turn was suggestive of a more severe presentation of autistic disorder.

According to the authors, the current findings indicate that there appears to be considerable structure within the restricted repetitive behavior exhibited by individuals with autistic disorder. The fact that these behaviors were found to be differentially related to subject characteristics and familiality adds to their validity, the researchers conclude. (41 References)
ABSENCE OF PREFERENTIAL LOOKING TO THE EYES OF APPROACHING ADULTS PREDICTS LEVEL OF SOCIAL DISABILITY IN 2-YEAR-OLD TODDLERS WITH AUTISM SPECTRUM DISORDER

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ARCH GEN PSYCHIATRY, 65:946-54, August 2008

From the first hours of life, typically developing human newborns give preferential attention to people. Four-day-old newborns distinguish between a face looking toward them and a face looking away, and by the age of three months, infants look more at a person’s eyes than at other parts of the face. Preferential attention to the eyes of others is an important facilitator of socialization and social adaptation not only in early childhood but also throughout later life. In children with autism, diminished and aberrant eye contact is a lifelong hallmark of disability. In the present investigation, the authors attempted to determine whether looking at the eyes of approaching adults is altered in autistic children by the age of two years, and whether these alterations are related to the child’s level of social disability.

Sixty-six children (mean age, 2.1 years) participated in the study and were grouped as follows: 15 toddlers with autism spectrum disorders (11 boys, four girls), 36 typically developing children (24 boys, 12 girls), and 15 toddlers with developmental delays but without autism (11 boys, four girls). The children were presented with 10 video clips. Each clip showed an actress looking directly into the camera, playing the role of a caregiver, and entreating the viewing toddler by engaging in childhood games (e.g. playing pat-a-cake, peek-a-boo, etc). The children’s visual fixation patterns were measured by eye tracking. The main outcome measure was preferential attention, which was measured as percentage of visual fixation time to four regions of interest (eyes, mouth, body, and object). The group of toddlers with autism fixated significantly less on the eye region relative to the typically developing group and the developmentally delayed, nonautistic group. The autism group also fixated significantly more on the mouth region than the other two groups. The typically developing group and the developmentally delayed, nonautistic group did not differ significantly from one another in terms of fixation to any of the four regions of interest. The fixation on eyes by the children with autism was correlated with their level of social disability; less fixation on eyes predicted greater social disability.

The current results show that by two years of age, children with autism already exhibit markedly different patterns of looking at the world. In addition, the relationship between fixation on eyes and level of social disability suggests that this measure may be useful for quantifying the social phenotype in autism early in development. (64 References)
People with autistic-spectrum disorder display pervasive abnormalities in socio-emotional communication as well as stereotyped and obsessional behavior. These symptoms not only have a profound impact on the autistic individual’s daily life but also have far-reaching social and economic consequences. However, the neurobiological determinants of such behavioral abnormalities are poorly understood. Although problems with self- and socially motivated behavior and social interaction are thought to result from a lack of perceived reward feedback in autistic individuals, no reported *in vivo* brain imaging studies have investigated reward mechanisms in autistic-spectrum disorder. In the present study, the authors used rapid, mixed-trial, event-related functional magnetic resonance imaging to examine the neural substrates of reward feedback within the context of a sustained attention task with monetary reward in adults with autism-spectrum disorder and in matched control subjects.

The study sample was composed of 10 healthy men (control subjects) and 10 right-handed men with normal IQ and with autism-spectrum disorder (seven with Asperger syndrome and three with high-functioning autism). Upon study entry, the participants were between 20 and 50 years of age and did not differ significantly from one another in terms of age, socioeconomic status, or IQ. When directly compared with control subjects, participants with autism-spectrum disorder showed significantly greater activation of the left anterior cingulate gyrus during reward achievement. This increased brain activation in the autistic subjects was correlated with clinical abnormalities in social interaction (as measured by the Autism Diagnostic Interview). Individuals with autism-spectrum disorder also had significantly reduced peri-ventricular white matter density in the left frontal lobe.

According to the authors of the present investigation, reward achievements, like other cognitive behavioral abnormalities, appear to be predominantly mediated by frontal left hemispheric structures and seem to require more frontal lobe brain activation in individuals with less social interaction abilities. Thus, the researchers conclude, neurodevelopmental delay of the left hemisphere in people with autism-spectrum disorder could influence brain activation patterns and behavioral outcomes. *(41 References)*
Autism spectrum disorders are characterized by impairments in social interaction, impairments in communication, restricted and repetitive behaviors, and a characteristic course. Empirical evidence from neuropsychological studies has led to the suggestion that an appropriate model for the repetitive behaviors often observed in autism is a deficit in executive functioning, a collection of mental processes responsible for planning, inhibition of prepotent or inappropriate behavioral responses, and execution of appropriate responses. Despite the fact that recent studies have indicated that the social and cognitive impairments in autism may be associated with neural processing deficits in specific brain regions, little is known about the brain mechanisms that mediate executive functioning deficits in autism. The authors of the present investigation used functional magnetic resonance imaging to examine the neural correlates of shifts in behavioral response and cognitive set in individuals with high-functioning autism and in neurotypical control subjects. All the participants performed a target detection task that was specifically designed to distinguish shifts in response from shifts in cognitive set.

Eighteen individuals with high-functioning autism (16 males, two females; mean age, 22.3 years) and 15 age- and IQ-matched comparison subjects (13 males, two females; mean age, 24.3 years) with no history of psychiatric or neurological disorders participated in the study. The individuals with high-functioning autism showed a lower degree of accuracy on response shifting trials, independent of whether those trials also required a shift in cognitive set. Compared with the control subjects, the autistic participants showed reduced activation in frontal, striatal, and parietal regions during these trials. Within the autism group, the severity of restricted, repetitive behaviors was negatively correlated with activation in anterior cingulate and posterior parietal regions.

According to the authors, the findings of the present study are consistent with current models of executive dysfunction in autism and provide novel insights into the putative neural mechanisms underlying the executive function deficits and stereotyped, repetitive behaviors often observed in individuals with autism spectrum disorders. (48 References)
DISPARITIES IN DIAGNOSIS AND ACCESS TO HEALTH SERVICES FOR CHILDREN WITH AUTISM: DATA FROM THE NATIONAL SURVEY OF CHILDREN’S HEALTH

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For children with autism, early diagnosis can optimize developmental outcomes, family coping, and family and community planning. Autistic children often have comorbid psychiatric and medical conditions. Thus, the identification of factors associated with delays in the early diagnosis of autism and with decreased access to health care has the potential to lead to interventions that could improve health and well-being. The aim of the present study was to evaluate traditionally underserved populations with regard to the prevalence of autism and access to services. The authors hypothesized that (1) differences occur in the age-related prevalence of autism between children of traditionally underserved populations and well-served populations; and (2) disparities based on race, ethnicity, and income exist in access to health care for families of children with autism.

Data were gathered from telephone surveys conducted from 2003 to 2004 for the National Survey of Children’s Health. The determination of autism was made on the basis of parental report. Of 102,353 children for whom valid data were available, 495 were identified as having autism. The overall weighted prevalence of autism was 46 per 10,000. For children between the ages of four and 17 years, the rate was 55 per 10,000 (one in 182 children). The prevalence of autism was lower for Latinos (26/10,000) than for non-Latinos (51/10,000). Whites and blacks had comparable rates of autism. The lowest preschool rate of autism (16/10,000) occurred among poor children. Latinos and poor families rated their children’s autism as more severe. Being black, Latino, or poor was associated with decreased access to health services, while having Medicaid or being enrolled in a State Children’s Health Insurance Program was linked with better access to some health care services.

The authors conclude that disparities in the prevalence and parent-reported severity of autism and in access to health care were found for children with autism. The researchers recommend that programs for children in general (e.g., universal screening for autism) and programs that target traditionally underserved groups of children, their families, and their health care providers should be tested and implemented in order to optimize case finding of children with autism and eliminate disparities in access to early intervention and to health care services. (68 References)
STIMULANT MEDICATION TREATMENT OF TARGET BEHAVIORS IN CHILDREN WITH AUTISM: A POPULATION-BASED STUDY

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J DEV BEHAV PEDIATR, 29:75-81, April 2008

Autism is a developmental disorder characterized by impairments in social interaction and communication and by restricted patterns of behavior and interests. In addition to these core symptoms, hyperactivity, impulsivity, disinhibition, and inattention frequently occur in children with autism. Previous studies have reported that between 34% and 55% of autistic children are treated with psychotropic medications, including antipsychotics, antidepressants, and psychostimulants. The current investigation provides detailed information on the use of psychostimulants in a large, population-based cohort of children with research-identified autism.

Among all children (aged 21 years or younger) residing in Olmsted County, Minnesota, between January 1, 1976 and December 31, 1997, 124 (95 males, 29 females) had been previously identified as fulfilling DSM-IV-based research criteria for autistic disorder. By means of detailed chart review, the authors abstracted information on all prescribed psychopharmacological medications for each of these children. Psychostimulants were used to treat 65 (52.4%) of the 124 subjects. The median age at which treatment began was 7.6 years, and the median duration of psychostimulant treatment was 3.1 years. Methylphenidate was the most frequently prescribed psychostimulant drug. A single type of stimulant was used in 32 subjects (49%), while 19 (29%) were treated with two different stimulants, and 14 (22%) received three different stimulants. While there was no difference in overall psychostimulant treatment rates between boys and girls, treatment was initiated at a significantly later age in girls, and girls were treated for a significantly shorter duration. There were 398 episodes of psychostimulant treatment, and favorable responses were associated with 276 (69.4%) of these episodes. In all, 67 (16.8%) of the 398 stimulant treatment episodes were associated with a side effect. At least one side effect was experienced by 43 (66%) of the 65 children treated with stimulants.

According to the authors, the current results indicate that psychostimulants are commonly prescribed to children (both boys and girls) with autism, and suggest that these medications may improve the target symptoms of hyperactivity, impulsivity, disinhibition, and inattention. (31 References)
GUANFACINE IN CHILDREN WITH AUTISM AND/OR INTELLECTUAL DISABILITIES

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J DEV BEHAV PEDIATR, 29:303-8, August 2008

Considerably higher rates of attention-deficit/hyperactivity disorder have been observed in children with developmental disabilities such as intellectual disability and autism (15%-25%) than in those seen in typically developing children (3%-5%). While psychostimulants have a long history of use in the treatment of hyperactivity and inattention in developmentally disabled children, the overall response rates in these children appear to be lower than those of typically developing children. In addition, there is evidence to suggest that children with developmental disabilities experience higher rates of adverse events. Guanfacine, an α2-adrenergic receptor agonist, has shown some promise as an alternative to psychostimulant medications. The authors of the present study conducted a six-week, double-blind, placebo-controlled, crossover trial of guanfacine (maximum daily dose, 3 mg) in 11 children with developmental disabilities and symptoms of inattention/hyperactivity.

The study subjects (10 boys, one girl; age range, 5 to 9 years; mean age, 7 years and 3 months) were recruited from a university-based outpatient specialty clinic and were required to have a diagnosis of intellectual disability (on the basis of the most recent school psychological assessment) and/or autism (autistic disorder or pervasive developmental disorder not otherwise specified). They were also diagnosed with attention-deficit/hyperactivity disorder or presented with clinically significant deficits in the areas of overactivity and inattention. All had previously been prescribed stimulant medication, but had either been nonresponders or experienced adverse side effects that had necessitated the discontinuation of medication. Eight of the 11 children were able to tolerate titration to the maximum 3-mg/day dose. Significant benefits were observed with guanfacine on the Hyperactivity subscale of the parent- and teacher-rated Aberrant Behavior Checklist (ABC) as well as on global ratings of improvement. However, no gains were noted on other ABC subscales. Of the 11 subjects, five (45%) were considered to be medication responders, on the basis of a 50% or greater decrease in the ABC Hyperactivity subscale score between the placebo and guanfacine conditions. Several side effects were reported, including drowsiness and irritability.

According to the authors, guanfacine appears to be a viable alternative to psychostimulants in the treatment of children with developmental disabilities. However, the researchers note, final conclusions cannot be drawn until larger double-blind studies have been conducted with the aim of assessing guanfacine’s short- and long-term efficacy and safety. (32 References) EAF
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PEDIATRICS, 121:725-31, April 2008

According to data gleaned from agencies reporting child abuse and neglect allegations across the United States, nearly 900,000 children experience some form of maltreatment, and the overwhelming majority of them experience it in the form of neglect. Some studies have suggested that neglect in early childhood may be an important predictor of later aggressive behavior. The goal of the present investigation was to examine the association between early childhood neglect (birth to age 2 years) and later childhood aggression at ages 4, 6, and 8 years, as compared with the associations between aggressive behavior and early childhood abuse and between aggression and later abuse and neglect.

A prospective cohort of 1,318 predominantly at-risk children (639 boys, 679 girls), recruited from four United States cities and one southern state, were monitored from birth to 8 years of age. Maltreatment was determined through review of local child protective service records. The Modified Maltreatment Classification Scheme (MMCS) was the coding system used to classify maltreatment across all sites. The MMCS allows for precise definition of neglect (failure to provide and/or lack of supervision), physical abuse, sexual abuse, and emotional maltreatment. Maltreatment status was determined for four non-overlapping time intervals: from birth to a child's second birthday, from age 2 to the fourth birthday, from age 4 to the sixth birthday, and from age 6 to the eighth birthday. A hierarchical, linear model approach (a special case of general, linear, mixed modeling) was used to predict aggressive behavior, as reported by the child’s primary caregiver at ages 4, 6, and 8 years. Sixty percent of the children had been reported to social services for abuse, neglect, or abuse and neglect before age 4; 20.6% were reported for maltreatment between the ages of 4 and 6 years and 17.2%, between the ages of 6 and 8 years. Only early neglect (from birth to age 2) significantly predicted aggression scores. Early abuse, later abuse, and later neglect were not significantly predictive, nor were the interaction terms controlling for the potential addictive effect of having been reported for both abuse and neglect.

According to the authors, the current data suggest that child neglect experienced during the first two years of life may be a more important precursor of childhood aggression than later neglect or physical abuse experienced at any age. (46 References)
POSTTRAUMATIC STRESS SYMPTOMS MEDIATE THE RELATION BETWEEN CHILDHOOD SEXUAL ABUSE AND NONSUICIDAL SELF-INJURY

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Previous research consistently has demonstrated a strong relationship between childhood abuse and nonsuicidal self-injury (NSSI), the direct and deliberate destruction of body tissue in the absence of suicidal intent. However, an explanation of the pathway through which a history of childhood abuse might lead to engagement in NSSI is lacking. It has also been suggested that childhood abuse is related to posttraumatic stress disorder (PTSD) and that PTSD symptoms are associated with some specific functions of NSSI. In the present investigation, the authors examined two specific PTSD symptom clusters (reexperiencing and avoidance/numbing) as potential mechanisms through which childhood abuse might be related to NSSI.

The study sample was composed of 86 adolescents (67 females, 19 males; mean age, 17 years), all of whom completed measures of childhood abuse, PTSD symptomatology, and NSSI. Fifty six of the participants (45 females, 11 males) had engaged in some form of NSSI (e.g., cutting or carving skin, hitting self, picking wound, biting self). To differentiate the effects of abuse type on NSSI, the researchers coded abuse type into three groups. No abuse (N=26) indicated that the participant did not endorse the occurrence of emotional, physical, or sexual abuse. Nonsexual abuse (N=42) indicated endorsement of the occurrence of emotional and/or physical abuse but not sexual abuse. Sexual abuse (N=18) indicated endorsement of the occurrence of sexual abuse; within this group, emotional and/or physical abuse also may have been endorsed. Analyses revealed a significant relationship between childhood sexual abuse in particular and the presence and frequency of NSSI. Reexperiencing symptoms (which include intrusive images of trauma and physiological reactivity secondary to reexperiencing) and avoidance/numbing symptoms (which include efforts to avoid reminders of trauma and difficulty feeling positive emotions) independently mediated the association between childhood sexual abuse and NSSI.

According to the authors, the current findings indicate that retrospectively reported childhood sexual abuse is associated with NSSI during adolescence. The present study provides support for a model in which episodic reexperiencing and avoidance/numbing symptoms constitute specific mechanisms through which childhood sexual abuse is associated with the subsequent presence and severity of NSSI. (19 References)
FAMILIAL TRANSMISSION OF SUICIDAL BEHAVIOR: FACTORS MEDIATING THE RELATIONSHIP BETWEEN CHILDHOOD ABUSE AND OFFSPRING SUICIDE ATTEMPTS

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J CLIN PSYCHIATRY, 69:584-96, April 2008

Self-reported childhood sexual abuse is known to be associated with major depression and with suicidal behavior. In the present study, the authors attempted to explore the familial transmission of risk for suicidal behavior by examining the relationship between reported childhood abuse in biological parents diagnosed with major depressive disorder and the risk for suicidal behavior in their offspring.

In all, 507 offspring (245 females, 262 males) of 271 parent probands with DSM-IV major depressive disorder (231 females, 40 males) were compared according to reported childhood abuse history on a number of demographic, diagnostic, and clinical variables related to risk for suicidal behavior. Both self-report and clinical interview measures were used to assess history of childhood physical and sexual abuse. The study was conducted from May 1997 to February 2004. The results showed that reported childhood sexual abuse (but not physical abuse) in the parent probands was related to suicidality and other risk factors for suicide attempts both in the probands themselves and in their biological offspring. More specifically, reported childhood sexual abuse in probands was correlated with a greater likelihood of the proband having made at least one lifetime suicide attempt; having comorbid posttraumatic stress disorder (PTSD) and dysthymic disorder; having exhibited more severe lifetime impulsivity, hostility, and aggression; and having an earlier age at onset of major depressive disorder. The offspring of sexually abused probands were significantly more likely to have made at least one lifetime suicide attempt, to have been sexually abused themselves, to have a diagnosis of PTSD, and to have higher levels of impulsivity. However, sexual abuse was not directly transmitted from proband to offspring; perpetrators of offspring sexual abuse were more likely to be from outside the home. A reported history of childhood physical abuse in the probands was related to more lifetime aggression in the offspring.

The authors conclude that reported childhood sexual abuse is a risk factor for suicidal behavior in both parent and offspring. Transmission of suicide risk across generations appears to be related to the familial transmission of sexual abuse and impulsivity. (71 References)
MEDIATORS OF THE RELATIONSHIP BETWEEN CHILDHOOD SEXUAL ABUSE AND SUICIDAL BEHAVIOR IN BORDERLINE PERSONALITY DISORDER

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J PERSONAL DISORD, 22:221-32, June 2008

A history of childhood sexual abuse (CSA) is associated with suicidal ideation, self-injury, and suicidal behavior in psychiatric patients and in nonclinical adult populations. CSA is especially prevalent among adult patients with borderline personality disorder (BPD), reportedly occurring in 40% to 76% of this group. Individuals with BPD who have experienced CSA are 10 times more likely to have attempted suicide and to have more lifetime suicide attempts than nonabused individuals with BPD. Despite a clear association between childhood abuse, especially CSA, and suicidal behavior in adults with BPD, specific variables that mediate this relationship have not been clearly determined. In the present study, the authors examined risk factors for suicidal behavior as potential mediators of the relationship between CSA and suicide attempts in adults with BPD.

The study sample was composed of 151 participants (115 women, 36 men; age range, 18 to 50 years; mean age, 28.3 years). Diagnostic, clinical, and psychosocial risk factors, as well as CSA and suicidal behaviors, were assessed by means of standardized interviews or self-rated measures. Assessment tools included the Structured Clinical Interview for DSM-III-R, the International Personality Disorders Examination (IPDE), the Diagnostic Interview for Borderline Patients (DIB), and the Social Adjustment Scale-Self-Report (SAS). Sixty-four of the participants reported a history of CSA, and 118 had made at least one suicide attempt. Among suicide attempters, the number of lifetime attempts ranged from one to 21, with a mean of 4.2. CSA predicted both attempter status and number of lifetime suicide attempts. The IPDE schizotypal score mediated the relationship between CSA and attempter status. The IPDE schizotypal score, the DIB psychosis score, and the SAS-leisure score emerged as mediators of the association between CSA and number of lifetime suicide attempts. Even with these mediators included in regression models, however, CSA remained a significant predictor of suicidal behavior in all cases. Thus, psychotic and schizotypal symptoms and poor social adjustment only partially mediated the relationship between CSA and adult suicidal behavior.

The authors note that psychotic and schizotypal symptoms in persons with BPD define a vulnerability to cognitive and perceptual distortions under stress. They increase the likelihood of suicidal behavior in adults with BPD, especially in the absence of mitigating social support. (60 References)
ALEXITHYMIA AND CHILDHOOD ABUSE AMONG PATIENTS ATTENDING PRIMARY AND PSYCHIATRIC CARE: RESULTS OF THE RADEP STUDY

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PSYCHOSOMATICS, 49:317-25, July-August 2008

Some authors have suggested that the background of alexithymia is related to affective development during early childhood. In recent years researchers have addressed the relationship between adult alexithymia and various forms of abuse experienced during childhood. However, the results of studies concerning associations (if any) between alexithymia and childhood adversity so far seem to be inconsistent. In the present investigation, the authors studied the associations between alexithymia and childhood emotional neglect, sexual abuse, and physical abuse, while taking into account the significance of concomitant psychopathology.

The current study is part of the larger Raisio Depression (RADEP) Study, which deals with outpatients attending three primary care health centers (PC patients) and three community mental health centers (MH patients) in southwestern Finland. In 2005, one to two years after baseline, questionnaires were mailed to 1,033 PC patients and 243 MH patients. Information was elicited with regard to alexithymia; depressive, manic, and psychotic symptoms; and childhood difficulties. In all, 696 of the PC patients and 161 of the MH patients responded with the alexithymia measure (Toronto Alexithymia Scale) adequately filled in; they formed the sample of the present investigation. Among the PC patients, the prevalence of alexithymia was 17.7% in men and 8.9% in women. In the MH group, 44.9% of the men and 29.5% of the women were alexithymic. No clear association emerged between alexithymia and childhood adversities in the MH patients. However, among the PC patients, the alexithymia total score as well as difficulty in identifying feelings and difficulty in describing feelings were found to be associated with childhood emotional, sexual, and physical abuse. After psychopathology was controlled, there still remained an association between difficulty in identifying feelings and most abuse and neglect variables.

The authors conclude that in primary care patients, but not in psychiatric patients, alexithymia, especially its dimension of difficulty in identifying feelings, is significantly associated with childhood neglect and abuse, even when patients’ concomitant psychopathology is taken into account. These findings serve to strengthen the theory of alexithymia as a developmental process that begins in childhood. (45 References)
CHILDHOOD SEXUAL ABUSE AND EATING DISORDERS IN FEMALES
Findings From the Victorian Adolescent Health Cohort Study

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ARCH PEDIATR ADOLESC MED, 162:261-7, March 2008

Clinicians have long suspected that childhood sexual abuse (CSA) has a causal relationship with eating disorders. However, epidemiological and empirical studies have failed to provide consistent evidence for this association. In the present investigation, the authors examined the relationship between CSA experienced before the age of 16 years and the onset of bulimia and anorexia nervosa symptoms in later adolescence in females.

Between August 1992 and March 2003, the researchers conducted an eight-wave longitudinal cohort study of adolescent and young adult health in Victoria, Australia. The cohort was defined in a two-stage cluster sample, in which two classrooms of 20 to 30 children were randomly selected from each of 44 schools drawn from a stratified frame of government, Catholic, and independent schools. A total of 1,936 persons participated at least once and survived to the age of 24 years, including 999 females. The mean age of the females at the start of follow-up was 14.91 years, and at completion, 24.03 years. Incident DSM-IV-defined partial syndromes of anorexia and bulimia were identified between wave 4 (mean age, 16.3 years) and wave 6 (mean age, 17.4 years) by means of the Branched Eating Disorder Test. Self-reported CSA experienced before the age of 16 years was ascertained retrospectively at the age of 24 years. After adjusting for age and background factors, the authors found that females who reported two or more episodes of CSA were almost five times more likely to develop bulimic syndrome during adolescence than females who reported no CSA. The association between CSA and bulimic syndrome persisted after adjustments were made for possible confounders or mediators measured six months earlier, including psychiatric morbidity and dieting behavior. There was only equivocal evidence of an association between a report of multiple episodes of CSA and the partial syndrome of anorexia nervosa.

The authors conclude that CSA appears to be a risk factor for the development of bulimic disorders in young females. The researchers suggest that developing less impulsive strategies for dealing with difficult emotions may be an important facet of efforts to prevent eating disorders or reduce their impact in female adolescents with a history of CSA. (36 References)
CHILDHOOD ABUSE, NONADHERENCE, AND MEDICAL OUTCOME IN PEDIATRIC LIVER TRANSPLANT RECIPIENTS

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 46:1280-9, October 2007

Psychosocial evaluations are an integral part of the routine pretransplantation evaluation procedure for solid organ transplant recipients. While the long-term sequelae of child abuse have been well documented, only a few studies have prospectively examined the possible associations between a history of child abuse, medication adherence, and poor medical outcome in patients with a life-threatening condition. In the present investigation, the authors assessed the relationships between a history of child abuse, nonadherence to medications, and medical outcome in children and adolescents who had received a liver transplant.

Patients were eligible for the study if they were between eight and 21 years of age at the time of assessment and had undergone liver transplantation at Mount Sinai Medical Center in New York six months or more before the evaluation. Evaluations took place in 2002, with abuse history being obtained by direct questioning of the child and parent and by review of pre- and posttransplantation psychosocial assessment records. Adherence to tacrolimus was assessed from January 1 to December 31 of 2003 by computing the SD of a series of medication blood levels for each patient. Biopsy-proven rejection episodes, degree of fluctuation of alanine aminotransferase (ALT), and maximal ALT levels were recorded as indicators of medical outcome. Of 72 eligible patients, 56 were evaluated. Five (four females, one male) had a documented history of child abuse. Compared with patients with no history of abuse, the abused children were significantly less adherent to their medication regimen, had poor disease control (higher maximal ALT), had greater fluctuations in ALT levels, and suffered more biopsy-proven rejection episodes in 2003 (two episodes in the abused cohort versus none in the nonabused group).

The authors conclude that a history of child abuse is a significant risk factor for poor outcome in transplant recipients and should be routinely evaluated. Special attention should be allotted to medication adherence in pediatric transplant recipients with a history of child abuse. (37 References)
CHILDHOOD MALTREATMENT AND EARLY ALCOHOL USE AMONG HIGH-RISK ADOLESCENTS

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Child maltreatment is believed to be prevalent among youth in the United States and has been identified as a predictor of subsequent maladaptive behaviors, including substance use. Several retrospective studies of adult reports of experiencing physical and sexual abuse before the age of 18 years have found that victimization is associated with problematic alcohol use in adolescence and adulthood. However, few studies have employed more proximal assessments to determine the link between child maltreatment and first alcohol use. The present authors examined the association between early child maltreatment and (1) preteen alcohol-use initiation and (2) heavy episodic drinking among students enrolled in a large epidemiologic study of adolescents.

Data were gathered from the Youth Violence Survey, a cross-sectional survey of all public school students enrolled in grades 7, 9, 11, and 12 in a school district located in a high-risk community (i.e., a community with high levels of poverty, unemployment, and serious crimes). The analysis sample (N=3,559) was limited to those students who provided complete information on all relevant variables and was composed of 1,849 girls and 1,710 boys. Early child maltreatment was defined as witnessing domestic violence, experiencing physical abuse, and/or experiencing sexual abuse before the age of 10 years. Outcome variables included ever drinking alcohol, preteen alcohol-use initiation, and heavy episodic drinking. Of the participants, 44% reported child maltreatment and 59% reported ever drinking alcohol. Witnessing domestic violence, experiencing physical abuse, and experiencing sexual abuse were significantly associated with preteen alcohol-use initiation (adjusted odds ratio [AOR] = 1.55, 95% confidence interval [CI]: 1.26-1.91; AOR = 2.10, 95% CI: 1.69-2.63; AOR = 1.57, 95% CI: 1.16-2.14, respectively). Students who experienced one or more types of child maltreatment were 1.5-3 times more likely to report preteen alcohol-use initiation. Heavy episodic drinking was found to be associated only with childhood sexual abuse in boys (AOR = 2.62, 95% CI: 1.52-4.50).

According to the authors of the current investigation, child maltreatment experienced in early childhood (before the age of 10 years), is associated with both early alcohol use and heavy episodic drinking. Prevention and treatment of the negative impact of early child maltreatment may serve to delay and reduce alcohol use. (28 References)
THREE POTENTIAL MEDIATORS OF THE EFFECTS OF
CHILD ABUSE AND NEGLECT ON ADULTHOOD
SUBSTANCE USE AMONG WOMEN

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Some studies have found that stress experienced in childhood can have
lasting effects and may influence substance use in adulthood. One stressor of
particular concern is childhood maltreatment, with many reports providing
support for a relationship between child abuse and later substance abuse.
However, few prospective studies of the effects of childhood maltreatment on
substance use have followed individuals into middle adulthood. In the
investigation presented here, the authors examined mechanisms that might
account for the association between early childhood abuse/neglect and
substance use and related problems in adult women. They hypothesized that
posttraumatic stress disorder (PTSD), life stressors, and delinquent/criminal
behavior measured in young adulthood would each independently mediate the
effects of early childhood abuse and neglect on substance use and related
problems in middle adulthood.

Data were gleaned from a cohort design study in which abused and neglected
children were matched with non-abused and non-neglected children and
followed prospectively into adulthood. In all, 582 women with court-documented
cases of early childhood abuse and/or neglect (occurring before the age of 12
years) and matched controls were interviewed in young adulthood (average age,
29 years) and again in middle adulthood (average age, 40 years). The researchers
evaluated the mediating effects of PTSD symptoms, stressful life events, and
delinquent and criminal behavior assessed in young adulthood on substance
use-related problems and illicit drug use measured in middle adulthood. The
results indicated that abuse and neglect in childhood predicted higher levels of
drug use and related problems in middle adulthood. PTSD, stressful life events,
and delinquent/criminal behavior partially mediated the effects of child abuse
and neglect on later illicit drug use and substance-use problems. However, when
all three mediators were considered simultaneously, the authors found that
PTSD remained the only significant partial mediator for illicit drug use, and
stressful life events remained the only significant partial mediator for substance
use-related problems.

Early interventions are needed with maltreated girls in order to recognize and
attend to PTSD symptoms and help them develop constructive strategies for
coping with stressful life events. (111 References)
THE DEXAMETHASONE/CORTICOTROPIN-RELEASING FACTOR TEST IN MEN WITH MAJOR DEPRESSION: ROLE OF CHILDHOOD TRAUMA

Christine Heim (Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, 101 Woodruff Circle, WMRB, Suite 4311, Atlanta, GA 30322; e-mail: cmheim@emory.edu); Tanja Mletzko; David Purselle; Dominique L. Musselman; and Charles B. Nemeroff


The combined dexamethasone/corticotrophin-releasing factor (CRF) test is considered to be the most sensitive measure of hypothalamic-pituitary-adrenal (HPA) axis hyperactivity and has been demonstrated to be altered in patients with major depression (MDD). Although childhood trauma is a known risk factor for MDD and patients with a history of childhood abuse and MDD demonstrate HPA hyperactivity, the dexamethasone/CRF test remains unstudied in this population. The authors of the present study attempted to determine the impact of childhood trauma on dexamethasone/CRF test results in patients with MDD.

Forty-nine healthy, medication-free men (age range, 18 to 60 years), without mania, psychosis, active substance abuse, or eating disorder, were recruited into the following four study groups: (1) normal control subjects with no childhood abuse history or psychiatric disorder (N=14); (2) men with a history of childhood abuse but without current MDD (N=14); (3) men with a history of childhood abuse and with current MDD (N=15); and (4) men with current MDD but with no childhood abuse history (N=6). There were no differences between the groups in terms of age, body mass index, or racial distribution. The presence or absence of childhood trauma was assessed with the Early Trauma Inventory. Other assessment tools included the Structured Clinical Interview for DSM-IV, the Hamilton Rating Scale for Depression 21-Items Version, the Clinician Administered PTSD scale, and the Life Event Survey. Plasma adrenocorticotropin (ACTH) and cortisol concentrations were measured in response to dexamethasone/CRF administration. The results showed that compared with non-abused men, men with histories of childhood trauma exhibited increases in ACTH and cortisol responses to dexamethasone/CRF. In particular, abused men with current MDD showed increased responsiveness as compared with normal control subjects and depressed men without childhood abuse experience. Increased response was associated with severity, duration, and earlier onset of the childhood abuse. The effects were not explained by the presence of concurrent posttraumatic stress disorder.

Childhood trauma increases HPA activity as measured with the dexamethasone/CRF test in adult men with MDD, potentially reflecting environmental risk for developing depression. (56 References)
BOOKS RECEIVED FOR REVIEW


Sleep Medicine, edited by Harold R. Smith, Cynthia L. Comella, and Birgit Högl. Cambridge University Press, 2008. 270 pages, $70.00 (paperback).
IN MEMORIAM

Charles W. Boren, M.D.
June 3, 1934 – March 28, 2008

It is with great sadness that we inform our readers of the passing of Dr. Charles W. Boren, former Psychiatrist-in-Chief of The Institute of Living and Editor of The Digest of Neurology and Psychiatry, in the spring of this year following an automobile accident in Hanover, New Hampshire.

A graduate of the Washington University School of Medicine in St. Louis, Missouri, Dr. Boren completed a rotating internship at St. Luke’s Hospital, and a residency in psychiatry at The Institute of Living in Hartford, Connecticut in 1964. With the exception of serving two years as a staff psychiatrist in the U.S. Navy from 1964-1966, the remainder of his career was spent at The Institute until his retirement in 1994. During this time, he served in a number of positions ranging from Staff Psychiatrist to Director of Psychiatric Education to Medical Director and, finally, to Psychiatrist-in-Chief.

He was honored by the residents in psychiatry when he was selected as the first recipient of the “Golden Lamp Award” for excellence in and dedication to teaching in 1974. He also held an academic appointment in the Department of Psychiatry at the University of Connecticut School of Medicine, first as an Associate Professor of Psychiatry from 1979-1991, then as Professor of Psychiatry from 1991-1994. Board-Certified in Psychiatry by the American Board of Psychiatry and Neurology, Charlie later served as an Examiner for the Board for many years. In addition to serving as Executive Secretary of the American Association of Directors of Psychiatric Residency Training (AADPRT), he was elected to Fellowship in the American College of Psychiatrists, the American Psychiatric Association, and was active in numerous state and local professional organizations.

Dr. Boren was dedicated to the care of patients and devoted to The Institute of Living and his fellow staff members and was mentor and friend to many. A worthy colleague and friend, he truly epitomized the meaning of the word physician. He is deeply missed.

Harold I. Schwartz, M.D.
Psychiatrist-in-Chief
Editor
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**BOOKS RECEIVED FOR REVIEW**
ASSOCIATION BETWEEN EXPOSURE TO CHILDHOOD AND LIFETIME TRAUMATIC EVENTS AND LIFETIME PATHOLOGICAL GAMBLING IN A TWIN COHORT

Jeffrey F. Scherrer, PhD (Washington University School of Medicine, Midwest Alcoholism Research Center, Department of Psychiatry, Campus Box 8134, 660 South Euclid, St. Louis, MO 63110); Hong Xian, PhD; Julie M. Krygiel Kapp, PhD; Brian Waterman, MPH; Kamini R. Shah, MHS; Rachel Volberg, PhD; and Seth A. Eisen, MD, MSc

J NERV MENT DIS, 195:72-8, January 2007

Very little is known about the association between traumatic life events and gambling problems. In the present study, the authors sought to estimate the strength of the association between exposure to lifetime traumatic events and gambling problems while accounting for the potential contribution of psychiatric disorders, genetic factors, and family environmental influences. The researchers hypothesized that childhood and lifetime traumatic events would be associated with problem gambling and pathological gambling, and that genetic and/or family environmental factors would partially explain the association between exposure to trauma and one or more symptoms of problem gambling.

In 2002, structured diagnostic interviews were conducted with 1,675 male twins in order to obtain information on exposure to traumatic events and pathological gambling. Respondents were between 45 and 60 years of age at the time of data collection, and they were asked if they had experienced any of the following: (1) life-threatening accident; (2) fire, flood, or natural disaster; (3) witnessing someone being badly injured or killed; (4) rape; (5) sexual molestation; (6) serious physical attack or assault; (7) physical abuse as a child; (8) serious neglect as a child; and (9) being threatened with a weapon, held captive, or kidnapped. Multinomial regression was used to analyze associations between each traumatic event and three levels of gambling behavior: at-risk gambling (1-2 symptoms), problem gambling (3-4 symptoms), and pathological gambling (5 or more symptoms). Analyses of data from twin pairs discordant for gambling behavior controlled for genetic and family environmental factors. The results showed that, after adjustment for covariates, being abused as a child (relative risk [RR]=2.31), being neglected as a child (RR=5.53), witnessing someone being badly hurt or killed (RR=2.83), and experiencing physical attack (RR=3.39) were associated with pathological gambling. Genetic and family environmental factors contributed significantly to the association between exposure to traumatic events and one or more symptoms of problem gambling.

The authors conclude that childhood and lifetime traumatic events are significantly associated with problem and pathological gambling. These associations are partially accounted for by psychiatric covariates and by genetic and family environmental factors. (29 References)
EPIDEMIOLOGY OF YOUTH GAMBLING PROBLEMS IN CANADA: A NATIONAL PREVALENCE STUDY

Jiun-Hau Huang, SM, ScD (Social Psychiatry Unit, Fernand-Seguin Research Centre, Louis-H Lafontaine Hospital, 7331 rue Hochelaga [Unit 218], Montreal, QC H1N 3V2, Canada; e-mail: jiun-hau.huang@umontreal.ca); and Richard Boyer, MA, PhD CAN J PSYCHIATRY, 52:657-65, October 2007

Youth gambling problems have become a significant public health issue, especially in light of the widespread expansion of legalized gambling in the United States and Canada. Earlier studies have indicated that an estimated 15.3 million adolescents in North America have engaged in gambling activities and that 2.2 million of these are problem or pathological gamblers. In the present investigation, the authors describe the epidemiology of gambling problems among young people in Canada (age range, 15 to 24 years) and determine whether gambling prevalence patterns differ by sex and/or geographic region.

Data for the study were drawn from the Canadian Community Health Survey: Mental Health and Well-Being (CCHS 1.2), a cross-sectional, national survey of Canadians who were 15 year of age and older and living in private dwellings throughout the Canadian provinces. Conducted by Statistics Canada between May and December of 2002 through the use of computer-assisted interviewing, the CCHS 1.2 had an overall response rate of 77%. Gambling problems were determined according to the Canadian Problem Gambling Index. All prevalence estimates used appropriate sampling weights and bootstrap variance estimation procedures developed by Statistics Canada. Multiple logistic regression modeling was employed to supplement prevalence comparisons by age, sex, and region. The results showed that among young Canadians between the ages of 15 and 24 years (N=5,666), 61.35% had gambled in the past 12 months; the national prevalence of moderate-risk or problem gambling was 2.22% (3.30% in male respondents and 1.10% in female respondents). Male respondents had a significantly higher prevalence of gambling problems than female respondents. Regional prevalence estimates of moderate-risk or problem gambling among Canadian youth were 1.37% in British Columbia, 2.17% in the Prairie provinces, 2.75% in Ontario, 2.12% in Quebec, and 1.71% in the Atlantic provinces.

According to the authors, the current findings indicate that Canadian youth between the ages of 15 and 24, particularly young men, are at greater risk for gambling problems than adults who are 25 years of age or older. More prevention and research efforts are needed to address the sex differences and interregional variability observed in the prevalence of gambling problems among young Canadians. (34 References)
A LATENT CLASS ANALYSIS (LCA) OF PROBLEM GAMBLING AMONG A SAMPLE OF COMMUNITY-RECRUITED GAMBLERS

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While rates of problem gambling in the general population are relatively low (2%-4%), problem gamblers experience multisystemic negative consequences, high comorbidity, and low treatment utilization. Using community advertising and telephone screening, the present authors recruited a diverse sample of lifetime gamblers (N=312) for a psychometric study of the newly developed Computerized-Gambling Assessment Module. The respondents (138 males, 174 females) ranged in age from 15 to 85 years (mean, 46.8 years). Latent Class Analysis enumerated and classified gambling subgroups by distinctive gambling patterns, on the basis of eight composite scales functioning as validators of latent class membership (i.e., diagnostic gambling symptoms, reasons for gambling, gambling “withdrawal-like” symptoms, problem gambling perceptions, gambling venues, financial sources for gambling, gambling treatment/help-seeking, and religiosity/spirituality.

Despite consistencies in classes of gamblers, the researchers found that a six-class solution was the best fitting model. Of the hypothesized eight factors used to measure problem gambling behaviors, the distinguishing clustering pattern of gambling was driven by the following six factors: number of diagnostic DSM/ICD-derived gambling symptoms, number of different reasons to gamble, number of gambling “withdrawal-like” symptoms, number of financial sources for gambling, number of different sources of perceived problem gambling, and number of gambling treatment/help-seeking sources that were endorsed. Of the six latent classes observed, Class 1 comprised over 57% of the study sample and was composed of nonproblem gamblers. Class 2 (low-risk gamblers) represented 3.5% of the sample; Class 3 (mild-risk gamblers), 12.2%; Class 4 (moderate-risk gamblers), 8.7%; Class 5 (high-risk gamblers), 12.2%; and Class 6 (severe-risk gamblers), 6.4%.

According to the authors, gambling severity is most strongly characterized not only by symptomatology but also by the number of gambling treatment/help-seeking sources used. The gambling typology supported by the current findings expands the understanding of the multifaceted nature of gambling pathology and also has direct clinical implications for prevention and intervention efforts that are specifically tailored for those gamblers who are at risk for impaired gambling behaviors. (44 References)

EAF
THE ROLE OF SELF-REPORTED IMPULSIVITY AND REWARD SENSITIVITY VERSUS NEUROCOGNITIVE MEASURES OF DISINHIBITION AND DECISION-MAKING IN THE PREDICTION OF RELAPSE IN PATHOLOGICAL GAMBLERS

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PSYCHOL MED, 38:41-50, January 2008

Disinhibition (the tendency to act upon acute impulses) and decision-making skills play an important role in theories on the causes and outcomes of addictive behaviors such as substance abuse and pathological gambling. In recent studies, both disinhibition and disadvantageous decision-making strategies, as measured by neurocognitive tests, were found to influence the course of substance use disorders. However, there is very little research on the factors that may influence relapse in pathological gamblers. The authors examined the effects of the following on relapse in a group of pathological gamblers: (1) self-reported impulsivity and reward sensitivity, and (2) neurocognitively assessed disinhibition and decision-making under conflicting contingencies.

The study sample was composed of 46 adult outpatients (37 males, nine females) who, at baseline, had abstained from gambling for less than three months. All underwent cognitive behavioral treatment for pathological gambling. Relapse was evaluated through telephone interviews held approximately one year after baseline assessment; 24 of the pathological gamblers were considered to be relapers (20 males, four females), and 22 (17 males, five females) were categorized as non-relapers. Logistic regression analysis revealed that longer duration of the gambling disorder and neurocognitive indicators of disinhibition (Stop Signal Reaction Time) and decision-making (Card Playing Task) were significant predictors of relapse (explaining 53% of the variance in relapse), while self-reported impulsivity and reward sensitivity did not significantly predict relapse. The overall classification accuracy was 76%, with a positive predictive accuracy of 76% (relapers correctly classified in the relapse group) and a negative predictive accuracy of 75% (non-relapers correctly classified in the non-relapse group).

The current data indicated that two endophenotypical measures of disinhibition and abnormal decision-making under conflicting contingencies were predictive of relapse in pathological gamblers, while phenotypical (self-report) measures were not. The assessment of neurocognitive functions may be useful not only for identifying and targeting pathological gamblers at risk for relapse but also for improving the efficacy of treatment in those with neurocognitive deficits. (75 References)
PATHOLOGICAL GAMBLERS DEMONSTRATE
FRONTAL LOBE IMPAIRMENT CONSISTENT WITH THAT
OF METHAMPHETAMINE-DEPENDENT INDIVIDUALS

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J NEUROPSYCHIATRY CLIN NEUROSCI, 19:298-303, Summer 2007

Pathological gambling has become a major public health concern. Prevalence
rates range from 2.5% to 10%, and its legal and social consequences include
bankruptcy, incarceration, domestic violence, and divorce. While much of the
research on pathological gambling has focused on its social consequences,
recent studies have attempted to determine whether the disorder is associated
with neurobiological dysfunction and whether such dysfunction is similar to that
seen in individuals with substance use disorders. Using tests frequently
administered by neuropsychologists, the authors of the present investigation
sought to determine whether pathological gambling is associated with frontal
lobe abnormalities.

The sample was composed of 10 non-treatment-seeking pathological
gamblers (nine males, one female), 25 non-treatment-seeking
methamphetamine-dependent individuals (18 males, seven females), and 19
comparison subjects (15 males, four females) who were neither pathological
gamblers nor methamphetamine-dependent. All participants were administered
the following measures of frontal lobe functioning: the Ruff Figural Fluency Test,
the Stroop Color-Word Test, and the Trail-Making Test, Part B. The pathological
gamblers, methamphetamine-dependent volunteers, and healthy comparison
subjects did not differ in terms of gender, education, estimated premorbid
intellectual functioning, or severity of self-reported depressive symptomatology.
However, multivariate analysis of variance revealed that the three groups
differed significantly with respect to their performance on measures of frontal
lobe functioning. The pathological gamblers performed significantly less well
than the comparison subjects on each of the three frontal lobe measures. The
performance of the pathological gamblers was similar to that of the
methamphetamine users on the Ruff Figural Fluency Test and the Stroop Color-
Word Test but was significantly worse than that of the methamphetamine users
on the Trail-Making Test, Part B. Overall magnitude of the effect size was large.

According to the authors, the current findings appear to be the first to
demonstrate that pathological gambling is associated with impairments across a
range of timed measures that are frequently used by neuropsychologists for the
purpose of documenting frontal lobe dysfunction. (32 References)
KNOWING WHEN TO STOP:
THE BRAIN MECHANISMS OF CHASING LOSSES

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Continued gambling to recover previous losses is frequently seen in both recreational and pathological gamblers. This behavior, known as “loss-chasing,” is strongly associated with impaired control over gambling behavior and is central to the development of pathological gambling. Despite this fact, very little is known about the neural mechanisms that mediate loss-chasing behavior. In the present study, the authors used functional magnetic resonance imaging to examine neural activity in healthy adults while they decided whether to chase losses or to quit gambling in order to prevent further losses. The researchers hypothesized that decisions to chase losses depend upon activity in neural pathways that are involved in the representation of reward expectancy, including the ventromedial prefrontal cortex; whereas decisions to quit chasing losses depend upon activity in neural circuits that are involved in visceral arousal and the anticipation of aversive consequences, including the dorsal anterior cingulate and the insula cortices.

Twenty-three healthy, right-handed, adult volunteers (13 men, 10 women; mean age, 25.68 years) were recruited for the study. They completed the South Oaks Gambling Screen, the Gambling Related Cognitions Scale, and an adapted 14-item questionnaire that provided an independent assessment of their propensity to chase in other gambling activities. All participated in a loss-chasing game. This consisted of 60 rounds of loss-chasing, each with a minimum of one and a maximum of six choices. At the beginning of each round, a loss was imposed and a decision made either to play (gamble further) or to quit (accept the loss) and end the round. Chasing losses was found to be associated with increased activity in cortical areas linked to incentive-motivation and an expectation of reward. On the other hand, quitting was associated with decreased activity in these areas but with increased activity in areas associated with anxiety and conflict monitoring. Activity within the anterior cingulate cortex associated with the experience of chasing and then losing predicted decisions to stop chasing losses at the next opportunity.

The authors conclude that the excessive loss-chasing behavior observed in pathological gamblers may involve a failure to appropriately balance activity within neural systems involved in coding conflicting motivational states. Similar mechanisms may underlie the loss-of-control over appetitive behaviors seen in other impulse control disorders. (53 References)
N-ACETYL CYSTEINE, A GLUTAMATE-MODULATING AGENT, IN THE TREATMENT OF PATHOLOGICAL GAMBLING: A PILOT STUDY

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Pathological gambling (PG), a significant public health problem, is associated with impaired functioning, reduced quality of life, and high rates of bankruptcy and divorce. At the present time, there is no treatment for PG that has been approved by the Food and Drug Administration, despite almost a decade of intense research. N-acetyl cysteine (NAC), an amino acid and cysteine pro-drug, seems to restore extracellular glutamate concentration in the nucleus accumbens and therefore offers promise in reducing addictive behavior. The present authors conducted a pilot study in order to examine the tolerability and efficacy of NAC in the treatment of PG. They hypothesized that on the basis of NAC’s potential to reduce drug cravings, it would reduce gambling cravings as well as the gambling behavior that results from cravings in individuals with PG.

Twenty-seven subjects (15 men, 12 women; age range, 21 to 65 years; mean age, 50.8 years) who met DSM-IV criteria for PG were treated in an eight-week, open-label trial of NAC. The primary outcome measure was the Yale Brown Obsessive Compulsive Scale Modified for Pathological Gambling (PG-YBOCS), with “response” being defined as a 30% or greater reduction in PG-YBOCS total score at end point compared with baseline. Subjects who “responded” to open-label NAC entered a six-week, double-blind phase and were randomly assigned to receive NAC or placebo. Scores on the PG-YBOCS decreased from a mean of 20.3 at baseline to 11.8 at the end of the open-label phase. Sixteen (59.3%) of the 27 subjects met responder criteria. Of the 16 responders, 13 entered the double-blind phase, with six being randomized to NAC and seven, to placebo. Of those assigned to receive NAC, 83.3% still met responder criteria at the end of the double-blind phase, as compared with only 28.6% of those assigned to receive placebo.

According to the authors, the efficacy of NAC demonstrated in the current pilot study lends support to the hypothesis that pharmacological manipulation of the glutamate system might target core symptoms of reward-seeking addictive behaviors such as gambling. However, given the open-label design of the current investigation and the small number of participants, the interpretation of the efficacy results is limited. Larger, longer, placebo-controlled, double-blind studies are needed. (37 References)
OLANZAPINE IN THE TREATMENT OF PATHOLOGICAL GAMBLING: A NEGATIVE RANDOMIZED PLACEBO-CONTROLLED TRIAL

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Pathological gambling, an important public health problem, is associated with bipolar disorder and dopamine dysfunction. A growing number of double-blind, placebo-controlled studies have suggested that pharmacotherapy may be helpful for some patients with pathological gambling. Olanzapine is a second-generation antipsychotic with mood-stabilizing properties and antagonistic activity at several dopamine receptors. The purpose of the present investigation was to evaluate the safety and efficacy of olanzapine in the treatment of individuals with pathological gambling.

In this 12-week, single-center, randomized, double-blind, placebo-controlled, flexible-dose (2.5-15 mg/day) trial, 42 outpatients who met DSM-IV-TR criteria for pathological gambling received olanzapine (N=21) or placebo (N=21). The primary outcome measure was the Pathological Gambling Adaptation of the Yale-Brown Obsessive Compulsive Scale (PG-YBOCS). The primary analysis of efficacy was a longitudinal analysis of the intent-to-treat sample, with treatment-by-time interaction as the effect measure. Forty subjects (20 receiving olanzapine and 20 receiving placebo) had at least one post-randomization efficacy measure. Eleven (52.4%) in the olanzapine group and six (28.6%) in the placebo group did not complete all 12 weeks of treatment. Five subjects discontinued prematurely because of adverse events (three from the olanzapine group and two from the placebo group); four because of lack of efficacy (three on olanzapine, one on placebo); and eight because of difficulties with protocol adherence (five on olanzapine, three on placebo). Of the remaining 25 subjects who completed 12 weeks of treatment, 10 were receiving olanzapine and 15 were on placebo. Compared with placebo, olanzapine was associated with a similar rate of reduction in total PG-YBOCS scores, as well as in gambling episodes/week, hours spent gambling/week, and Clinical Global Impressions-Severity of Illness scale scores. The mean daily dose of olanzapine at endpoint was 8.9 mg/day.

The authors conclude that olanzapine was not found to be superior to placebo in reducing gambling symptoms, gambling frequency, or severity of illness. In addition, it was associated with only a fair degree of tolerability and a relatively high treatment discontinuation rate. (52 References)
12-MONTH FOLLOW-UP STUDY OF DRUG TREATMENT IN PATHOLOGICAL GAMBLERS
A Primary Outcome Study

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Pathological gambling (PG), a relatively common and highly disabling impulse control disorder, shares features with obsessive-compulsive spectrum disorder, other impulse control disorders, and addictive disorders. In previous studies, a wide range of pharmacological agents, including selective serotonin reuptake inhibitors, antiepileptic drugs, and opioid antagonists, have proven to be effective in the short-term treatment of PG. In the present naturalistic, long-term, follow-up outcome study, the authors assessed the rate of relapse in a group of pathological gamblers after the discontinuation of active treatment.

The sample was composed of 43 male pathological gamblers (age range, 19 to 69 years) who had responded fully to one of four drug treatment regimens (fluvoxamine, topiramate, bupropion SR, or naltrexone) in several previous acute open-label (12-week) comparison studies. Full response was defined as the absence of gambling for a duration of one month in addition to improvement on the Clinical Global Impressions Improvement scale. These full responders were then followed prospectively for an additional nine-month period, which included a three-month open-label drug continuation phase and a six-month medication-free follow-up phase. Follow-up visits were performed monthly throughout the course of the study. At every follow-up visit, a comprehensive psychiatric diagnostic evaluation was performed on all patients, the Clinical Global Impression Improvement scale was administered, and symptoms of gambling were assessed by means of a self-report instrument and collateral family reports. Most patients did not relapse during the six-month, medication-free, follow-up phase, with relapse being strictly defined as the occurrence of gambling behavior at any time during this medication-free follow-up. Three of six patients who had been on fluvoxamine (50%), three of nine who had received topiramate (33%), seven of 18 who had been on bupropion SR (39%), and four of 10 who had been on naltrexone (40%) relapsed during the medication-free follow-up.

According to the authors, the current results indicate that, for a significant number of pathological gamblers, a six-months’ response to active drug treatment may be associated with sustained remission after discontinuation of the drug. The researchers suggest that the mechanism of this remission may be related to changes in central nervous system neurotransmitters or changes in neuromotivational pathways. (25 References)
Both problem gambling and pathological gambling are associated with financial problems, psychiatric distress, and poor health. Problem gamblers spend a median of about $400 per month on gambling, while pathological gamblers typically wager $2,000 or more each month. However, limited research exists with regard to methods for reducing problem gambling, and few problem or pathological gamblers seek treatment. In the current study, the authors evaluated the efficacy of three brief interventions for the treatment of problem gambling: (1) one session consisting of 10 minutes of brief advice, (2) one session of motivational enhancement therapy (MET), or (3) a four-session intervention that consisted of one session of MET plus three sessions of cognitive-behavioral therapy. Each of these three interventions was compared with an assessment-only control condition.

The study sample was composed of 180 problem gamblers who were randomly assigned as follows: 48 to the assessment-only control condition, 37 to brief advice, 55 to MET, and 40 to MET plus cognitive-behavioral therapy. Gambling was assessed at baseline, at six weeks, and at nine-month follow-up. Of those assigned to assessment only, 47 completed the Week 6 evaluation, and 42 completed the Month 9 evaluation. Of those assigned to brief advice, 35 completed the Week 6 evaluation, and 31, the Month 9 evaluation. Of those allocated to MET, 52 completed the Week 6 evaluation, and 48, the Month 9 evaluation. Of those allocated to receive MET plus cognitive-behavioral therapy, 38 completed the Week 6 evaluation, and 34, the Month 9 evaluation. Relative to assessment only, brief advice was the only condition that significantly decreased gambling between baseline and Week 6, and it was associated with clinically significant reductions in gambling at Month 9. Compared with the assessment-only control condition, MET plus cognitive-behavioral therapy was found to be associated with significantly reduced gambling on one measure between Week 6 and Month 9.

According to the authors, the current data suggest that screening for gambling problems, especially in high-risk populations such as substance abusers and general medical patients, may uncover fairly high proportions of problem gamblers. A very brief and directive intervention may assist in reducing gambling problems among these individuals. (66 References)
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STRIATAL FUNCTION IN GENERALIZED SOCIAL PHOBIA:
A FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY

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BIOL PSYCHIATRY, 61:396-404, February 1, 2007

Generalized social phobia (GSP), also known as social anxiety disorder, is characterized by an excessive or unreasonable fear of social interactions in which an individual anticipates being negatively evaluated by others. In persons with GSP, social fears usually begin during childhood or adolescence and often persist into adulthood. Information biases in those with GSP may include an excessively negative interpretation of external social events, an enhanced detection of negative responses from other people, an imbalance of attention between external and self processing, and an exaggerated recall of negative aspects of an event. Although some neurobiological investigations point to the involvement of the amygdala in GSP, few have examined other neural regions. Clinical, preclinical, and dopamine receptor imaging studies that have found altered dopaminergic functioning in GSP are suggestive of an association between the disorder and striatal dysfunction. To the best of the authors’ knowledge, the present report is the first functional magnetic resonance imaging (fMRI) study to examine the neural correlates of GSP during the performance of a cognitive task that was not aimed at inducing anxiety or engaging emotional systems. The researchers attempted to determine whether subjects with GSP and healthy controls displayed different activation in striatal regions while engaged in a cognitive task (Serial Reaction Time) that has been shown to reliably activate striatal regions.

Ten adult, unmedicated subjects with a primary DSM-IV diagnosis of GSP (six women, four men; mean age, 29.1 years) and 10 age-, gender-, and education-matched healthy comparison subjects (six women, four men; mean age, 28.4 years) underwent fMRI while performing the implicit sequence learning task. The results showed that the GSP and the comparison subjects did not differ significantly on the behavioral performance of the task. However, as compared with the healthy controls, the GSP subjects displayed significantly reduced neural activation related to implicit learning in the left caudate head, the left inferior parietal lobe, and the bilateral insula.

In accordance with previous findings of altered dopaminergic function in persons with GSP, the current study found evidence of striatal dysfunction. The authors hypothesize that abnormal left caudate functioning may contribute to the information biases observed in GSP. (76 References)
A FAMILY STUDY OF CO-MORBIDITY BETWEEN GENERALIZED SOCIAL PHOBIA AND GENERALIZED ANXIETY DISORDER IN A NON-CLINIC SAMPLE

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J AFFECT DISORD, 100:103-13, June 2007

While high rates of comorbidity between generalized social phobia (GSP) and generalized anxiety disorder (GAD) have been found in both clinic-based and community-based samples, the reason for this finding remains unclear. In the family aggregation study presented here, the authors examined six models of comorbidity between GSP and GAD in a nonclinical sample of female probands and their first-degree relatives (16 years of age or older).

The study sample was composed of 115 probands and 403 of their first-degree relatives (115 mothers, 111 fathers, 97 brothers, and 80 sisters). Psychiatric data were obtained on probands and relatives by means of both direct and family history interviews. Of the 115 probands, 37 had GSP but no lifetime history of GAD, 22 had GAD but no lifetime history of GSP, 15 had comorbid GSP/GAD, and 41 had no lifetime history of GSP or GAD (controls). Of the 403 first-degree relatives, 130 were related to probands with GSP; 72 were related to those with GAD; 55 were related to those with comorbid GSP/GAD; and 146 were related to the control probands. When the relatives of probands in each of the three anxiety groups were compared with the relatives of controls, an increased rate of pure GSP was found in the relatives of the probands with GSP only and the relatives of the probands with comorbid GSP/GAD. In addition, the relatives of the probands with comorbid GSP/GAD were found to have an increased rate of both pure GAD and comorbid GSP/GAD. An increased rate of pure GSP was found in the relatives of the GSP-only probands when compared with the relatives of the GAD-only probands. An increased rate of pure GAD was found in the relatives of the probands with comorbid GSP/GAD when compared with the relatives of the probands with GSP only.

According to the authors, the findings of the current investigation are most consistent with a comorbidity model that points to the independent familial transmission of GSP and GAD. The researchers recommend that assortative mating and individual-specific environmental factors be examined as possible sources for the high rate of comorbidity observed between these two disorders.

(38 References)
THE RELATIONSHIP BETWEEN AVOIDANT PERSONALITY DISORDER AND SOCIAL PHOBIA: A POPULATION-BASED TWIN STUDY

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AM J PSYCHIATRY, 164:1722-8, November 2007

One of the most studied and controversial interactions between axis I and axis II psychiatric disorders is that between social phobia and avoidant personality disorder. The purpose of the present investigation was to determine the sources of comorbidity for social phobia and dimensional representations of avoidant personality disorder. More specifically, the authors attempted to estimate the extent to which these two disorders are influenced by common genetic and shared or unique environmental factors and to what extent these factors are specific to each disorder.

The study sample was composed of 1,427 young adult female-female twin pairs (age range, 19 to 36 years; mean age, 28.1 years) who were evaluated by means of personal interview for the presence of avoidant personality disorder and social phobia. Assessment tools used were the Structured Interview for DSM-IV Personality and the Composite International Diagnostic Interview. Bivariate Cholesky models were fitted through use of the Mx statistical program. The prevalence of avoidant personality disorder was 2.7%, and the prevalence of lifetime social phobia was 5%. Among subjects with avoidant personality disorder, 32.5% also met criteria for social phobia; 18.3% of subjects with social phobia also satisfied criteria for avoidant personality disorder. Among subjects with 12-month social phobia, 26.1% had co-occurring avoidant personality disorder; the prevalence of avoidant personality disorder in subjects who met criteria for generalized social phobia was 30.6%. The best-fitting model included only genetic and individual-specific environmental factors and indicated that, within the limits of study design and statistical power, the covariation between social phobia and avoidant personality disorder could be explained solely by common genetic factors, that is, the genetic risk factors for the two disorders appeared to be identical. On the other hand, the environmental risk factors influencing avoidant personality disorder and social phobia appeared to be unique to each disorder.

These data suggest that, given a high degree of genetic liability on the avoidant personality disorder/social phobia dimension, the probability of developing one or the other of these disorders is a result of different sets of environmental experiences; individuals exposed to both sets of environmental factors may develop both disorders. (40 References)
LOW EXTRAVERSION AND HIGH NEUROTICISM AS INDICES OF GENETIC AND ENVIRONMENTAL RISK FOR SOCIAL PHOBIA, AGORAPHOBIA, AND ANIMAL PHOBIA

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AM J PSYCHIATRY, 164:1714-21, November 2007

Phobias run in families, and some twin studies suggest that the modest familial aggregation observed in general population samples is mainly due to genetic factors. However, exactly what is inherited remains unclear. The present authors examined the extent to which two major personality dimensions (extraversion and neuroticism) indexed the genetic and environmental risk for three phobias (social phobia, agoraphobia, and animal phobia) in a large sample of twins ascertained through a population-based registry.

Lifetime phobias and personality traits were assessed by means of diagnostic interview and self-report questionnaire, respectively, in 7,800 twins drawn from female-female, male-male, and opposite-sex pairs. Sex-limited trivariate Cholesky structural equation models were used to decompose the correlations among extraversion, neuroticism, and each phobia. In the best-fitting models, genetic correlations were moderate and negative between extraversion and both social phobia and agoraphobia; that between extraversion and animal phobia was effectively zero. Genetic correlations were high and positive between neuroticism and both social phobia and agoraphobia; that between neuroticism and animal phobia was moderate. All of the genetic risk factors for social phobia and agoraphobia were shared with those that influenced extraversion and neuroticism. On the other hand, only a small proportion of the genetic risk factors for animal phobia (16%) was shared with those that influenced personality. Shared environmental experiences were not a source of correlations between personality traits and phobias, and unique environmental correlations were relatively modest.

According to the authors, the current results suggest that the familial co-occurrence of certain personality traits and phobias has a genetic, not a shared environmental, basis. Furthermore, genetic factors that influence individual variation in extraversion and neuroticism appear to account entirely for the genetic liability to social phobia and agoraphobia, but not to animal phobia. Although geneticists often seek a single basic dimension for an endophenotype, the present findings appear to indicate that the greatest genetic risk for social phobia or agoraphobia involves genetic liability to both low extraversion and high neuroticism. (39 References)
THE EFFECTS OF MATERNAL SOCIAL PHOBIA ON MOTHER-INFANT INTERACTIONS AND INFANT SOCIAL RESPONSIVENESS

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J CHILD PSYCHOL PSYCHIATRY, 48:45-52, January 2007

Social phobia is a persistent, disabling condition in which the central psychopathological feature is an intense fear of scrutiny and negative evaluation by others; it often manifests itself in avoidance of social encounters and markedly restricted social functioning. While social phobia aggregates in families, the genetic contribution to intergenerational transmission is modest, and environmental influences such as the quality of parenting are likely to be significant. Research aimed at the effects of social phobia on parenting has been subject to problems of small sample size, heterogeneity of samples, and lack of specificity of observational frameworks. Attempting to address these problems, the authors of the present investigation recruited a large sample of mothers with social phobia and their infants and compared their behavior with that of a non-anxious control group in a situation designed to elucidate the index mothers’ social difficulties, namely, being required to converse with an unfamiliar person and manage their infant’s engagement with the stranger.

At 10 weeks postpartum, the researchers assessed 84 mothers with social phobia, 89 control mothers, and 50 mothers with generalized anxiety disorder (GAD) during face-to-face interactions with their infants and during a social challenge (engaging with a stranger). The contributions to infant social responsiveness of both maternal behaviors and early infant characteristics (neonatal irritability) were examined. The results showed that mothers with social phobia were no less sensitive to their infants during face-to-face interactions than control mothers. However, when interacting with the stranger, the mothers with social phobia appeared to be more anxious, engaged less with the stranger themselves, and were less encouraging of the infant’s interaction with the stranger; the infants of index mothers also showed reduced social responsiveness to the stranger. These differences did not apply to mothers with GAD and their infants. Regression analyses indicated that the reduction in social responsiveness in infants of mothers with social phobia was predicted by neonatal irritability and the degree to which the mother encouraged the infant to interact with the stranger.

According to the authors, the current findings indicate that mothers with social phobia display specific parenting difficulties, and that their infants show early signs of reduced social responsiveness that are related to both individual infant differences and a lack of maternal encouragement to engage in social interactions. (37 References)
TREATMENT OF SOCIAL PHOBIA: RANDOMISED TRIAL OF
INTERNET-DELIVERED COGNITIVE-BEHAVIOURAL
THERAPY WITH TELEPHONE SUPPORT

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BR J PSYCHIATRY, 190:123-8, February 2007

Although there are effective psychosocial treatments for social phobia, many
individuals with this disorder refrain from seeking therapy because of the fear of
embarrassment associated with help-seeking. While internet-based cognitive-
behavioral self-help can serve as a viable alternative, treatment adherence is a
problem. In the randomized, controlled trial presented here, the authors
attempted to evaluate the effects of a nine-week program of internet-based
cognitive-behavioral therapy that was designed to increase treatment adherence
through the addition of short weekly telephone calls from the therapist. There
were nine calls in all, with a total duration of 95 minutes.

The study sample was composed of a treatment group (N=29) and a control
group (N=28). All subjects met DSM-IV criteria for social phobia. Those in the
control group (20 women, eight men; age range, 22 to 51 years; mean age, 32.9
years) remained on a waiting list and received no treatment. Those in the
treatment group (17 women, 12 men; age range, 19 to 52 years; mean age, 32.4
years) received internet-administered self-help that included minimal therapist
contact via e-mail supplemented by short weekly telephone calls. Primary
outcome measures were the Liebowitz Social Anxiety Scale self-report version,
the Social Phobia Scale, the Social Interaction Anxiety Scale, and the Social
Phobia Screening Questionnaire. In addition, general anxiety, depression, and
quality of life were assessed by means of the Beck Anxiety Inventory, the
Montgomery-Åsberg Depression Rating Scale, and the Quality of Life Inventory.
The results showed that compared with the control subjects, the treated
participants experienced greater reductions on the measures of social anxiety,
fear, avoidance, depression, and general anxiety. Adherence to treatment was
high, with 93% of the treatment group finishing the complete treatment package.
All improvements were maintained at one-year follow-up.

According to the authors, the current findings provide support for the use of
internet-based treatment that is supplemented by short, weekly telephone calls.
They recommend that future studies examine the specificity of internet-based
self-help interventions, the role of community online support, and the non-
specifics of therapist contact that are likely to be present in both telephone and
internet consultations. (22 References)
TREATMENT OF SOCIAL PHOBIA THROUGH PURE SELF-HELP AND THERAPIST-AUGMENTED SELF-HELP

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BR J PSYCHIATRY, 191:246-52, September 2007

Although treatments for social phobia appear to be fairly effective, traditional models of delivery are associated with limitations such as cost, availability of mental health workers, and reluctance of individuals with this disorder to seek treatment. Self-help and minimal therapist treatments may serve as alternatives to more traditional therapies. For example, bibliotherapeutic interventions have been successfully applied to a wide range of difficulties, including anxiety disorders. The current study was designed to evaluate the efficacy of two forms of self-help through the use of bibliotherapeutic materials in the amelioration of social phobia: (1) pure bibliotherapy that involved almost no contact with the researchers and (2) therapist-augmented bibliotherapy in which printed material was supplemented with five group sessions conducted by a therapist. Benchmarks for these conditions were provided through comparisons with a no-treatment waiting-list condition and a standard, 10-session, therapist-led group therapy condition.

In all, 224 study participants with severe generalized social phobia were randomly assigned to one of four treatment conditions: standard group treatment (N=59), “pure” self-help (N=56), self-help augmented with minimal therapist assistance (N=57), and waiting list (N=52). Assessments covering diagnoses, symptoms and degree of life interference were conducted at pretreatment, at 12 weeks, and at 24 weeks. At post-intervention, a larger percentage of patients in the pure self-help group than in the waiting-list group no longer had a diagnosis of social phobia, although this percentage decreased slightly over the next three months. Symptoms of social anxiety and degree of life interference did not differ significantly between these two groups. The augmented self-help condition proved to be more efficacious than the waiting-list condition on all measures. Augmented self-help was comparable to standard group treatment, with both producing marked improvements in symptoms of social phobia and life interference.

According to the authors, self-help augmented by therapist assistance shows promise as a less resource-intensive method for the management of social phobia. However, they conclude, pure self-help appears to have limited efficacy in the treatment of this disorder. (30 References)
NEFAZODONE IN THE TREATMENT OF GENERALIZED SOCIAL PHOBIA: A RANDOMIZED, PLACEBO-CONTROLLED TRIAL

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J CLIN PSYCHIATRY, 68:288-95, February 2007

Generalized social phobia (GSP) is an anxiety disorder characterized by excessive fear of exposure to social and performance situations. A variety of drug classes have been shown to be effective in the treatment of GSP, including serotonergic antidepressants. Nefazodone is an antidepressant medication whose primary action is the inhibition of presynaptic 5-HT reuptake. However, nefazodone differs from other selective serotonin reuptake inhibitors in that it appears to have the additional action of blocking postsynaptic 5-HT$_{2A}$ receptors.

The present authors conducted a 14-week, randomized, double-blind study to evaluate the efficacy, safety, and tolerability of nefazodone in the treatment of patients with GSP.

The study sample was composed of 105 patients whose diagnosis of GSP was confirmed through use of the Structured Clinical Interview for DSM-IV. Four Canadian outpatient anxiety clinics participated in the trial. Fifty-two patients (24 men, 28 women; mean age, 34.6 years) were randomly assigned to receive nefazodone (300-600 mg/day, flexible dose) and 53 (26 men, 27 women; mean age, 37 years), to receive placebo. Primary outcome measures were the Clinical Global Impressions-Improvement scale score (CGI-I) and the Liebowitz Social Anxiety Scale score. Patients were evaluated at weeks 1, 2, 3, 5, 7, 9, 12, and 16. In the intent-to-treat sample, 16 (31.4%) of 51 subjects taking nefazodone and 12 (23.5%) of 51 subjects taking placebo were rated as much or very much improved on the CGI-I at study endpoint. No significant differences between the nefazodone and the placebo groups were found on the measures of social phobia, with the exception of the Social Phobia Scale. Nefazodone-treated patients reported significantly more adverse events than placebo-treated patients, although there were no significant differences between the two groups in liver function tests.

The present findings suggest that nefazodone is not an effective agent in the treatment of patients with GSP. The authors conclude that serotonin reuptake inhibition may not be the only mechanism of action required for efficacy to occur in the treatment of GSP. (73 References)
A RANDOMIZED CONTROLLED TRIAL OF VENLAFAXINE ER VERSUS PLACEBO IN PEDIATRIC SOCIAL ANXIETY DISORDER

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Social anxiety disorder, also called social phobia, is characterized by extreme worry about negative evaluation, humiliation, or embarrassment in social situations. Generalized social anxiety disorder (GSAD), which typically begins in adolescence but can occur earlier, is associated with significant distress and long-term functional impairment. The purpose of the current randomized, masked controlled trial conducted in 48 academic and community centers across the United States was to evaluate the efficacy of the serotonin-norepinephrine reuptake inhibitor venlafaxine extended release (ER) in the treatment of children and adolescents with GSAD.

A volunteer sample of 293 outpatients (age range, eight to 17 years) who met diagnostic criteria for social anxiety disorder (generalized subtype) and who were enrolled between February 2000 and March 2003 participated in the study. Venlafaxine ER or placebo was titrated from a starting daily dose of 37.5 mg to a maximum daily dose of 225 mg over a period of 16 weeks. The primary outcome measures were the Social Anxiety Scale, child or adolescent version (SAS-CA) and (for responder analysis) a (dichotomized) Clinical Global Impressions-Improvement (CGI-I) score. Of the 293 randomized patients, 285 were included a priori in the intent-to-treat efficacy analysis population (137 venlafaxine ER-treated patients, 148 placebo-treated patients), and 290 were included in the safety analysis population (140 venlafaxine ER-treated patients, 150 placebo-treated patients). Intent-to-treat random regression analyses of SAS-CA scores showed a statistically significant advantage for venlafaxine ER over placebo. On the CGI-I responder analysis, 56% (95% confidence interval [CI], 47%-64%) of venlafaxine ER-treated patients responded, a percentage that was statistically superior to that of the placebo group (37% [95% CI, 29%-45%]). Adverse events occurred more frequently in the venlafaxine ER group than in the placebo group; the most commonly observed were anorexia, nausea, weight loss, dizziness, and nervousness. There were no suicides or suicide attempts; however, three patients in the venlafaxine ER group, but none in the placebo group, developed treatment-emergent suicidality.

According to the authors, the current results indicate that venlafaxine ER is an effective and reasonably well-tolerated treatment for children and adolescents with GSAD. As is the case with other antidepressants, however, careful clinical monitoring for adverse events, including treatment-emergent suicidality, is essential. (25 References)
Approximately 5% of youths suffer from social phobia, the third most commonly occurring psychiatric disorder in the United States. In addition to experiencing social fear, these children and adolescents report general anxiety, depression, loneliness, impaired peer acceptance, and poor social skills. While pharmacological and psychological interventions have proven to be effective in the treatment of youths with social phobia, there appear to be no comparisons of different active interventions, particularly those comparing pharmacotherapies and psychological treatments. To address these limitations, the authors of the present study compared the efficacy of fluoxetine, pill placebo, and Social Effectiveness Therapy for Children (SET-C) in the treatment of children and adolescents with social phobia. SET-C includes group social skills training, peer generalization sessions, and individualized in vivo exposure.

In all, 139 subjects who were between the ages of seven and 17 years and who had a primary diagnosis of social phobia were randomly assigned to one of the three treatment conditions for a period of 12 weeks. Of these, 122 completed at least one treatment session and were classified as intent-to-treat patients (57 who received SET-C, 33 who received fluoxetine, and 32 who received pill placebo). There were no differences between the 17 pretreatment dropouts/administrative removals and the 122 participants in the intent-to-treat sample. Outcome was evaluated through use of self-reports, parent ratings, independent evaluator ratings, and behavioral assessments. The results indicated that both fluoxetine and SET-C were more effective than placebo in terms of reducing social distress and behavioral avoidance and increasing general functioning. SET-C was superior to fluoxetine on each of these measures and was the only treatment superior to placebo in terms of improving social skills, decreasing anxiety in specific social interactions, and enhancing ratings of social competence. While fluoxetine appeared to exert maximum effect by week 8, SET-C provided continued improvement through week 12. All treatment gains were maintained at one-year follow-up, without further intervention.

According to the authors, both fluoxetine and SET-C are effective in the treatment of children and adolescents with social phobia. SET-C appears to provide additional benefit, perhaps as a result of its enhancement of social competence through social skills training. (43 References)
BOOKS RECEIVED FOR REVIEW


Abstracts and Reviews of Selected Literature in Psychiatry, Neurology, and their Allied Fields

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LONELINESS AND RISK OF ALZHEIMER DISEASE

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ARCH GEN PSYCHIATRY, 64:234-40, February 2007

While social isolation has been found to be associated with increased risk of dementia and cognitive decline, little is known about the relationship (if any) between dementia and emotional isolation (loneliness). It is uncertain how much feeling alone (i.e., loneliness), as distinct from being alone (i.e., social isolation) contributes to the risk of dementia in old age. In the present longitudinal clinicopathologic study, the authors attempted to determine whether loneliness is associated with increased risk of Alzheimer disease (AD).

Some 823 older persons were recruited from senior citizen facilities in and around Chicago, Illinois. All were free of dementia at study enrollment. At baseline and annually thereafter for up to four years, the participants underwent uniform evaluations that included assessment of loneliness with a five-item scale, clinical classification of dementia and AD, and detailed testing of cognitive functioning. In those who died, a uniform postmortem examination of the brain was conducted to quantify AD pathologic abnormalities and cerebral infarctions. During follow-up, 76 subjects developed dementia that met clinical criteria for AD. Compared with unaffected persons, those who developed AD were more likely to be older, to be male, and to have a lower household income. Individuals who developed AD also had lower levels of cognitive functioning, higher levels of loneliness and disability, and lower levels of social and cognitive activity. A person with a high degree of loneliness (score 3.2, 90th percentile) was more than twice as likely to develop clinical AD during follow-up than a person with a low degree of loneliness (score 1.4, 10th percentile). Controlling for indicators of social isolation did not affect this finding. Loneliness was associated with a lower level of cognition at baseline and with more rapid cognitive decline during follow-up. There was no significant change in loneliness, and mean degree of loneliness during the study was robustly associated with cognitive decline and development of AD. In 90 participants who died and in whom autopsy of the brain was performed, loneliness was not found to be related to summary measures of AD pathology or to cerebral infarction.

According to the authors, the results of the current investigation suggest that while loneliness may contribute to the risk of an AD-like dementia in late life, it appears to do so through some mechanism other than AD pathology and/or cerebral infarction. (50 References)
CONSCIENTIOUSNESS AND THE INCIDENCE OF ALZHEIMER DISEASE AND MILD COGNITIVE IMPAIRMENT

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ARCH GEN PSYCHIATRY, 64:1204-12, October 2007

Conscientiousness refers to an individual’s tendency to control impulses and to be goal directed. While this personality trait has been found to be related to morbidity and mortality in old age, its association (if any) with the development of Alzheimer disease (AD) is not known. The aim of the present investigation was to test the hypothesis that a higher level of conscientiousness would be associated with a decreased risk of developing AD. Data were drawn from the Religious Orders Study, a longitudinal clinicopathologic investigation of aging and AD in older Catholic clergy members recruited from more than 40 groups across the United States.

The participants were 997 older Catholic nuns, priests, and brothers; all were without dementia at study enrollment. At baseline, they underwent a structured clinical evaluation and completed a standard 12-item measure of conscientiousness. Thereafter, evaluations were conducted annually for up to 12 years. Those who died underwent a uniform neuropathologic evaluation from which previously established measures of amyloid burden, tangle density, Lewy bodies, and chronic cerebral infarction were derived. The main outcome measures were clinical diagnosis of AD and change in previously established measures of global cognition and specific cognitive functions. Conscientiousness scores ranged from 11 to 47 (mean, 34), with higher values indicating higher levels of the trait. During follow-up, 176 people developed AD. A proportional hazards regression model adjusted for age, sex, and education indicated that the risk of developing AD was reduced by about 89% in a person with a high conscientiousness score (90th percentile) as compared with a person with a low conscientiousness score (10th percentile). Controlling for other personality traits, activity patterns, vascular conditions, and other risk factors did not substantially alter the results. Conscientiousness was also associated with a decreased incidence of mild cognitive impairment and reduced cognitive decline. In those who died and underwent brain autopsy, conscientiousness was not related to neuropathologic measures, but it modified the association of neurofibrillary pathologic changes and cerebral infarction with cognition proximate to death.

The authors conclude that level of conscientiousness appears to be associated with the incidence of mild cognitive impairment and AD but not with the pathologic hallmarks of these conditions. (69 References)
IMPACT OF FRONTAL SYSTEMS BEHAVIORAL FUNCTIONING IN DEMENTIA ON CAREGIVER BURDEN

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Providing care for an individual with dementia can have significant emotional and physical health consequences. It is estimated that as many as 50% of dementia caregivers experience depression, anxiety, and feelings of burden, strain, and stress (Schulz, 1995). Behavioral problems in the dementia patient are some of the strongest predictors of caregiver burden, although the impact of specific types of behavioral problems on burden is limited. The present authors investigated the contribution of frontal systems behavioral functioning (i.e., apathy, executive dysfunction, and disinhibition) on caregiver burden.

The study sample was composed of 72 caregivers of patients with mild (N=47) or moderate (N=25) dementia. All caregivers resided with the care recipient and had been providing a minimum of four hours of daily care for at least six months. Most of the caregivers were women (N=56), spouses of the patients (N=44), and Caucasian (N=69). The caregivers completed the Frontal Systems Behavior Scale as well as measures of mood, perceived burden, and patient ratings of functional impairment. Regression analyses indicated that frontal systems behavioral problems in the care recipient predicted caregiver burden after dementia severity and caregiver depression were controlled. Closer analysis of subscales revealed that behaviors associated with executive dysfunction and disinhibition were predictive of caregiver burden, whereas patient apathy was not. Frontal systems behavioral problems failed to predict caregiver depression when the authors controlled for dementia severity. When dementia subtypes were compared, no differences on outcome measures emerged. Spousal and adult child caregivers reported similar levels of perceived burden, depressive symptomatology, and severity of behavioral problems, despite the fact that spousal caregivers reported more intact activities of daily living in the care recipient than did adult child caregivers.

According to the authors, the current data are consistent with previous findings demonstrating that behavioral disturbance in the dementia patient is one of the strongest contributors to caregiver burden. Behavioral strategies for dementia patients that are aimed toward increasing daily structure, creating routines, and assisting with sequencing may be particularly useful in dementia caregiver interventions. (37 References)
THE INFLUENCE OF NEUROPSYCHOLOGICAL FUNCTIONING ON NEUROPSYCHIATRIC PROBLEMS IN DEMENTIA

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J NEUROPSYCHIATRY CLIN NEUROSCI, 19:50-6, Winter 2007

Dementia is characterized by multiple cognitive deficits, and most patients exhibit neuropsychiatric problems while experiencing this disease. Although the relationship between specific neuropsychiatric problems and the global severity of dementia is well established, only a few studies have examined the relationships between specific cognitive deficits and neuropsychiatric problems. The aim of the present investigation was to determine the influence of specific neurological impairments on the development of a broad range of neuropsychiatric problems in patients with dementia.

The study sample consisted of 126 dementia patients (50 men, 76 women; age range, 53 to 92 years; mean age, 75.8 years) who were evaluated every six months for a period of two years. Neuropsychiatric problems were assessed by means of the Neuropsychiatric Inventory (NPI). The neuropsychological test battery covered the domains of language, memory, executive functioning, attention, orientation, perception, and praxis. The results showed no main effects of time and no interaction effects between time and cognitive variables for any of the neuropsychiatric problems. There were no significant findings demonstrating a relationship between any of the cognitive function variables and the NPI subsyndromes of mood/apathy or hyperactivity or the separate symptoms of depression and apathy. There were significant main effects of language impairment on the psychosis subsyndrome of the NPI and on the symptoms of delusions and aberrant motor behavior. Separate analyses revealed specific significant main effects of language expression on psychosis, delusions, and total NPI scores. No significant relationship was found between language comprehension and any neuropsychiatric problem. However, there were significant main effects of abstract reasoning on psychosis, delusions, and aberrant motor behavior.

According to the authors, the current findings indicate that impairments in language expression and abstract reasoning are related to the emergence of psychosis, aberrant motor behavior, and total level of neuropsychiatric problems in dementia patients. These results imply that clinicians should be more alert to communication and executive deficits in patients with dementia, since such deficits point to persons who are more prone to develop these types of noncognitive symptoms. (44 References)
POSITRON EMISSION TOMOGRAPHY METABOLIC CORRELATES OF APATHY IN ALZHEIMER DISEASE

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ARCH NEUROL, 64:1015-20, July 2007

While cognitive impairment is the hallmark of Alzheimer disease (AD), neuropsychiatric symptoms occur frequently. Apathy is the most common behavioral manifestation and is reported to occur in 29% to 72% of AD patients. Clinical studies, single-photon emission computed tomography studies, magnetic resonance imaging studies, and pathologic correlations of apathy in AD have suggested an association with frontal dysfunction but without a definitive localization. The purpose of the present investigation was to examine the association between apathy and cortical metabolic rate on positron emission tomography (PET) in patients with AD.

Forty-one subjects with probable AD underwent [18F] fluorodeoxyglucose PET imaging as well as neuropsychiatric and cognitive assessments. Global subscale scores from the Scale for the Assessment of Negative Symptoms in Alzheimer Disease were used to designate the presence or absence of clinically meaningful apathy. Whole-brain voxel-based analyses were performed by means of statistical parametric mapping software. Two sample statistical parametric mapping analyses yielded significance maps comparing relative regional activity in subjects with and without apathy. Of the sample, 14 subjects (34%) had apathy, and 27 (66%) did not. Statistical parametric mapping analysis revealed significant reduced activity in the bilateral anterior cingulate region extending inferiorly to the medial orbitofrontal region and the bilateral medial thalamus in the subjects with apathy as compared with those without apathy. The results remained the same after the researchers individually covaried for the effects of global cognitive impairment, depressed mood, and education.

The authors conclude that apathy in AD patients (independent of the severity of global cognitive impairment, age, cognitive symptom duration, education, and depressed mood) is associated with reduced metabolic activity in the bilateral anterior cingulate gyrus and in the medial orbitofrontal cortex and may be associated with reduced activity in the medial thalamus. These findings, they note, point to a specific neurobiological basis for the expression of apathy in AD. The current data reinforce the confluence of evidence from other investigational modalities in implicating medial frontal dysfunction and related neuronal circuits in the neurobiology of apathy in AD and other neuropsychiatric diseases. (25 References)
COGNITIVE DECLINE IN ALZHEIMER DISEASE
Impact of Spirituality, Religiosity, and QOL

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NEUROLOGY, 68:1509-14, May 1, 2007

Increased levels of quality of life (QOL) have been shown to have a beneficial effect on health outcomes, morbidity, and mortality. Similarly, higher levels of spirituality and religiosity have been found to be correlated with lower morbidity and mortality, enhanced QOL and well-being, and lower levels of depression and psychological stress. Possible mechanisms by which spirituality/religiosity may affect health outcomes include a more favorable immune profile, enhanced cognitive stimulation, quicker response to acute health crises, and higher compliance with treatment. Although QOL, spirituality, and religiosity have been associated with better outcomes in many disorders, including neurologic disease, their impact on rate of cognitive decline in Alzheimer disease (AD) merits further investigation. The objective of the present longitudinal study was to assess the effects of QOL, spirituality, and religiosity on the rate of progression of cognitive decline in persons with AD.

The sample was composed of 70 patients with probable AD (age range, 49 to 94 years; mean age, 78.43 years). Each subject underwent a uniform structured evaluation. The Mini-Mental State Examination (MMSE) was used to monitor the rate of cognitive decline. Religiosity and spirituality were measured through the use of standardized scales designed to assess spirituality, religiosity, and organizational and private religious practices. The researchers conducted a multiple regression analysis to provide an estimate of the unique contribution of QOL, spirituality, and religiosity scores over and above other demographic and clinical variables in predicting the rate of cognitive decline in AD. After controlling for baseline level of cognition, age, sex, and education, the authors found that a slower rate of cognitive decline was associated with higher levels of spirituality \(p < 0.05\) and private religious practices \(p < 0.005\). These two predictors in the multiple regression model accounted for 16.5% of the variance of the annual decline in MMSE score. There was no correlation found between rate of cognitive decline and QOL measures.

According to the authors, the results of the current investigation indicate that higher levels of spirituality and private religious practices, but not quality of life, are associated with a slower progression of Alzheimer disease. Further studies are needed, they note, to replicate the present findings and to better understand the meaning of the observed relationship between spirituality/religiosity and cognitive decline. (51 References)
NURSING HOME PLACEMENT, DAY CARE USE, AND COGNITIVE DECLINE IN ALZHEIMER’S DISEASE

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AM J PSYCHIATRY, 164:910-5, June 2007

Progressive decline in cognitive function is the principal clinical manifestation of Alzheimer’s disease. As the dementia progresses, affected individuals require increasing levels of care, and many are eventually placed in nursing homes. Although the transition from the community to institutional residence is a life event of enormous significance, little is known about the relationship of such placement to the course of cognitive decline in dementia or whether the previous use of adult day care services modifies this correlation in any way. In the present study, the authors examined the associations of day care use and nursing home placement with trajectories of global cognitive decline in Alzheimer’s disease.

The participants were 432 older persons with clinically diagnosed Alzheimer’s disease (mean age at baseline, 80.3 years); all were recruited from health care settings in the Chicago area. At baseline, they lived in the community and were using day care services an average of 1.7 days per week. At six-month intervals for a period of up to four years, they completed nine cognitive tests, with a composite measure of global cognition being derived from the results. The researchers used mixed-effects regression models to characterize individual paths of change in cognitive function and their relation to level of day care use at baseline and subsequent institutionalizations. On average, cognition declined at a gradually increasing rate over the course of the study. Nursing home placement was associated with a decrease in the level of cognition and an acceleration in the rate of cognitive decline. Day care use at baseline was not related to cognitive decline in initial analyses, but it interacted with nursing home placement in that a higher level of adult day care use substantially reduced the association of placement with accelerated cognitive decline. Level of education interacted with placement in that more schooling was associated with a greater increase in cognitive decline upon nursing home placement, but prior day care use also attenuated this association.

According to the authors, the results of the current study suggest that the transition from the community to a nursing home is particularly difficult for individuals with Alzheimer’s disease and that those planning for their care should consider the possibility that experiences in adult day care programs may help prepare affected persons for institutional living. (26 References)
MORTALITY RISK IN PATIENTS WITH DEMENTIA TREATED WITH ANTIPSYCHOTICS VERSUS OTHER PSYCHIATRIC MEDICATIONS

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While neuropsychiatric symptoms are present in more than 80% of persons with dementia, research examining the treatment of such symptoms is modest, and no medication has been approved by the Food and Drug Administration for this indication. However, antipsychotics and other types of psychiatric medications are used for the management of neuropsychiatric symptoms in demented individuals. The purpose of the present retrospective study was to compare 12-month mortality risks among patients who had recently filled prescriptions for conventional antipsychotics, atypical antipsychotics, or other nonantipsychotic psychiatric medications in outpatient settings following a diagnosis of dementia.

Data were gathered from national Department of Veterans Affairs registries (fiscal years 2001-2005) on patients who were older than 65 years of age and who began outpatient treatment with psychiatric medication after receiving a dementia diagnosis (N=10,615). Twelve-month mortality rates were compared in patients taking antipsychotics (N=4,534) and those taking other psychiatric medications (N=6,081). The authors controlled for confounding variables by using multivariate models and propensity-scoring methods. Secondary analyses included a no-medication group (N=12,821) and examination of mortality causes. The overall mortality in the cohort was 18%. Twelve-month mortality was found to differ significantly by medication type. Mortality among patients taking conventional antipsychotics (25.2%), atypical antipsychotics (22.6%), or both types of antipsychotics (29.1%) was significantly higher than that among users of other psychiatric medications (14.6%). The adjusted mortality risks for all individual classes of nonantipsychotics, except for anticonvulsants, were significantly lower than the risk for antipsychotics. Mortality risks did not change over 12 months. The proportion of patients who died from cerebrovascular, cardiovascular, or infectious causes appeared to be no higher among those receiving antipsychotics than among those taking nonantipsychotic psychiatric medications.

The authors conclude that antipsychotic drugs taken by patients with dementia seem to be associated with higher mortality rates than most other medications used for the management of neuropsychiatric symptoms. However, this association is not yet well understood. (38 References) 

EAF
ANTIAGGRESSIVE EFFECT OF CYPROTERONE VERSUS HALOPERIDOL IN ALZHEIMER’S DISEASE: A RANDOMIZED DOUBLE-BLIND PILOT STUDY

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Alzheimer’s disease (AD) is commonly accompanied by aggressive behavior. While numerous drugs have been investigated in the search for a specific antiagressive action in dementia, the results have been disappointing in the majority of cases. In the present randomized, double-blind pilot study, the authors evaluated the efficacy and safety of the antiandrogen cyproterone acetate in the control of aggression associated with AD.

The study sample was composed of 27 elderly patients (19 women, eight men; mean age, 80.7 years) who were referred to the University of Guadalajara Psychogeriatric Clinic and who were diagnosed with AD and associated aggressive behavior (mean Staff Observation Aggression Scale [SOAS] score ≥ 2). Twenty-two of the patients resided in a nursing home, while five lived in their own home or the home of a relative. After a single-blind, psychotropic drug washout period of 15 days, each patient was randomly assigned to receive stable doses of cyproterone (100 mg/day) or haloperidol (2 mg/day) for 90 days. Thirteen patients were assigned to the cyproterone group and 14, to the haloperidol group. Of the 27 patients, 24 completed the trial, with three (all from the haloperidol group) dropping out prematurely because of adverse events. The primary outcome measure was the SOAS score. The baseline aggression level in the sample was mild, as indicated by a mean SOAS score of 4.48. Efficacy analyses for all intent-to-treat patients indicated that nine subjects (69.2%) in the cyproterone group achieved complete elimination of aggression at endpoint, while only two patients (14.2%) in the haloperidol group did so. Ten patients (71.4%) taking haloperidol experienced adverse effects, while only four (30.7%) taking cyproterone had adverse events.

According to the authors, cyproterone showed significantly better efficacy and safety than haloperidol in controlling mild aggression associated with AD. However, they note, additional research is needed to determine whether the current findings can be ratified in a larger study and generalized to patients whose aggression is more severe. (47 References)
THE INFLUENCE OF GALANTAMINE ON REACTION TIME, ATTENTION PROCESSES, AND PERFORMANCE VARIABILITY IN ELDERLY ALZHEIMER PATIENTS

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Alzheimer disease (AD), the most common cause of dementia, is characterized mainly by memory dysfunction and cognitive decline. Treatment with acetylcholinesterase inhibitors has been shown to improve cognition and global functioning in patients with mild to moderate AD. Although attention deficits are known to appear early in the course of AD, attention has been less considered as a possible therapeutic target. The purpose of the present open-label, prospective trial was to examine the effect of galantamine on reaction time (RT), selective attention (SA), alternating attention (AA), errors, and interindividual and intraindividual variability in elderly patients with mild to moderate AD.

The study sample consisted of 41 outpatients with AD (31 women, 10 men; mean age, 80.8 years). The participants were evaluated at baseline and after eight and 22 weeks of galantamine treatment by means of an RT test that allowed differentiation between the decision and movement time components of the total RT. The various tasks of the RT test allowed calculation of SA (the capacity to ignore irrelevant stimuli) and AA (the capacity to switch attention from one subject to another). Standard AD evaluation tests were performed at baseline and again at 22 weeks. Of the 41 patients, eight were completely lost to follow-up. The average daily dose of galantamine was 14.9 mg at eight weeks and 21 mg at 22 weeks. After eight and 22 weeks of treatment, an improvement in decision time and RT was found at all complexity levels. In terms of movement time, improvements were less pronounced and were not present at both follow-up moments or at all complexity levels. SA, but not AA, improved significantly after 22 weeks. A decrease in the number of errors was noted. At both eight and 22 weeks, the interindividual and intraindividual variability decreased at several complexity levels. Changes in Mini Mental State Evaluation scores were found to be correlated with changes in SA.

According to the authors, the current findings provide support for the argument that galantamine treatment improves various parameters of reaction time, attention, and interindividual and intraindividual variability in elderly patients with AD. However, they note, because the present study was not a controlled trial, further investigation is needed. (43 References)
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PREVALENCE, CORRELATES, DISABILITY, AND COMORBIDITY OF DSM-IV DRUG ABUSE AND DEPENDENCE IN THE UNITED STATES
Results from the National Epidemiologic Survey on Alcohol and Related Conditions

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The abuse of, and dependence on, illicit substances is a widespread problem in the United States (US) and is associated with substantial societal, personal, and economic costs. However, current and comprehensive information on the epidemiology of DSM-IV 12-month and lifetime drug use disorders among the general population has been lacking. The aim of the current study was to present detailed data on the prevalence, correlates, disability, and comorbidity of drug abuse and dependence.

By means of the Alcohol Use Disorder and Associated Disabilities Interview Schedule of the National Institute on Alcohol Abuse and Alcoholism, face-to-face interviews were conducted with a large representative sample of US adults (N=43,093) in 2001 and 2002. The overall response rate was 81%. The results indicated that 2.0% of adult Americans had experienced a drug use disorder in the preceding 12 months, and 10.3% had developed a drug use disorder at some time during their lives. The 12-month and lifetime prevalences of drug abuse (1.4% and 7.7%, respectively) exceeded the corresponding rates for drug dependence (0.6% and 2.6%, respectively). Rates of drug abuse and dependence were generally higher among men; Native Americans; respondents between the ages of 18 and 44 years; adults of lower socioeconomic status; those residing in the West; and those who were never married or were widowed, separated, or divorced. When the authors controlled for psychiatric disorders, associations of drug use disorders with other substance use disorders and antisocial personality disorder were diminished but remained strong. Associations of drug dependence with most mood disorders and generalized anxiety disorder also remained significant. Lifetime treatment- or help-seeking behavior was uncommon (8.1%, abuse; 37.9%, dependence) and was associated with psychiatric comorbidity but not with sociodemographic characteristics.

The authors conclude that most individuals with drug use disorders have never been treated, and treatment disparities exist among those at high risk, despite substantial disability and comorbidity. (105 References)
PREVALENCE, CORRELATES, DISABILITY, AND COMORBIDITY OF
DSM-IV ALCOHOL ABUSE AND DEPENDENCE IN THE UNITED STATES
Results from the National Epidemiologic Survey on
Alcohol and Related Conditions

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ARCH GEN PSYCHIATRY, 64:830-42, July 2007

Alcohol use disorders (abuse and dependence) are maladaptive patterns of alcohol consumption manifested by symptoms that lead to clinically significant impairment or distress. However, up-to-date information on the epidemiology of alcohol use disorders in the United States (US) is lacking. The main objective of the current study was to present nationally representative findings on the prevalence, correlates, psychiatric comorbidity, and treatment of DSM-IV alcohol abuse and dependence.

In 2001 and 2002, face-to-face interviews were conducted with a representative sample of US adults (N=43,093). The survey response rate was 81%. The data showed that 8.5% of American adults had experienced alcohol use disorders in the prior 12 months (abuse, 4.7%; dependence, 3.8%), while 30.3% had experienced alcohol use disorders during their lifetimes (abuse, 17.8%; dependence, 12.5%). The duration of alcohol use disorders was often chronic, with a mean duration of nearly four years for alcohol dependence. Alcohol dependence was significantly more prevalent among men, whites, Native Americans, younger and unmarried adults, and those with lower incomes. Current alcohol abuse was more prevalent among men, whites, and younger and unmarried individuals, while lifetime rates were highest among middle-aged Americans. Significant disability was particularly associated with alcohol dependence. Only 24.1% of those with alcohol dependence were ever treated. Strong associations between other substance use disorders and alcohol use disorders were lower but remained significant when other comorbidity was controlled. Again, when the researchers controlled for other comorbidity, significant associations between mood, anxiety, and personality disorders and alcohol dependence were reduced in number and magnitude.

According to the authors, the current findings indicate that alcohol abuse and dependence are highly prevalent disorders that go largely untreated and that continue to represent a widespread and serious personal and public health problem in the United States. (129 References)
AMPHETAMINE-INDUCED DOPAMINE RELEASE: MARKEDLY BLUNTED IN COCAINE DEPENDENCE AND PREDICTIVE OF THE CHOICE TO SELF-ADMINISTER COCAINE

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AM J PSYCHIATRY, 164:622-9, April 2007

Dopamine is an important mediator of the reinforcing effects of cocaine, according to the authors of the current report, and alterations in dopamine function could be involved in cocaine dependence. The aim of the present investigation was to characterize pre- and post-synaptic dopamine function in recently detoxified cocaine-dependent individuals. Using positron emission tomography, the researchers assessed the dopamine response to an acute amphetamine challenge in the striatal subregions of cocaine-dependent and healthy comparison subjects. The authors also investigated the relationship between this dopamine response and the choice to self-administer cocaine in a laboratory model of relapse.

In all, 24 cocaine-dependent participants (19 men, five women; mean age, 39 years) and 24 matched healthy subjects (19 men, five women; mean age, 38 years) underwent $^{11}$Craclopride scans during a baseline condition and following intravenous amphetamine administration (0.3 mg/kg). The cocaine-dependent subjects also completed cocaine self-administration sessions in which a priming dose of cocaine was followed by the choice to either self-administer subsequent doses of cocaine or receive a monetary reward. Cocaine dependence was associated with a marked reduction in amphetamine-induced dopamine release in each of the functional subregions of the striatum (limbic striatum: $-1.2\%$ in cocaine-dependent subjects versus $-12.4\%$ in healthy subjects; associative striatum: $-2.6\%$ versus $-6.7\%$, respectively; sensorimotor striatum: $-4.3\%$ versus $-14.1\%$). In the cocaine-dependent subjects, blunted dopamine transmission in the ventral striatum and anterior caudate was associated with the choice for cocaine in the self-administration sessions; those individuals with greater impairment in presynaptic dopamine in these regions were more likely to choose cocaine over an alternative reinforcer (money).

The current findings suggest that cocaine dependence is associated with impairment in presynaptic dopamine function and that this impairment plays a critical role in maintaining the habitual, maladaptive patterns of behavior that are indicative of addiction. (36 References)
STROKE IN YOUNG ADULTS WHO ABUSE AMPHETAMINES OR COCAINE
A Population-Based Study of Hospitalized Patients

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ARCH GEN PSYCHIATRY, 64:495-502, April 2007

The abuse of stimulant drugs is increasing in the western United States. Over the past two decades, a mounting body of evidence has pointed to a link between the abuse of stimulant drugs and the occurrence of strokes in young people. While numerous case reports and animal studies support the existence of such a link, epidemiologic investigations have yielded conflicting results. The aim of the present cross-sectional study was to determine whether young adults who abuse amphetamines or cocaine are at a higher risk of having a stroke.

Drawing from a quality indicators’ database of 3,148,165 discharges (persons between 18 and 44 years of age) from Texas hospitals, the authors estimated the secular trends (from January 1, 2000 to December 31, 2003) in the abuse of various drugs and the occurrence of strokes. Definitions from the Agency for Healthcare Research and Quality’s stroke mortality Inpatient Quality Indicator were used to ascertain stroke incidence. The researchers developed separate logistic regression models of risk factors for hemorrhagic (N=937) and ischemic (N=998) stroke discharges of adults between the ages of 18 and 44 years in 2003, and for mortality risk in patients with stroke. Among patients admitted to Texas hospitals, cocaine was reported to be the second most frequently abused drug, after alcohol, and amphetamines were the fifth most frequently abused. From 2000 to 2003, the rates of abuse of cocaine, cannabis, opioids, and amphetamines increased significantly, with the rate of increase being greatest for amphetamines. The rate of strokes also increased, particularly among amphetamine abusers. When discharges in 2003 (N=812,247) were examined, amphetamine abuse was found to be associated with hemorrhagic stroke (adjusted odds ratio [OR], 4.95; 95% confidence interval [CI], 3.24-7.55) but not with ischemic stroke; cocaine abuse was associated with both hemorrhagic (OR, 2.33; 95% CI, 1.74-3.11) and ischemic (OR, 2.03; 95% CI, 1.48-2.79) stroke. Amphetamine abuse (but not cocaine abuse) was associated with a higher risk of death after hemorrhagic stroke (OR, 2.63; 95% CI, 1.07-6.50).

According to the authors, the current data suggest that increases in stimulant abuse may increase the rate of hospital admissions for strokes as well as stroke-related mortality. (69 References)
SIX-MONTH TREATMENT OUTCOMES OF COCAINE-DEPENDENT PATIENTS WITH AND WITHOUT PTSD IN A MULTISITE NATIONAL TRIAL

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While an association between substance use disorder (SUD) and posttraumatic stress disorder (PTSD) has been well established, few studies have examined treatment outcome in individuals with this dual diagnosis. The present authors evaluated six-month treatment outcomes among 428 cocaine-dependent adult outpatients with (N=34) and without (N=394) PTSD as part of a controlled, randomized, multisite clinical trial of the efficacy of manual-based psychotherapies for SUD.

All the study participants met DSM-IV criteria for cocaine dependence (current or in early partial remission) and had used cocaine in the 30-day period prior to intake; 77.1% were male, 57.5% were white, 40% were black, 1.2% were Hispanic, 0.7% were Native American, and 0.7% were Asian. Most were employed (57.6%); 38.4% were unemployed, and 4% were students, homemakers, retirees, or persons with disabilities. Assessments were completed at baseline and monthly during the six-month active treatment phase. Using longitudinal mixed-effects models, the authors compared outcomes in the SUD-PTSD patients (N=34) with those in the SUD-only patients (N=394) and also examined rates of within-group change. Compared with SUD-only patients, SUD-PTSD patients were more impaired to begin with and remained so across time on all psychological and interpersonal outcomes, including global psychological severity, addiction-related psychiatric problems, problems with interpersonal relatedness, and addiction-related family and social problems. SUD-PTSD patients also reported more severe addiction-related medical problems than SUD-only patients. While the SUD-PTSD patients showed no improvement over time on the majority of addiction-related outcomes (i.e., Addiction Severity Index alcohol, legal, employment, and psychiatric composites), the SUD-only patients improved significantly in each of these areas. However, both groups improved significantly over time in terms of drug use, addiction-related family and social problems, and global psychological severity.

The authors conclude that the greater impairment and relative lack of improvement seen in SUD-PTSD patients (compared with SUD-only patients) suggest that these dual-diagnosis patients may need treatments that more directly target their areas of difficulty. (54 References)
A STEPPED CARE STRATEGY USING BUPRENORPHINE AND METHADONE VERSUS CONVENTIONAL METHADONE MAINTENANCE IN HEROIN DEPENDENCE: A RANDOMIZED CONTROLLED TRIAL

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Morbidity and mortality are high in heroin dependence, although both can be reduced with the administration of methadone or buprenorphine. While the efficacy of methadone maintenance therapy is the most well-documented, safety concerns limit its use. Buprenorphine therapy offers a lower risk of overdose and improved access; however, its efficacy may be lower. In the study presented here, the authors compared adaptive, buprenorphine-based stepped care with optimal methadone maintenance treatment.

The randomized controlled trial, conducted between 2004 and 2006, consisted of a 24-day, uniform, double-blind induction phase followed by single-blind flexible dosing based on structured clinical criteria, for a total of six months. In all, 96 self-referred subjects with heroin dependence were randomly assigned to a methadone maintenance arm (33 men, 15 women; mean age 36.5 years) or a stepped care arm (43 men, five women; mean age, 34.8 years). In the stepped care arm, subjects were initially treated with buprenorphine/naloxone and then switched to methadone if necessary. All subjects underwent intensive behavioral treatment. The primary outcome measure was retention in treatment. Secondary outcomes were completer analyses of problem severity (Addiction Severity Index) and proportion of urine samples free of illicit drugs. Overall, the six-month retention rate was 78%. The outcomes of stepped treatment and methadone maintenance were virtually identical. Among completers of stepped therapy, 46% remained on buprenorphine/naloxone. The proportion of urine samples free of illicit opiates increased over time and ultimately reached 80% in both treatment arms. Problem severity decreased significantly and uniformly in both the stepped care and methadone maintenance arms.

According to the authors, the current results suggest that in the treatment of heroin dependence, buprenorphine should neither replace methadone nor be viewed as a less effective alternative to methadone when the latter is not available. Instead, buprenorphine should generally be used as the first-line treatment in heroin dependence, with provisions being made for rapid progression to methadone when necessary. (34 References)
SUBSTANCE USE-DISORDER TREATMENT AND A DECLINE IN ATTEMPTED SUICIDE DURING AND AFTER TREATMENT

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J STUD ALCOHOL DRUGS, 68:503-9, July 2007

A history of suicide attempts is common in patients entering treatment for substance use disorders (SUDs). However, relatively little is known about the frequency of suicidal behavior during treatment or in the interval immediately following a treatment episode. In the present study, the authors examined the prevalence and treatment-related predictors of suicide attempts during and after SUD treatment. They attempted to determine whether treatment setting, length of treatment, availability of psychiatric treatment, and use of psychiatric services during treatment would predict a suicide attempt in the year following treatment (above and beyond baseline suicidality).

The study participants (N=3,733) were drawn from a national sample of patients in publicly funded SUD treatment centers (31 outpatient programs, 23 residential programs). Of these patients, 1,691 were treated in outpatient settings, and 2,042 were treated in residential facilities. The patients were assessed at the start of an episode of SUD treatment, again at discharge from treatment, and/or at one year after treatment. The authors used mixed-model logistic regression analyses to estimate the relative strength of the association between different aspects of treatment and suicide attempts during and after treatment. At treatment entry, approximately 26% of the patients reported a lifetime suicide attempt; of these, 67% stated that some or all of these attempts were made subsequent to drug or alcohol use. In all, 2% of the patients reported making a suicide attempt during the episode of SUD treatment. The rate of suicide attempts was found to be significantly lower in the year following treatment (4%) than in the year before treatment (9%). Patients treated in residential facilities were less likely to attempt suicide during treatment than those treated in outpatient programs. The rate of suicide attempts in outpatient settings was approximately three times higher than the rate in residential settings. A longer course of treatment was associated with a lower likelihood of a posttreatment suicide attempt.

The authors conclude that treatment providers need to be aware of the high prevalence of suicide attempts before SUD treatment, as well as the likelihood that a sizable minority of patients may engage in suicidal behavior either during or soon after SUD treatment. Whenever possible, a combination of residential treatment and longer treatment episodes should be considered as methods for reducing the likelihood of suicide attempts. (30 References)
SIX-MONTH CHANGES IN SPIRITUALITY, RELIGIOUSNESS, AND HEAVY DRINKING IN A TREATMENT-SEEKING SAMPLE

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J STUD ALCOHOL DRUGS, 68:282-90, March 2007

Many addiction clinicians, recovering individuals, and clergy members have experienced, observed, and promoted changes in spirituality and/or religiousness (S/R) as important, if not crucial, components of successful recovery. However, there are few empirical investigations of S/R changes in patients with alcohol use disorders. In the present naturalistic study, the authors examined six-month changes in 10 dimensions of S/R in a sample of alcoholics entering outpatient substance-disorder treatment; they also attempted to determine whether these changes were associated with drinking outcomes.

Longitudinal survey data were collected from 123 outpatients (mean age, 38.8 years) with alcohol use disorders; 66.2% were male, 83% were white, and 39% were married or cohabiting. S/R dimensions were as follows: Loving God Scale; Controlling God Scale; Beliefs; S/R practices; Daily Spiritual Experiences; Meaning, Values, Beliefs; Forgiveness; Positive Religious Coping; Negative Religious Coping; and Purpose in Life. Drinking behaviors were assessed with the Timeline Followback Interview. Alcoholics Anonymous (AA) participation and attendance were also measured. From baseline to six-month follow-up, half of the S/R variables changed significantly. In particular, behavioral and experiential dimensions appeared to be most sensitive to change. More specifically, S/R practices, Daily Spiritual Experiences, Forgiveness, Positive Religious Coping, and Purpose in Life increased. Values, beliefs, self-assessed religiousness, perceptions of God, and the use of negative religious coping did not change. All measures of alcohol use and consequences of alcohol use showed significant reductions over time. Multiple logistic regression analyses revealed that increases in Daily Spiritual Experiences and in Purpose in Life scores were associated with increased odds of no heavy drinking at six months, even after the researchers controlled for AA involvement and gender.

According to the authors of the current investigation, because spiritual practices and experiences increased significantly over time, whereas spiritual and religious beliefs did not, the results suggest that proactive and experiential dimensions of spirituality, rather than cognitive dimensions of spirituality, contributed to recovery and to less drinking during the first six months of the recovery effort. (51 References)

EAF
RACIAL AND ETHNIC DISPARITIES IN SSRI AVAILABILITY IN SUBSTANCE ABUSE TREATMENT

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PSYCHIATR SERV, 58:55-62, January 2007

Historically, the issue of racial and ethnic disparities in mental health care has been understudied, although interest in understanding and documenting these differences is growing. The substantial rate of co-occurrence of psychiatric and substance use disorders suggests that specialty substance abuse treatment facilities may be important sites for the delivery of psychotropic medications. However, the literature indicates that there may be associations between the percentage of racial and ethnic minority clients and the availability of selective serotonin reuptake inhibitors (SSRIs) in these facilities. The present authors considered the issue of racial and ethnic disparities by modeling the likelihood of SSRI availability as a function of the racial and ethnic composition of a treatment center’s caseload. They also attempted to determine whether any identified disparities were mediated by organizational-level control variables.

Survey data from the National Treatment Center Study, comprising nationally representative samples of 326 publicly funded and 339 privately funded substance abuse treatment centers, were used to measure the availability of SSRI medications from 2004 to 2006 (dependent variable). Independent variables included the percentages of African-American and Hispanic clients, type of center, organizational affiliation, region, size, accreditation status, presence of an integrated care program, and physician availability. SSRIs were available in 48% of the surveyed treatment centers. Logistic regression analysis indicated that greater minority representation in centers’ caseloads was negatively associated with the availability of SSRIs. The negative association between the percentage of African-American clients and the availability of SSRIs was fully mediated by the addition of factors related to treatment inputs, such as the presence of a physician on staff or under contract and the presence of an integrated care program. However, the negative association between the percentage of Hispanic clients and SSRI availability remained significant after the researchers controlled for organizational characteristics and treatment inputs.

The authors conclude that although SSRIs were available in nearly half of the substance abuse treatment centers surveyed, racial and ethnic disparities were found to exist in the availability of these medications. Future research should continue to consider racial and ethnic disparities in the availability of psychiatric services at the organizational level. (45 References)
BUILDING BETTER COGNITIVE-BEHAVIORAL THERAPY:
IS BROAD-SPECTRUM TREATMENT MORE EFFECTIVE
THAN MOTIVATIONAL-ENHANCEMENT THERAPY FOR
ALCOHOL-DEPENDENT PATIENTS TREATED WITH NALTREXONE?

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Significant strides in the treatment of alcohol dependence have been made over the last three decades, with advances in combined behavioral and psychopharmacological therapies dominating the literature. In the current study, the authors examined the efficacy, during treatment, of a second-generation cognitive-behavioral therapy for alcoholism (broad-spectrum treatment), as well as the effectiveness of motivational-enhancement therapy, when both were offered in conjunction with a therapeutic dose of naltrexone.

The sample consisted of 149 alcohol-dependent patients who completed a three-month controlled trial in which they were randomly assigned to receive broad-spectrum treatment (BST) and naltrexone (N=73) or motivational-enhancement therapy (MET) and naltrexone (N=76). The primary outcome measures were percentage of days abstinent (PDA) and percentage of heavy drinking days (PHDD). The average PDA did not differ significantly by treatment group at baseline. However, at the end of the three-month treatment period, patients receiving BST had a significantly higher PDA than patients receiving MET. BST was found to be increasingly more effective than MET (with respect to PDA) in patients whose baseline support for drinking was higher. The effect remained significant when the authors controlled for pretreatment PDA. Although the average PHDD was lower among subjects treated with BST than among those treated with MET, the difference was not significant.

The authors conclude that in aggregate, the current findings suggest that it is either the combination of naltrexone and BST or the unique properties of BST that account for BST's superiority over MET and naltrexone. The results of this initial trial indicate that a second-generation cognitive-behavioral therapy such as BST may have a meaningful clinical advantage over brief interventions such as MET, at least when combined with naltrexone. The present study provides considerable support for the intriguing thesis that an eclectic treatment focused on the unique psychosocial resource deficiencies of the individual client may hold considerable promise in providing comprehensive treatment for alcohol dependence in a focused and efficient manner. (34 References)
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ABNORMAL ATTENTION MODULATION OF FEAR CIRCUIT FUNCTION IN PEDIATRIC GENERALIZED ANXIETY DISORDER

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ARCH GEN PSYCHIATRY, 64:97-106, January 2007

The presence of pediatric generalized anxiety disorder (GAD) confers a major risk for the development of adult psychopathologic abnormalities. Numerous mechanisms may underlie this association, with one possibility being that early neural dysfunction associated with anxiety may persist into adulthood. Functional magnetic resonance imaging (fMRI) studies of anxious adults implicate abnormal neural activation and disrupted attention to facial-threat cues in adult anxiety disorders. However, almost no research has examined the associations among pediatric anxiety, attention to threat, and neural activity. In the present case-control study, the authors attempted to determine whether attention modulates amygdala and cortical responses to facial-threat cues differently in adolescents with GAD and in healthy adolescents.

The sample was composed of 15 medication-free adolescents who met DSM-IV criteria for anxiety disorders and 20 healthy age- and sex-matched controls. The main outcome measure was blood oxygenation level-dependent signal as determined by fMRI. During imaging, the study participants completed a face-emotion rating task that systematically manipulated attention. Two main fMRI findings emerged. First, group differences in right amygdala activation varied with participants’ attentional focus. Adolescents with GAD exhibited greater activation than controls during fearful-face vs happy-face viewing when attending to subjective fear. Second, between-group differences in amygdala response emerged against a backdrop of strong co-activation in a distributed fear circuit for the sample as a whole. Functional connectivity analyses demonstrated strong relationships between changes in amygdala activity and activity throughout a ventrally and medially distributed circuit. Furthermore, analyses of task-related changes in the prefrontal cortex (PFC) revealed between-group differences in the anterior cingulate cortex and ventral PFC that paralleled those found in the right amygdala. Between-group differences occurred only when participants’ attention focused on subjective fear.

The current study is the first to provide evidence that in juveniles, GAD-associated patterns of pathologic fear circuit activation are particularly evident during certain attention states. (50 References)
SLEEP-RELATED PROBLEMS AMONG CHILDREN AND ADOLESCENTS WITH ANXIETY DISORDERS

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Adequate sleep is essential for health and for normal growth and development in children. Insufficient sleep has been associated with such impairments as decreased attention, impulsivity, behavioral problems, and decrements in school performance. In the present investigation, the authors evaluated sleep-related problems (SRPs) in a large group of children and adolescents with anxiety disorders. The frequencies of eight specific SRPs (has insomnia, is reluctant or refuses to sleep alone, is reluctant or refuses to sleep away from home, has nightmares, is overtired without good reason, sleeps more than most kids, sleeps less than most kids, and talks/walks in sleep) were examined in relation to age, gender, type of anxiety disorder (generalized, separation, or social), anxiety severity, and functional impairment. The researchers also assessed the impact of pharmacological treatment (fluvoxamine versus pill placebo) on the reduction of SRPs.

The study sample was composed of 128 children and adolescents (65 males, 63 females; age range, six to 17 years) who met DSM-IV criteria for generalized anxiety disorder, separation anxiety disorder, and/or social anxiety disorder. All were enrolled in a double-blind, placebo-controlled, clinical trial of fluvoxamine for youth with anxiety disorders. Clinician and parent reports of SRPs were assessed before and after treatment. In all, 88% of the total sample reported at least one SRP, and 55% reported three or more. The most commonly reported SRPs were insomnia, nightmares, and refusal/reluctance to sleep alone. Although there were no gender or age differences in total number of SRPs, nightmares were significantly more common among the girls than among the boys, and younger children (6-11 years old) were more likely than older children (12-17 years old) to have nightmares and refuse to sleep alone. Total SRPS were positively associated with anxiety severity and interference in family functioning. Significantly greater reductions in SRPS were found in the fluvoxamine-treated children than in those who received placebo.

According to the authors, the current findings indicate that SRPs are commonly associated with childhood anxiety disorders. The results also suggest that there is a need to take note of and assess sleep disturbances in clinical and research settings. (31 References)
JUVENILE MENTAL HEALTH HISTORIES OF ADULTS
WITH ANXIETY DISORDERS

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AM J PSYCHIATRY, 164:301-8, February 2007

Anxiety disorders are among the most commonly occurring psychiatric difficulties throughout the life course. In an attempt to inform classification systems, target research efforts, and inform preventions, the authors examined the developmental histories of adults with anxiety disorders by employing a prospective, follow-back design.

Data were drawn from a longitudinal investigation of the health and behavior of a representative birth cohort (N=1,037). The participants were evaluated several times when they were between 11 and 32 years of age, with psychiatric diagnoses being assigned according to DSM criteria. For those adults diagnosed with an anxiety disorder at age 32, follow-back analyses were used to ascertain the first diagnosis of anxiety disorders and other juvenile mental disorders. The anxiety disorders diagnosed at age 32 were generalized anxiety disorder, obsessive-compulsive disorder (OCD), posttraumatic stress disorder (PTSD), panic disorder, agoraphobia, specific phobia, and social phobia. Among the seven anxiety disorders diagnosed at age 32, the one-year prevalence rates ranged from 2% (PTSD, OCD, and panic) to 9% (social phobia). Virtually all persons with an anxiety disorder at age 32 had met criteria for a psychiatric disorder at an earlier age; of these, at least 50% had met diagnostic criteria for a psychiatric disorder by age 15. Over 75% of those diagnosed with an anxiety disorder at age 32 had been diagnosed with an anxiety disorder at an earlier age, and over one-third had an anxiety disorder before the age of 15. Adults with most types of anxiety also had a juvenile history of depression. There was some evidence of specificity. For example, adults with panic disorder did not have histories of juvenile disorders, whereas those with other anxiety disorders did. Adults with PTSD had histories of conduct disorder, whereas those with other anxiety disorders did not. Adults with specific phobias had histories of juvenile phobias but not other anxiety disorders.

According to the authors, the strong comorbidity between different types of anxiety disorders, coupled with the lack of specificity in the developmental histories of adults with anxiety disorders, provides support for a hierarchical approach to classification, with a broad class of anxiety disorders containing individual disorders within it. (35 References)
THE RELATIONSHIP OF ANXIETY DISORDERS, ANXIETY SENSITIVITY AND PULMONARY DYSFUNCTION WITH DYSPNEA-RELATED DISTRESS AND AVOIDANCE

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J NERV MENT DIS, 194:951-7, December 2006

Little is known about the factors that mediate the relationship between anxiety disorders and respiratory-related distress and disability. Anxiety sensitivity is a dispositional construct defined by an excessive fear of anxiety-related sensations and based on the belief that such sensations are harmful. In the present study, the authors hypothesized that elevations in anxiety sensitivity would be associated with greater severity of dyspnea, greater dyspnea-related avoidance, and poorer subjective assessment of health in patients with dyspnea who had been referred for pulmonary function testing, regardless of objective evidence of pulmonary dysfunction.

A total of 182 patients (mean age, 52 years) who were undergoing pulmonary function testing for the evaluation of dyspnea were screened with a patient-rated Primary Care Evaluation of Mental Disorders (PRIME-MD); they also completed the Anxiety Sensitivity Index (ASI) and a series of questionnaires designed to assess severity and avoidance. Pulmonary function testing revealed objective pulmonary dysfunction in 73.6% of the sample. Nearly half (49.6%) of the patients suffered from dyspnea “most days a week,” while 24.5% experienced dyspnea “several days a week,” 19.4% had it “a few days a month,” and 6.5% experienced it “only with chest infections.” Results of the PRIME-MD indicated that, regardless of pulmonary findings, nearly half (48%) of the patients screened positive for at least one anxiety disorder; 35% screened positive for generalized anxiety disorder; 14%, for posttraumatic stress disorder; 18%, for panic disorder; 9%, for social phobia; 5%, for obsessive-compulsive disorder; and 34%, for anxiety disorder not otherwise specified. In a regression model, ASI scores were found to be independently associated with the subjective severity of dyspnea and dyspnea-related avoidance, after statistical adjustment were made for the presence of anxiety disorders and depression and for evidence of pulmonary dysfunction on pulmonary function testing.

According to the authors, the current data appear to indicate that strategies designed to identify, measure, and address high levels of anxiety sensitivity should be examined in order to reduce subjective distress and improve functioning in patients with dyspnea. (60 References)
CROSS-CULTURAL DIFFERENCES IN SOMATIC PRESENTATION IN PATIENTS WITH GENERALIZED ANXIETY DISORDER

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J NERV MENT DIS, 194:962-6, December 2006

Mood and anxiety disorders generally include symptoms that reflect somatic experiences (e.g., fatigue or palpitations) as well as psychological experiences (e.g., feeling sad or afraid). Previous cross-cultural studies of depression have reported a higher rate of somatic symptom presentation in Asian populations as opposed to Western populations. However, little is known about cultural differences in the expression of distress in patients with anxiety disorders. In the present investigation, the authors examined anxiety symptoms in two culturally diverse groups: one in Nepal (N=30), and one in the United States (N=23).

All the subjects had presented to an urban mental health setting (Kathmandu, Nepal or Boston, Massachusetts) with a chief complaint of anxiety. All met DSM-IV criteria for generalized anxiety disorder (GAD). They were asked to complete the Beck Anxiety Inventory (BAI), a 21-item Likert self-report questionnaire designed to measure common symptoms of anxiety, such as “nervous” and “unable to relax.” Each symptom is rated on a 4-point scale ranging from 0 (not at all) to 3 (severe), with possible total scores ranging from 0 to 63. The two groups were compared in terms of BAI total scores as well as somatic and psychological subscale scores. There was no significant difference between the Nepali and the American groups in BAI total scores. However, the Nepali subjects had higher scores on the somatic subscale, while the American subjects had higher scores on the psychological subscale. The Nepali group had significantly higher scores on the following single items: “numbness or tingling,” “wobbliness in legs,” “dizzy or lightheaded,” “feeling of choking,” “indigestion or discomfort in abdomen,” “feeling hot,” “hands trembling,” and “faint.” The American group had significantly higher scores on the following single items: “unable to relax,” “nervous,” and “fear of dying.”

In the present study, the authors found that Nepali patients with GAD had higher rates of somatic complaints than American patients with GAD. The researchers recommend that general medical practitioners be aware of this somatic focus when evaluating patients from different cultures, since such a focus may obscure psychological or emotional distress. Further research is needed to better understand culturally-based explanatory models for a somatic focus in mood and anxiety disorders, and their impact on compliance with, and response to, treatment interventions. (18 References)
USE OF ALCOHOL AND DRUGS TO SELF-MEDICATE ANXIETY DISORDERS IN A NATIONALLY REPRESENTATIVE SAMPLE

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J NERV MENT DIS, 194:818-25, November 2006

The comorbidity of anxiety disorders and substance use disorders has been clearly established in several previous studies. The self-medication hypothesis suggests that individuals with a primary anxiety disorder use alcohol and drugs to reduce symptoms of anxiety. The goals of the present investigations were: (1) to assess the prevalence of self-medication among people with various types of anxiety disorders; (2) to determine whether self-medication is associated with an increased likelihood of comorbidity with other mental disorders; and to ascertain the association between self-medicating behavior and measures of distress, including suicidal behavior.

Data were obtained from a nationally representative sample (N=5,877; age range, 15 to 54 years). A modified version of the Composite International Diagnostic Interview was used to assign DSM-III-R psychiatric diagnoses. In all, 1,447 individuals were determined to have some type of anxiety disorder. Of these, 324 (21.9%) reported engaging in self-medicating behavior. This subgroup was then compared with the remainder of the sample (N=5,553), which comprised all individuals (including those with anxiety disorders) who did not self-medicate. Among the respondents who were diagnosed with an anxiety disorder, those with a generalized anxiety disorder exhibited the highest prevalence of self-medication (35.6%). The subgroup that endorsed self-medicating behavior had significantly higher rates of every DSM-II-R disorder, including major depression, dysthymia, bipolar I disorder, alcohol abuse with or without dependence, drug abuse with or without dependence, and antisocial personality disorder. Among those with an anxiety disorder, self-medication was also significantly associated with a greater likelihood of experiencing distress, having suicidal ideation, and making suicide attempts. Multiple regression analysis revealed that self-medicating behavior continued to be significantly associated with suicidal ideation and suicide attempts, even after the researchers controlled for sociodemographic and diagnostic variables.

The authors conclude that self-medication appears to be a common problem among individuals with anxiety disorders and that self-medicating behavior is associated with greater psychiatric comorbidity and increased rates of suicidal ideation and suicide attempts. The current findings underscore the importance of the clinical assessment of comorbidity and suicidality in persons who suffer from anxiety disorders and who use drugs and/or alcohol to reduce their anxiety symptoms. (51 References)
EFFICACY AND SAFETY OF EXTENDED-RELEASE VENLAFAXINE IN THE TREATMENT OF GENERALIZED ANXIETY DISORDER IN CHILDREN AND ADOLESCENTS: TWO PLACEBO-CONTROLLED TRIALS

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AM J PSYCHIATRY, 164:290-300, February 2007

While anxiety disorders are the most commonly occurring psychiatric illnesses in children and adolescents, most pediatric patients with anxiety disorders do not receive treatment or are misdiagnosed, treated incorrectly, or poorly monitored. The authors of the present investigation evaluated the efficacy, safety, and tolerability of extended-release venlafaxine in the treatment of pediatric generalized anxiety disorder.

Two randomized, double-blind, placebo-controlled trials (study 1 and study 2) were conducted at 59 sites in 2000 and 2001. Study participants (age range, 6 to 17 years) who met DSM-IV criteria for generalized anxiety disorder were assigned to receive a flexible dosage of extended-release venlafaxine (N=157) or placebo (N=163) for a period of eight weeks. The primary outcome measure was the composite score of nine delineated items from the generalized anxiety disorder section of a modified version of the Schedule for Affective Disorders and Schizophrenia for School-Age Children; the primary efficacy variable was the baseline-to-endpoint change in this composite score. Secondary outcome measures were overall score on the nine delineated items, Pediatric Anxiety Rating Scale, Hamilton Anxiety Rating Scale, Screen for Child Anxiety Related Emotional Disorders, and the severity of illness and improvement scores from the Clinical Global Impression scale (CGI). The extended-release venlafaxine group showed significant improvements on the primary and secondary outcome measures in study 1 and significant improvements in some secondary outcome measures but not the primary outcome measure in study 2. In a pooled analysis, the venlafaxine group exhibited a significantly greater mean decrease in the primary outcome measure than the placebo group. The response rate as indicated by a CGI improvement score of less than 3 was significantly greater with extended-release venlafaxine than with placebo (69% versus 48%). Common adverse events were asthenia, anorexia, pain, and somnolence. Significant changes in height, weight, blood pressure, pulse, and cholesterol levels were observed in the extended-release venlafaxine group.

The authors conclude that extended-release venlafaxine may prove to be an effective, well-tolerated, short-term treatment for children and adolescents with generalized anxiety disorder. (37 References)
PSYCHIATRIC TREATMENT IN PRIMARY CARE PATIENTS WITH ANXIETY DISORDERS: A COMPARISON OF CARE RECEIVED FROM PRIMARY CARE PROVIDERS AND PSYCHIATRISTS

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AM J PSYCHIATRY, 164:276-82, February 2007

More than half of patients with a psychiatric problem receive treatment for their symptoms from a primary care physician rather than a mental health specialist. Although anxiety disorders are among the most common mental health problems seen in the primary care setting, very few studies have investigated the nature of mental health treatments for primary care patients with anxiety disorders. The authors of the present study examined psychiatric treatment received by primary care patients with anxiety disorders and compared the treatment they received from primary care physicians with the therapy they received from psychiatrists.

Patients at 15 primary care sites were screened for the presence of anxiety symptoms. Those who screened positive underwent a full diagnostic interview (Structured Clinical Interview for DSM-IV). Several other assessment tools were administered, and information on psychiatric treatments received and providers of pharmacotherapy were collected. In all, 539 primary care patients met criteria for one or more anxiety disorders. Of these, 52.7% were receiving some form of treatment for their psychiatric problems; 24.5% were receiving both psychopharmacological treatment and psychotherapy, 21% were receiving medication only, and 7.2% were receiving psychotherapy only. Patients receiving pharmacotherapy were treated with similar medications, often at similar dosages, whether their prescriber was a primary care physician or a psychiatrist. One exception was that patients were less likely to be taking benzodiazepines if their provider was a primary care physician. Those receiving medications from a primary care provider were also less likely to be receiving psychotherapy. In general, patients with more functional impairment, more severe symptoms, and comorbid depression were more likely to receive mental health treatment. Members of racial/ethnic minority groups were less likely to be treated. Frequently endorsed reasons for not receiving pharmacotherapy were that the primary care physician did not recommend it and that the patient did not believe in taking medications for emotional problems.

In the present study, the authors found that nearly half the primary care patients with anxiety disorders did not receive treatment. However, when they were treated, the care received from primary care physicians and psychiatrists was relatively similar. (26 References)
DULOXETINE TREATMENT FOR ROLE FUNCTIONING IMPROVEMENT IN GENERALIZED ANXIETY DISORDER: THREE INDEPENDENT STUDIES

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J CLIN PSYCHIATRY, 68:518-24, April 2007

In previous epidemiologic and clinical investigations, generalized anxiety disorder (GAD) has been associated with various role functioning impairments, medical and psychiatric comorbidity, and diminished well-being. Using data from three independent clinical studies, the authors of the present report examined the efficacy of duloxetine treatment for improving functional outcomes in adult outpatients who met DSM-IV criteria for GAD.

All three studies were randomized, double-blind, placebo-controlled multicenter trials conducted between June 2004 and November 2005. Study 1 involved 42 treatment centers in seven countries. Studies 2 and 3 were conducted independently at outpatient centers (62 separate sites) throughout the United States. Study 1 was a nine-week, fixed-dose trial in which duloxetine 60 mg (N=168) and duloxetine 120 mg (N=170) were compared with placebo (N=175). The other two studies were 10-week, flexible-dose trials in which duloxetine 60-120 mg (study 2, N=168; study 3, N=162) was compared with placebo (study 2, N=159; study 3, N=161). The main functional outcome measure for each study was the Sheehan Disability Scale (SDS). Additional assessment tools included the Quality of Life Enjoyment and Satisfaction Questionnaire Short Form and the European Quality of Life 5 Dimensions. In all three studies, duloxetine-treated patients improved significantly more than placebo-treated patients on SDS global functioning scores. In each study, the duloxetine group demonstrated significantly greater improvement than the placebo group across the SDS domains of work, social life, and family/home responsibility. At treatment endpoint, duloxetine patients were more likely than placebo patients to obtain an SDS global functioning score in the normative range; across the studies, approximately 47% of duloxetine patients and 28% of placebo patients achieved this outcome. Compared with placebo-treated patients, duloxetine-treated patients also reported greater increases in quality of life, well-being, and health.

The authors conclude that in the three independent studies reported here, duloxetine consistently reduced role functioning disabilities associated with GAD and enhanced patients’ well-being and quality of life. (35 References)
AN OPEN-LABEL TRIAL OF ARIPIPRAZOLE AUGMENTATION FOR TREATMENT-RESISTANT GENERALIZED ANXIETY DISORDER

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J CLIN PSYCHOPHARMACOL, 22:207-10, April 2007

Generalized anxiety disorder (GAD), a common condition characterized by excessive worrying, is associated with significant functional and vocational impairment. GAD tends to have a chronic course, and remission is uncommon. Aripiprazole, a second-generation atypical antipsychotic, has not yet been studied prospectively in patients with primary GAD. The authors conducted a pilot study of the efficacy and tolerability of aripiprazole as an adjunctive therapy in patients with treatment-resistant GAD.

The sample consisted of nine patients (three men, six women; age range, 18 to 65 years; mean age, 35 years). Entry criteria included a primary DSM-IV diagnosis of GAD, a Hamilton Anxiety Rating Scale (HAMA) score of 14 or higher, and a Clinical Global Impression Scale (CGI) score of at least 4 (moderately ill). The patients reported significant levels of anxiety at baseline, with the mean HAMA score being 26.2, and the mean CGI score being 5 (markedly ill). At baseline, eight of the nine patients had a secondary diagnosis of depression. Five were taking selective serotonin reuptake inhibitors, and four were taking other antidepressants. The patients’ current medication regimen was augmented with open-label aripiprazole over a six-week period. Dosing was begun at 10 mg per day and was adjusted at each visit on the basis of tolerability and response. Primary outcomes were measures of anxiety symptoms (HAMA) and overall improvement (CGI). Secondary outcomes included disability and quality of life as measured by the Medical Outcome Study Short Form (SF-36), depression as assessed by Hamilton Rating Scale for Depression (HDRS), and extrapyramidal symptoms as measured by the Extrapyramidal Symptom Rating Scale. Both primary outcome measures showed significant improvement from baseline to endpoint. The mean HAMA improved to 14.2, and eight patients were rated as much improved (CGI=2) or very much improved (CGI=1). According to the HAMA, five patients were responders (50% or greater reduction in scores), and one was a remitter (final score of less than 10). The mean HDRS score improved significantly from 21.6 at baseline to 11.8 at endpoint, and scores on multiple subscales of the SF-36 also improved. In general, the drug was well tolerated, although one patient did terminate early because of unresolved akathisia.

According to the authors, although the present study is small and open-label in design, the findings do suggest that aripiprazole may be a useful adjunctive treatment for those GAD patients who are suboptimally responsive to antidepressant therapy. (17 References)
BOOKS RECEIVED FOR REVIEW


Abstracts and Reviews of Selected Literature in Psychiatry, Neurology, and their Allied Fields

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**Olanzapine Versus Risperidone in the Treatment of Manic or Mixed States in Bipolar I Disorder: A Randomized, Double-Blind Trial**
BIOLOGICAL RISK FACTORS IN PEDIATRIC BIPOLAR DISORDER

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BIOL PSYCHIATRY, 60:936-41, November 1, 2006

Although there is some variability in criteria across research groups, elated or expansive mood, irritability, and grandiosity appear to be the core features of pediatric bipolar disorder (PBD). Identifying potential biological risk factors is a promising strategy not only for delineating the etiopathogenesis of PBD but also for facilitating early detection and intervention. Using a cross-sectional design, the authors of the current investigation attempted to determine whether neurodevelopmental and biomedical abnormalities are more common in individuals with PBD than in those without this disorder.

The study sample (98 subjects; age range, 5 to 18 years; mean age, 11.5 years) consisted of three demographically matched groups: healthy controls (N=28), children diagnosed with PBD only (N=37), and children diagnosed with PBD and attention deficit hyperactivity disorder (N=33). Family psychiatric history was obtained by interviewing the subjects’ parents and having them complete the Family History Screen. A subject’s family history was considered to be positive if any first-degree relative had received a diagnosis of bipolar disorder (BD). Additional measures were administered to obtain comprehensive information on perinatal risk factors, developmental milestones, history of traumatic brain injury, serious medical illnesses, and history of hospitalizations for medical problems. Results of logistic regression indicated that only family history and perinatal risk significantly predicted a diagnosis of PBD. A diagnosis of PBD was 15 times higher among those subjects with a family history of BD. The mean number of perinatal risk factors in the total sample was .53. For every additional perinatal risk factor, such as prenatal exposure to drugs or birth complications, the risk of having a diagnosis of PBD increased more than sixfold. No evidence was found to support the theory that combinations of risk factors (e.g., family history plus perinatal risk) were associated with greater risk than individual biological risk factors.

According to the authors of the present investigation, having a positive family history of bipolar disorder in a first-degree relative and being exposed to perinatal insults may elevate the risk for developing PBD. The presence of these risk factors, especially in the context of clinical signs of affect dysregulation, should alert clinicians to screen for PBD. (46 References)
PHENOMENOLOGY OF CHILDREN AND ADOLESCENTS WITH BIPOLAR SPECTRUM DISORDERS

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ARCH GEN PSYCHIATRY, 63:1139-48, October 2006

There are relatively few published studies that examine the clinical phenomenology of pediatric bipolar disorder. Children and adolescents who present with manic symptoms frequently do not meet the full DSM-IV diagnostic criteria for bipolar I disorder (BP-I). The purpose of the present investigation was to assess the clinical presentation and family history of children and adolescents with BP-I, bipolar II disorder (BP-II), and bipolar disorder not otherwise specified (BP-NOS).

The study sample was composed of 438 children and adolescents (mean age, 12.7 years); 255 had BP-I, 30 had BP-II, and 153 had BP-NOS. Subjects were assessed by means of semistructured interviews with the child or adolescent and a parent or primary caregiver. The subject’s primary caretaker was interviewed at intake about his/her personal psychiatric history and the psychiatric status of the subject’s first- and second-degree relatives. Children and adolescents with BP-NOS were not diagnosed as having BP-I primarily because they did not meet DSM-IV duration criteria for a manic or mixed episode. There were no significant differences between the BP-I and BP-NOS groups in terms of age at onset; duration of illness; lifetime rates of comorbid diagnoses, suicidal ideation, and major depression; family history; and types of manic symptoms that were present during the most serious lifetime episode. Compared with the subjects with BP-NOS, those with BP-I had more severe manic symptoms; greater overall functional impairment; and higher rates of hospitalization, psychosis, and suicide attempts. Elevated mood was present in 81.9% of the BP-NOS group and 91.8% of the BP-I group. Subjects in the BP-II group had higher rates of comorbid anxiety disorders than those in the other two groups. Compared with subjects in the BP-I group, those in the BP-II group had less functional impairment and lower rates of psychiatric hospitalization.

According to the authors of the present investigation, children and adolescents with BP-II and BP-NOS have a phenotype that exists on a continuum with that of children and adolescents with BP-I. They also note that elevated mood appears to be a common feature of children and adolescents with BP-spectrum illness. (38 References)
FAMILIALITY OF POLARITY AT ILLNESS ONSET IN BIPOLAR AFFECTIVE DISORDER

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Bipolar affective disorder is a clinically heterogeneous illness, and clinical features that run in families may help to define more homogeneous phenotypes. One of the features of bipolar affective disorder that varies across individuals is the polarity of the initial episode at onset of illness. The authors of the present investigation attempted to determine whether polarity at illness onset, which is related to the severity and course of the illness, is a familial feature of bipolar affective disorder.

As part of a large, multisite, genetic linkage study, detailed clinical data were collected on 507 families ascertained through sibling pairs affected with bipolar I disorder or schizoaffective bipolar disorder. Polarity at onset was assessed in 971 affected individuals (340 males, 631 females) from these families. Self-reported ages at onset of mania and major depression were used to code polarity at onset as manic, major depressive, or both (mania and major depression occurring in the same onset year). Familial clustering was estimated by means of mixed-effects regression analysis, and the relationship between polarity at onset and several other clinical features was evaluated. As a preliminary test of genetic validity, the researchers assessed the impact of polarity at onset on genetic linkage findings previously detected in the current sample. The results indicated that polarity at onset was significantly familial in this sample. This finding largely reflected relative pairs concordant for mania at onset, which occurred significantly more frequently than would be expected by chance. Mania at onset substantially increased the genetic linkage signal on chromosome 16p (maximum lod score=4.5) but had no effect on linkage to chromosome 6q. On average, mania at onset occurred at a later age than major depression at onset and was less likely to be complicated by panic attacks or alcoholism.

According to the authors, the present findings indicate that polarity at onset is a familial feature of bipolar affective disorder. The current results also suggest that polarity at onset, particularly mania at onset, may be genetically informative. Polarity at onset may help define subtypes of bipolar affective disorder that are more homogeneous in terms of clinical features and underlying genetic etiology. (25 References)
WHAT IS FAMILIAL ABOUT FAMILIAL BIPOLAR DISORDER?
Resemblance Among Relatives Across a Broad Spectrum of Phenotypic Characteristics

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ARCH GEN PSYCHIATRY, 63:1368-76, December 2006

The phenotype increasingly has become a focus of genetic research in bipolar affective disorder (BPAD) and other genetically complex conditions. Current diagnostic criteria define a phenotype that is highly heritable, yet clinically variable. One approach in attempting to identify the most promising phenotypic variables for use in gene mapping is to assess which traits are most familial and then use these traits to define subtypes among individuals affected with the broader disorder. The aim of the present study was to examine the familiality of phenotypic features in families ascertained through individuals with BPAD.

The current sample was composed of 1,246 individuals (529 males, 717 females; mean age, 49 years) from 172 multiplex families recruited within the framework of a bipolar disorder (BP) genetics study. Of these 1,246 subjects, 253 had a diagnosis of BP-I, 215 had BP-II, 150 had recurrent unipolar disorder, 12 had schizoaffective BP, 354 could not be unequivocally assigned to a major mood disorder diagnosis, and 262 were considered to be unaffected by a major mood disorder. The familiality of 40 diverse phenotypic features was examined through the use of mixed-effects regression analyses. Substance abuse, alcoholism, psychosis, history of suicide attempt, and level of social functioning were found to be strongly familial. An additional 15 variables showed a nominally significant familial effect, but they did not withstand conservative correction for multiple testing. These included age at onset, diagnostic subtype, healthiest level of functioning, suicidal ideation in depression, poor judgment in hypomania, and several comorbid conditions.

Taken together, the findings of the present study suggest that definitions of the affected phenotype of BPAD might usefully consider comorbid conditions and social functioning in addition to traditional symptoms. People whose bipolar disorder is complicated by substance abuse, psychosis, and poor social relations may differ genetically from those individuals whose illness shows none of these features. According to the authors, the systematic assessment of familiality may help to resolve this genetically complex disorder into more homogeneous subtypes that are better suited for genetic studies and other biological investigations. (77 References)
SUBSYNDROMAL DEPRESSIVE SYMPTOMS ARE ASSOCIATED WITH FUNCTIONAL IMPAIRMENT IN PATIENTS WITH BIPOLAR DISORDER: RESULTS OF A LARGE, MULTISITE STUDY

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Studies of patients with unipolar depression have demonstrated a relationship between subthreshold depressive symptoms and impairment in role functioning. However, there is very little research that examines this association in persons with bipolar disorder. In the present investigation, the authors attempted to evaluate the relationship between subsyndromal depressive symptoms and role functioning in individuals with bipolar disorder.

The sample consisted of 759 adult outpatients who had a DSM-IV diagnosis of bipolar disorder, were enrolled in the Stanley Foundation Bipolar Network between March 1996 and November 2002, and were followed longitudinally for assessment of their course of illness. On the basis of cutoff scores obtained from administration of the Inventory for Depressive Symptomatology-Clinician Rated, the patients were assigned to one of three groups: not depressed (N=292), subsyndromally depressed (N=291), and syndromally depressed (N=176). The Life Functioning Questionnaire was used to assess degree of role function impairment in four domains: duties at work/school, duties at home, family life, and friendships. The subsyndromally depressed group was significantly more likely than the nondepressed group to report impairment at work (64% vs. 31%), in functioning at home (75% vs. 38%), in their relationships with family (59% vs. 34%) and friends (56% vs. 18%), and in overall life functioning (70% vs. 32%). The proportion of impaired subjects in the subsyndromally depressed group was closer to the proportion of impaired subjects found in the syndromally depressed group than to the proportion found in the nondepressed group.

According to the authors, the current findings clearly demonstrate the public health significance of subsyndromal depression in the bipolar population. Since patients with bipolar disorder are two to three times more likely to develop depressive symptoms rather than hypomanic symptoms between acute episodes of illness, and since subsyndromal depressive symptoms are predictive of relapse into syndromal depression, the researchers note, there is a need to consider treating subsyndromal depressive symptoms. (67 References)
THE RELATIONSHIP BETWEEN SMOKING AND SUICIDAL BEHAVIOR, COMORBIDITY, AND COURSE OF ILLNESS IN BIPOLAR DISORDER

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J CLIN PSYCHIATRY, 67:1907-11, December 2006

The prevalence of nicotine dependence in people with bipolar disorder is markedly greater than that found in the general population. This elevated rate of smoking may contribute to the increased risk of death from natural causes in the bipolar population. In the retrospective study presented here, the authors explored the relationship between smoking, severity of bipolar disorder, psychiatric comorbidity, and suicidal behavior.

The sample was composed of 399 outpatients (183 males, 216 females) who had bipolar disorder and who were treated in a bipolar specialty clinic between December 1999 and October 2004. The Affective Disorders Evaluation and the Mini-International Neuropsychiatric Interview were used to assess diagnosis, mood state, course of illness, level of functioning, and psychiatric comorbidity. Of the 399 bipolar patients who were evaluated, 155 (39%) had a history of daily smoking, and 244 (61%) had never smoked. Having ever smoked was associated with earlier age at onset of first depressive episode, earlier age at onset of first manic episode, lower Global Assessment of Functioning (GAF) scores, higher Clinical Global Impressions-Bipolar Disorder (CGI-BP) scale scores, history of a comorbid anxiety disorder, history of alcohol dependence, history of alcohol abuse, history of substance dependence, history of substance abuse, and lifetime history of a suicide attempt. In a logistic regression model with history of smoking as the dependent variable and age at onset of depression, age at onset of mania, history of having made a suicide attempt, GAF scores, CGI-BP scores, and a lifetime history of an anxiety disorder, alcohol dependence, alcohol abuse, substance dependence, and substance abuse as covariates, the only two variables that continued to be significantly associated with smoking in these bipolar patients were a history of having made a suicide attempt and a history of substance dependence.

According to the authors, the current findings indicate that in patients with bipolar disorders, a history of smoking is associated with a more severe course of illness and greater comorbidity in terms of anxiety, alcohol use, and substance use disorders. They also note that smoking may be independently associated with suicidal behavior in bipolar patients. (18 References)
SUB-SYNDROMAL AND SYNDROMAL SYMPTOMS IN THE LONGITUDINAL COURSE OF BIPOLAR DISORDER

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BR J PSYCHIATRY, 189:118-23, August 2006

There have been few detailed longitudinal symptom studies of persons with bipolar disorder. In the investigation presented here, the authors attempted to examine the course of bipolar disorder over an 18-month period in a group of bipolar patients who were receiving mental health care.

The study sample was composed of 204 bipolar patients (71 males, 133 females; mean age, 42 years). The participants were interviewed every eight weeks, and weekly ratings of depression, mania, and overall symptom severity were obtained. The subjects had experienced a median of 11 previous bipolar episodes; 67 had received a lifetime diagnosis of a comorbid nonbipolar disorder, 89 had a history of previous substance abuse or dependence, and 179 were receiving mood stabilizers at baseline. Over the course of the 18-month follow-up, the patients were symptomatic 53% of the time; they experienced subsyndromal symptoms 23% of the time, minor symptoms 20% of the time, and major symptoms 10% of the time. Depressive symptoms were present three times longer than manic symptoms. Individuals who were experiencing a bipolar episode at baseline spent 33% of the 18-month follow-up with substantial subsyndromal symptoms, 22% of the time with minor symptoms, 17% of the time with major symptoms, and 28% of the time with no symptoms. Patients who were not experiencing a bipolar episode at baseline spent 19% of the follow-up period with substantial subsyndromal symptoms, 6% of the time with minor symptoms, and 55% of the time with no symptoms. Changes in symptom level were frequent. Over the 18 months of follow-up, there was an average of 5.4 changes in depression level, three changes in level of manic symptoms, and six changes in overall symptom severity level. Individuals who were experiencing a bipolar episode at baseline underwent a mean of 6.6 changes in symptom level during follow-up, while those who were not experiencing an episode at baseline underwent a mean of 5.7 changes in symptom level over the 18 months.

According to the authors, the results of the current investigation indicate that subsyndromal residual symptoms are an important problem in individuals who suffer from a recurrent bipolar disorder. Continuation and/or maintenance treatment may well be necessary, especially for those who have experienced an episode over the past year. (29 References)
ADEQUACY OF TREATMENT RECEIVED BY DIAGNOSED AND UNDIAGNOSED PATIENTS WITH BIPOLAR I AND II DISORDERS

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For many patients with bipolar disorder, there is a gap between optimal pharmacotherapy and the drug treatment that they are actually receiving. The aim of the current study was to investigate the adequacy of pharmacotherapy in a representative sample of patients with a research diagnosis of bipolar I or II disorder, including both those patients who had and who not yet received a clinical diagnosis of bipolar disorder.

As part of the Jorvi Bipolar Study, between January 1, 2002, and February 28, 2003, a total of 1,630 psychiatric inpatients and outpatients from three Finnish cities were systematically screened for the presence of bipolar I and II disorders by means of the Mood Disorders Questionnaire. Through the use of structured clinical interviews, 191 patients (mean age, 38 years) were diagnosed with bipolar disorder (90 with bipolar I and 101 with bipolar II). Information was collected on clinical history, diagnosis, and therapy, and the adequacy of treatment received was evaluated. Of the 162 patients with previous episodes of bipolar disorder, only 34 (20.9%) were being treated with a mood stabilizer at the onset of the index episode. Of these 162 patients, 54 had a clinical diagnosis of bipolar disorder before the onset of the index episode, and 30 (55.5%) of these 54 were receiving a mood stabilizer before the index episode started. Only 81 (42.4%) of the 191 patients who were assigned a research diagnosis of bipolar disorder were classified as having received adequate acute-phase treatment; men received adequate treatment more often than women, bipolar I patients more often than bipolar II patients, and inpatients more often than outpatients. The factor found to be most strongly independently associated with adequate treatment was a clinical diagnosis of bipolar disorder. In addition, rapid cycling, polyphasic index episode, and depressive index phase were independent predictors of inadequate treatment.

The authors conclude that a clinical diagnosis of bipolar disorder is by far the most important prerequisite for receiving adequate treatment. Problems in treatment seem to be associated mainly with outpatient settings, where adequate therapy for individuals with bipolar depression is a major concern. In addition, the longitudinal course of bipolar disorder appears to pose an obstacle to the provision of adequate treatment. (46 References)
MAINTENANCE MODEL OF INTEGRATED PSYCHOSOCIAL TREATMENT IN PEDIATRIC BIPOLAR DISORDER: A PILOT FEASIBILITY STUDY

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 46:205-12, February 2007

Pediatric bipolar disorder (PBD) is characterized by mixed mood states, rapid cycling, excessive elation, prominent irritability, frequent comorbid conditions, and a chronic and refractory course. PBD is associated with behavioral and academic difficulties in school, poor social skills, conflictual relationships with siblings, and stressed parents. In the open pilot study presented here, the authors evaluated the feasibility of a maintenance model of the child- and family-focused cognitive-behavioral therapy program (CFF-CBT), an integrated treatment plan that consists of psychosocial booster sessions and optimized pharmacotherapy. The researchers attempted to determine whether positive effects seen after the acute phase of treatment could be sustained over time with the use of this maintenance model.

The sample was composed of 34 PBD patients (24 boys, 10 girls; age range, 5 to 17 years; mean age, 11.3 years) who underwent CFF-CBT during the acute phase of treatment and then received the maintenance model over a follow-up period of three years. Twenty-eight of the participants had a primary diagnosis of PBD type 1, three were considered to have PBD type 2, and three were classified as having PBD not otherwise specified. All but five of the patients had other Axis I disorders, with the most prevalent comorbid conditions being attention deficit/hyperactivity disorder (73.5%), oppositional defiant disorder (35%), and learning disorders (32%). Symptom changes were assessed by means of the Children’s Global Impressions Scale-Bipolar, and global functioning was measured by means of the Children’s Global Assessment Scale. The results indicated that participation in the maintenance model of CFF-CBT was associated with positive effects in symptoms and functioning over the three-year follow-up period. There were no significant differences found between assessment scale scores obtained after the acute phase of treatment and scores obtained at years 1, 2, and 3 of follow-up, indicating the maintenance of clinically significant improvements.

The current findings demonstrate that three years after the acute phase of treatment, those PBD patients who received CFF-CBT maintenance therapy were able to sustain the positive effects of the initial intervention. According to the authors, the refractory nature and low recovery rates associated with PBD may be preventable through the use of an ongoing integrated program of pharmacotherapy and psychosocial treatment. (19 References)
OLANZAPINE VERSUS RISPERIDONE IN THE TREATMENT OF
MANIC OR MIXED STATES IN BIPOLAR I DISORDER:
A RANDOMIZED, DOUBLE-BLIND TRIAL

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Contemporary treatment guidelines now include the use of an atypical
antipsychotic (either as monotherapy or add-on therapy) as a first-line treatment
option in manic patients. In the present three-week, randomized, controlled,
double-blind, parallel multicenter study, the authors compared the efficacy of
two atypical antipsychotics (olanzapine and risperidone) in the treatment of
nonpsychotic acute manic or mixed episodes. The study was conducted at 30
sites in the United States between July 2001 and June 2002.

In all, 329 hospital inpatients who met DSM-IV criteria for bipolar I disorder,
manic or mixed episode, without psychotic features, were randomly assigned to
receive olanzapine (N=165) or risperidone (N=164). The mean modal dose was
14.7 mg/day for olanzapine and 3.9 mg/day for risperidone. The primary
outcome measure was mean change in Young Mania Rating Scale (YMRS) total
score. Secondary measures included the 21-item Hamilton Rating Scale for
Depression (HAM-D-21), the Montgomery-Asberg Depression Rating Scale
(MADRS), the Clinical Global Impressions-Bipolar Version (CGI-BP) severity of
illness scale, and the Cognitive Test for Delirium (CTD). Quality of life (Short
Form Health Survey [SF-12]), psychological well-being (Psychological General
Well-Being [PGWB]), and sexual functioning were also assessed. Significantly
more olanzapine-treated patients (78.7%) than risperidone-treated patients
(67%) completed the study. Comparison of the efficacy of the two drugs showed
that there was no difference in mean change on the YMRS, MADRS, CTD,
PGWB, or SF-12 measures or in remission or response rates. Olanzapine-treated
patients exhibited greater improvement in HAM-D-21 scores over the course of
the study. Olanzapine-treated patients experienced higher elevations in liver
function enzymes and greater increases in weight, while risperidone-treated
patients were more likely to experience prolactin elevation and sexual
dysfunction.

The authors conclude that olanzapine and risperidone were associated with
similar improvements in the symptoms of acute mania after three weeks of
administration. The two treatments also yielded similar response and remission
rates, but differed in rates and times to discontinuation and in adverse event
profiles. (40 References)
Abstracts and Reviews of Selected Literature in Psychiatry, Neurology, and their Allied Fields

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REPORTED CHILDHOOD ONSET OF SELF-MUTILATION AMONG BORDERLINE PATIENTS

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Self-mutilation is one of the most compelling and distressing symptoms of borderline personality disorder (BPD). The purpose of the present investigation was to determine the percentage of borderline patients who first engaged in self-mutilation as children and to compare the parameters of their self-harm with those of borderline patients who first harmed themselves at an older age. Only behaviors that were engaged in with the purpose of deliberately inflicting physical damage to one’s body (without suicidal intent) were considered (e.g., cutting, burning, punching oneself).

The study sample was composed of 290 inpatients (233 females, 57 males; age range, 18 to 35 years; mean age, 26.9 years) who met diagnostic criteria (both DSM-III-R and Revised Diagnostic Interview for Borderlines) for BPD. Past experiences of deliberate self-harm were assessed by means of the Lifetime Self-Destructiveness Scale, a semistructured interview that is designed to elicit information regarding the age that deliberate physically self-destructive behavior began, the types of self-destructive behaviors, the number of instances, and the duration of self-harm. In all, 90.5% (N=262) of the patients reported a history of self-mutilation. Of these, 32.8% (N=86) reported first harming themselves as children (12 years of age or younger), 30.2% (N=79) reported first harming themselves as adolescents (between 13 and 17 years of age), and 37% (N=97) reported first harming themselves as adults (18 years of age or older). Using logistic regression analyses and controlling for baseline age, the authors found that borderline patients with a childhood onset of self-mutilation reported more episodes of self-harm, a longer duration of self-harm, and a greater number of self-harm methods than those with either an adolescent or adult onset. Of those with a childhood onset of self-mutilation, two thirds reported harming themselves at least 50 times, three quarters reported harming themselves over a period of 15 years or longer, and half reported using at least four different methods of self-mutilation.

According to the authors, the results of the current investigation suggest that a sizable minority of borderline patients first engage in self-harm as children and that the course of their self-mutilative behavior may be particularly malignant. (26 References)
Borderline personality disorder (BPD) is a severe, chronic illness that is characterized by affective, impulsive, and interpersonal symptoms. It is also considered to be the paradigmatic adult disorder of social attachment. Using a reliable self-report instrument based on an empirically derived model of attachment, the authors of the present study attempted to characterize the social attachment patterns of clinically stable adults with BPD along two fundamental dimensions (attachment-anxiety and attachment-avoidance). They also evaluated the relationships between adult attachment disturbances and the following: five types of childhood maltreatment (emotional abuse, sexual abuse, physical abuse, emotional neglect, physical neglect), current interpersonal problems, and current clinical symptoms.

The subjects were 40 outpatients who met DSM-IV criteria for BPD. For comparison purposes, healthy control subjects were recruited from the community. The results indicated that compared with the control group, the BPD group had significantly elevated scores on each of the two fundamental social attachment dimensions. The overall distribution of attachment types was significantly different in the two groups. In the BPD group, the most prevalent attachment type was the fearful type; this type was found to be significantly more frequent in the BPD group than in the control group. In the BPD group, attachment-anxiety was specifically associated with childhood sexual abuse, while attachment-avoidance was associated with all five types of childhood maltreatment. The two attachment dimensions had divergent associations with current interpersonal problems, impulsivity subtypes, and mood symptoms. For example, in terms of current symptom profiles, elevated attachment-anxiety was associated with hostility and both attentional and motor impulsivity, whereas elevated attachment-avoidance scores were found to be related to depressive symptoms as well as to nonplanning impulsivity.

The authors conclude: (1) that BPD is characterized by adult attachment disturbances; (2) that these disturbances are strongly related to childhood maltreatment, current interpersonal problems, and current core clinical symptoms of BPD; and (3) that the diverse problems of BPD patients may arise from two basic mechanisms, each of which may be associated with a different type of attachment disturbance, developmental history, and clinical outcome. (45 References)
THE RELATIONSHIP OF BORDERLINE PERSONALITY DISORDER, LIFE EVENTS AND FUNCTIONING IN AN AUSTRALIAN PSYCHIATRIC SAMPLE

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J PERSONAL DISORD, 20:205-17, June 2006

Current research suggests that personality disorders (PDs), and borderline personality disorder (BPD) in particular, are associated with an increased frequency of major life events and disruptions in life functioning, especially in the interpersonal domain. Exposure to life events in individuals with BPD may lead to an exacerbation of symptoms associated with the disorder, including an increase in suicide attempts and self-injurious behaviors. In the present study, the authors investigated the impact of recent life events, daily hassles, and daily uplifts on psychosocial functioning in patients with PDs. They also examined the role of perceived coping effectiveness and perceived stress of recent life events.

In all, 97 participants (45 males, 52 females; age range, 18 to 64 years; mean age, 39 years) underwent clinical interviews and completed measures of functioning, recent life events (occurring within the past six months), and daily hassles and uplifts (occurring within the past month). For purposes of comparison, the sample was divided into three diagnostic groups: the Axis I only group (N=30), the BPD group (N=23), and the Other PD group (N=44). No significant age or gender differences were found among the groups. Compared with the other two groups, the BPD group reported the poorest levels of functioning, especially with regard to interpersonal relationships. The BPD group also reported more negative life events, particularly in the interpersonal relationships, personal health, crime, and financial domains. The BPD group experienced less daily uplifts and more daily hassles, and found attempting to cope with employment circumstances to be particularly stressful and difficult. The intensity of daily hassles was found to be predictive of functioning independently of a BPD diagnosis. A greater frequency of life events was closely associated with a non-BPD diagnosis in predicting a decrease in psychosocial functioning.

According to the authors, the present findings indicate that, compared with individuals with no PD diagnosis and those with other PD diagnoses, persons with BPD have lower levels of psychosocial functioning, perceive daily hassles as being more intense, and experience a greater total number of life events. However, the researchers note, the presence of recent life events does not appear to be directly related to psychosocial functioning in individuals diagnosed with BPD. (28 References)
TEMPERAMENTAL AND ENVIRONMENTAL RISK FACTORS FOR BORDERLINE PERSONALITY DISORDER AMONG INNER-CITY SUBSTANCE USERS IN RESIDENTIAL TREATMENT

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Borderline personality disorder (BPD) is characterized by persistent problems with emotional, behavioral, cognitive, and interpersonal functioning. There is a general consensus that BPD is best accounted for within the context of a diathesis-stress model, with the disorder appearing to arise from a combination of biologically based temperamental vulnerabilities and childhood adversity. Despite the presence of a growing body of evidence that implicates a variety of temperamental and environmental risk factors in the development of BPD, the unique contribution of each remains unclear. Furthermore, the extent to which these factors are associated with BPD in underserved and diverse populations is not known. In the current study, the authors examined the temperamental and environmental factors uniquely associated with BPD in inner-city drug users.

The mixed-gender sample was composed of 93 individuals (age range, 21 to 63 years; mean age, 41.51 years) who were primarily of African-American descent (92.5%) and who were receiving residential substance use treatment. Assessment instruments included the Multidimensional Personality Questionnaire-Brief Form, the Childhood Trauma Questionnaire-Short Form, and the Structured Clinical Interview for DSM-IV, Axis II (SCID-II). Results of the SCID-II interviews revealed that 25.8% (N=24) of the participants met diagnostic criteria for BPD. With regard to the contribution of temperamental factors, the findings indicated that BPD was associated with higher impulsivity and emotional instability/vulnerability, lower well-being, and several interpersonal manifestations of positive and negative temperament (i.e., greater alienation and lower achievement and social closeness). In terms of environmental factors, the authors found a relationship between BPD and several forms of abuse and neglect (including emotional and physical abuse and emotional and physical neglect). Only emotional instability or vulnerability, impulsivity, and emotional abuse emerged as unique predictors of BPD.

According to the authors, the current investigation fits well within theoretical accounts of BPD and represents one of the few extensions of such work to more underserved at-risk populations. They recommend that future studies extend their findings by means of prospective, longitudinal investigations and the use of objective measures of abuse. (57 References)
PREDICTORS OF 2-YEAR OUTCOME FOR PATIENTS WITH BORDERLINE PERSONALITY DISORDER

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AM J PSYCHIATRY, 163:822-6, May 2006

The primary purpose of the present report was to determine whether baseline characteristics of individuals with borderline personality disorder would be predictive of variations in outcome at a two-year follow-up. The current investigation took place within the context of a series of prior studies that were characterized by the use of widely divergent predictor variables, often assessed retrospectively and, if measured prospectively, without established reliability.

The sample (75% female; 71% Caucasian; age range, 18 to 45 years) was composed of 160 patients with borderline personality disorder, all of whom were recruited from the four clinical sites of the Collaborative Longitudinal Personality Disorders Study. The patients were assessed at baseline and at six, 12, and 24 months with the Structured Clinical Interview for DSM-IV Axis I disorders; a modified version of the Diagnostic Interview for Personality Disorders; the Longitudinal Interval Follow-up Evaluation; and the Childhood Experiences Questionnaire-Revised. Univariate Pearson’s correlation coefficients were calculated on several primary predictor variables, and with two forward stepwise regression models, outcome was assessed in terms of global functioning (as measured by Global Assessment of Functioning [GAF] Scale scores) and number of borderline personality disorder criteria met. The results indicated that more severe baseline psychopathology (i.e., higher levels of borderline personality disorder criteria and functional disability) and a history of childhood trauma were predictive of a poor outcome. The data also suggested that the quality of a borderline patient’s current relationships may have prognostic significance.

According to the authors, the findings of the present investigation indicate that when developing a two-year prognosis for patients with borderline personality disorder, assessments of severity, both symptomatic (i.e., criteria-based) and functional (i.e., based on GAF Scale scores), are of the greatest importance. The researchers also suggest that a thorough examination of borderline patients’ current relationships and past relational histories (specifically, histories of early childhood maltreatment) may add to estimates of the expected prognoses. (33 References)
PREDICTION OF THE 10-YEAR COURSE OF BORDERLINE PERSONALITY DISORDER

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The purpose of the present study was to determine the most clinically relevant baseline predictors of time to remission in patients with borderline personality disorder. A total of 290 inpatients (233 women, 57 men; mean age, 26.9 years) who met both Revised Diagnostic Interview for Borderlines and DSM-III-R criteria for borderline personality disorder were assessed during their index admission with a series of semistructured interviews and self-report measures. Diagnostic status was reassessed at five contiguous two-year time periods. Discrete survival analytic methods, which controlled for baseline severity of borderline psychopathology and time, were used to estimate hazard ratios.

Of the 290 original participants, 275 were reinterviewed at two years, 269 at four years, 264 at six years, 255 at eight years, and 249 at 10 years. Of the 275 borderline patients with at least one follow-up interview, 242 (88%) achieved remission. Of the 242 patients who experienced a remission of their borderline personality disorder, 95 (39.3%) first remitted by their two-year follow-up, 54 (22.3%) first remitted by the four-year follow-up, 53 (21.9%) first remitted by their six-year follow-up, 31 (12.8%) first remitted by the eight-year follow-up, and nine (3.7%) first remitted by their 10-year follow-up. Sixteen variables were found to be significant bivariate predictors of earlier time to remission (younger age; no prior psychiatric hospitalization; no history of childhood sexual abuse; less severe childhood abuse of a verbal, emotional, or physical nature; less severe childhood neglect; less severe violence witnessed as a child; higher degree of childhood competence; no family history of mood or substance use disorder; absence of posttraumatic stress disorder and anxious cluster personality disorders; low neuroticism; high extroversion; agreeableness; conscientiousness; and a good vocational record in the two-year period prior to index admission). Seven of these factors remained significant in multivariate analyses: younger age, absence of childhood sexual abuse, no family history of substance use disorder, good vocational record, absence of an anxious cluster personality disorder, low neuroticism, and high agreeableness.

The results suggest that prediction of symptomatic outcome for borderline personality disorder is multifactorial in nature. It encompasses predictors that are routinely assessed in clinical practice and factors (particularly aspects of temperament) that are rarely addressed. (31 References)

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Presently there exists only a modest body of methodologically sound research that addresses the interface of borderline personality disorder and bipolar disorder. In the investigation presented here, the authors attempted to determine whether borderline personality disorder is a variant of bipolar disorder by examining the rates of co-occurrence in both disorders, studying the effects of co-occurrence on a longitudinal course, and evaluating whether the presence of either disorder confers the risk for new onsets of the other.

A prospective repeated-measures design with reliable independent diagnostic measures and four years of follow-up was used to assess 196 patients with borderline personality disorder and 433 patients with other personality disorders (i.e., schizotypal personality disorder, avoidant personality disorder, and obsessive-compulsive disorder). The results showed that bipolar I and bipolar II disorders were significantly more common in the patients with borderline personality disorder than in the patients with other personality disorders. Comorbid bipolar I or bipolar II disorder was found to have occurred in 19.4% (38/196) of borderline patients but in only 7.9% (34/433) of those with other personality disorders. However, the presence of a co-occurring bipolar disorder appeared to have no appreciable clinical effect on the subsequent course of borderline personality disorder. Although only 8.2% of the patients with borderline personality disorder developed new onsets of bipolar disorder, this rate was higher than the percentage of patients with other personality disorders who developed new onsets of bipolar disorder (3.1%). Patients with other personality disorders and co-occurring bipolar disorder generally experienced more new onsets of borderline personality disorder (25%) than did patients with other personality disorders but no comorbid bipolar disorder (10%).

According to the authors, the results of the present investigation demonstrated a modest association between borderline personality disorder and bipolar disorder. (36 References)
Borderline personality disorder (BPD) is marked by chronic instability in multiple areas (i.e., emotional dysregulation, self-harm, impulsivity, and identity disturbance). Its prevalence is estimated to be between 1% and 2.5% in the general population and between 10% and 50% in psychiatric inpatient and outpatient settings. However, only limited effects of current treatments have been documented. Using a multicenter, randomized, two-group design, the authors of the present study compared the effectiveness of two prolonged outpatient treatments in achieving full recovery from BPD: schema-focused therapy (SFT) and psychodynamically based transference-focused therapy (TFP).

In all, 88 BPD patients drawn from four community mental health centers were randomized to SFT (N=45) or TFP (N=43). Both treatments were offered in 50-minute sessions twice a week. The main outcome measures were scores on the Borderline Personality Disorder Severity Index, fourth version (BPDSI-IV); quality of life; general psychopathologic dysfunction; and measures of SFT/TFP personality concepts. Assessments were made before randomization and then every three months for three years. Data were available for 44 SFT patients and 42 TFP patients. Sociodemographic and clinical characteristics of the groups were similar at baseline. Survival analyses revealed a higher dropout risk among the TFP patients. Using an intention-to-treat approach, the authors found statistically and clinically significant improvements for both treatments on all measures after one, two, and three years. After three years of treatment, survival analyses revealed that significantly more SFT patients recovered or showed reliable clinical improvement on the BPDSI-IV. Analysis of covariance showed that they also improved more in general psychopathologic dysfunction and measures of SFT/TFP personality concepts. The SFT patients also exhibited greater improvement in quality of life than the TFP patients.

In this study, three years of SFT or TFP brought about significant changes in patients’ personalities, as evidenced by reductions in all BPD symptoms and general psychopathologic dysfunction, improvements in quality of life, and changes in associated personality features. (57 References)
EFFICACY AND TOLERABILITY OF QUETIAPINE IN THE TREATMENT OF BORDERLINE PERSONALITY DISORDER: A PILOT STUDY

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J CLIN PSYCHIATRY, 67:1042-6, July 2006

Borderline personality disorder is characterized by marked impulsivity and a pervasive pattern of instability with regard to self-image, affect, and interpersonal relationships. Second-generation antipsychotics with favorable tolerability profiles have offered new treatment options in the management of this disorder. The present authors conducted a twelve-week, open-label pilot study to determine the efficacy and tolerability of quetiapine (200-400 mg/day) in the treatment of patients with borderline personality disorder.

The sample was composed of 14 outpatients (eight females, six males; mean age, 29.64 years) with a DSM-IV diagnosis of borderline personality disorder. The patients were assessed at baseline, at week 4, and at week 12 with the following measurements: the Clinical Global Impressions (CGI) severity index, the Brief Psychiatric Rating Scale (BPRS), the Hamilton Rating Scale for Depression (HAM-D), the Hamilton Rating Scale for Anxiety (HAM-A), the Social and Occupational Functioning Assessment Scale (SOFAS), the Borderline Personality Disorder Severity Index (BPDSI), and the Barrett Impulsiveness Scale-version 11 (BIS-11). Adverse effects were evaluated by means of the Dosage Record and Treatment Emergent Symptom Scale. Eleven patients (six females, five males; mean age, 30.55 years) completed the study. Of the three patients (21.4%) who dropped out, two did so because of adverse effects (excessive somnolence) and one because of noncompliance. The mean daily dose of quetiapine was 309.09 mg. Significant improvement was observed in the following measures: CGI severity item, BPRS mean score, HAM-A mean score, SOFAS mean score, BPDSI total score, two BPDSI items (“impulsivity” and “outbursts of anger”), and BIS-11 mean score. Among the 11 patients who completed the trial, adverse effects were mild to moderate in intensity, with the most commonly reported being somnolence, dry mouth, and dizziness.

According to the authors, the present results suggest that quetiapine appears to be an effective and well-tolerated antipsychotic treatment for patients with borderline personality disorder. It may be a particularly good therapeutic option when high levels of impulsiveness or aggressiveness are present. The researchers note that double-blind, controlled studies are needed to verify the findings of the current open-label trial. (38 References)
ARIPIPRAZOLE IN THE TREATMENT OF PATIENTS WITH BORDERLINE PERSONALITY DISORDER: A DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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AM J PSYCHIATRY, 163:833-8, May 2006

Aripiprazole is a relatively new atypical antipsychotic agent that has been used successfully in the treatment of patients with schizophrenia and schizoaffective disorder. While a few neuroleptic drugs have been employed in the therapy of patients with borderline personality disorder, the use of aripiprazole in the treatment of this disorder has not yet been evaluated. In the present double-blind, placebo-controlled study, the authors investigated the influence of aripiprazole on the multifaceted psychopathological symptoms and aggressive tendencies in patients with borderline personality disorder.

The sample was composed of 52 subjects (43 women, nine men) who met criteria for borderline personality disorder according to the Structured Clinical Interview for DSM-III-R Personality Disorders. All were randomly assigned in a 1:1 ratio to receive 15 mg/day of aripiprazole (N=26; mean age, 22.1 years) or placebo (N=26; mean age, 21.2 years) for a period of eight weeks. The subjects were assessed weekly. Primary outcome measures were changes in scores on the following: the symptom checklist (SCL-90-R), the Hamilton Depression Rating Scale (HAM-D), the Hamilton Anxiety Rating Scale (HAM-A), and the State-Trait Anger Expression Inventory. Self-injury and side effects were evaluated by means of a nonvalidated questionnaire. According to the intent-to-treat principle, significant changes in scores on most scales of the SCL-90-R, the HAM-D, and the HAM-A, and on all scales of the State-Trait Anger Expression Inventory were observed in the aripiprazole-treated subjects after eight weeks. Self-injury occurred in both the aripiprazole and the placebo groups. Neither serious side effects nor suicidal acts were seen over the course of the study. Reported side effects were headache, insomnia, nausea, numbness, constipation, and anxiety.

The authors conclude that aripiprazole appears to be a safe and effective therapeutic agent for improving not only the symptoms of borderline personality disorder but also the health-related quality-of-life and interpersonal problems associated with this illness. (50 References)
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THE CLOSE LINK BETWEEN SUICIDE ATTEMPTS AND MIXED (BIPOLAR) DEPRESSION: IMPLICATIONS FOR SUICIDE PREVENTION

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J AFFECT DISORD, 91:133-8, April 2006

Some studies have shown that among patients with major mood disorders (unipolar depression, bipolar I disorder, bipolar II disorder), those with bipolar II illness are at the greatest risk for both attempted and completed suicide. It has also been demonstrated that in patients with major mood disorders, suicidal behavior occurs most frequently during major depressive episodes, less frequently during periods of dysphoric (mixed) mania, and almost never during episodes of euphoric mania or euthymia. Recently, reports have shown a significant relationship between suicidal ideation and mixed depression. The aim of the present investigation was to explore the prevalence and clinical characteristics of mixed depression in nonviolent suicide attempters.

The study sample was composed of 100 outpatients (age range, 18 to 65 years) who had attempted suicide by nonviolent means (drug overdose or poisoning). All were examined within 24 hours of their attempt and were administered the modified Mini International Neuropsychiatric Interview, an instrument that assesses the symptoms of 16 Axis I psychiatric diagnoses. Mixed depression was defined as a major depressive episode (MDE) or a dysthymic disorder that was accompanied by three or more co-occurring intradepressive hypomanic symptoms. In all, 89% had a current MDE or dysthymic disorder. Mixed depression was found to be present in 63% of the total sample and in 71% of the 89 suicide attempters with a current MDE or dysthymic disorder. Irritability, distractibility, and psychomotor agitation were present in more than 90% of the patients with mixed depression. The rate of mixed depression was significantly higher in bipolar than nonbipolar depressed suicide attempters (90% vs 62%, respectively). Compared with suicide attempters without mixed depression (N=37), those with mixed depression (N=63) were significantly more likely to be female; to exhibit suicidality; and to have MDEs, bipolar II disorders, anxiety disorders (panic, social phobia, generalized anxiety disorder), substance abuse disorders, and (by definition) co-occurring hypomanic symptoms.

In the present study, the authors found a very high rate of mixed depression in a sample of depressed suicide attempters. In addition, the rates of mixed depression found among bipolar and nonbipolar depressed suicide attempters were much higher than those previously reported in nonsuicidal depressed unipolar and bipolar II depressed outpatients. The current data highlight the necessity of detecting and treating mixed (bipolar) depression in the prevention of suicidal behavior. (46 References)
ASSOCIATION OF PSYCHOSIS WITH SUICIDALITY IN PEDIATRIC BIPOLAR I, II AND BIPOLAR NOS PATIENTS

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J AFFECT DISORD, 91:33-7, March 2006

Bipolar (BP) disorder is a chronic mental illness that affects between 1% and 3% of the United States population. The onset of BP disorder before age 18 is associated with suicidal ideation and suicide attempts, and adolescents with BP disorder have a higher risk for completed suicide than adolescents with other psychiatric disorders. In the present study, the authors examined the relationship (if any) between the presence of psychotic symptoms and suicidality in pediatric BP patients. On the basis of previous findings in adult BP patients, the researchers hypothesized that when compared with nonpsychotic pediatric BP patients, pediatric BP patients with psychotic symptoms would have a higher frequency of suicidality, a greater number of lifetime psychiatric hospitalizations, and poorer social functioning (as determined by Global Assessment of Functioning Scale [GAF] scores).

The study sample was composed of 43 pediatric BP patients (25 males, 18 females; age range, eight to 17 years; mean age, 11.2 years); 25 were classified as BP I, three as BP II, and 15 as BP not otherwise specified. Of these 43 children and adolescents, 17 (11 males, six females) had a lifetime history of psychotic symptoms, and 26 (14 males, 12 females) did not. The patients were interviewed with the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version. Indicators of suicidality (thoughts of death, suicidal ideation, suicide plans, suicide attempts), psychiatric diagnoses, psychotic symptoms, psychiatric hospitalizations, and GAF scores were assessed by trained raters. When the pediatric BP patients with a lifetime history of psychotic symptoms were compared with the BP patients without psychotic symptoms, the authors found that those with psychotic symptoms were more likely to have thoughts of death (100% vs 69.2%), to have suicidal ideation (94.1% vs 42.3%), and to have suicide plans (64.7% vs 15.4%). In addition, previous psychiatric hospitalizations were found to have occurred significantly more frequently among the psychotic BP patients (82.4%) than among the nonpsychotic BP patients (46.2%).

The authors conclude that psychotic symptoms in pediatric BP patients are associated with suicidal ideation, suicide plans, and psychiatric hospitalizations and are a risk factor for suicidality in these patients. (24 References)
RISK FACTORS FOR COMPLETED SUICIDE IN SCHIZOPHRENIA AND OTHER CHRONIC PSYCHOTIC DISORDERS: A CASE-CONTROL STUDY

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SCHIZOPHR RES, 84:132-43, May 1, 2006

Despite an increased risk for suicide among individuals diagnosed with psychotic disorders, possible risk factors for completed suicide in this population remain largely unexamined. Using a case-control design, the authors of the present study investigated clinical and behavioral risk factors for suicide completion in persons with schizophrenia and other chronic psychotic disorders.

The sample was composed of 81 Caucasian subjects (62 males, 19 females) who had been diagnosed with schizophrenia or a chronic psychotic disorder; of these, 45 were suicide completers (36 males, nine females; mean age, 34.45 years), and 36 served as matched controls (26 males, 10 females; mean age, 34.95 years). A psychological autopsy method was used to diagnose axis I and axis II DSM-IV psychiatric disorders and to assess personality, impulsivity, hostility, and lifetime history of aggression. Proxy-based interviews with an average of two informants per subject were conducted by means of SCID-I and SCID-II interviews and a series of personality trait measurements. The results showed that an increased risk of suicide was associated with a family history of suicidal behavior. Compared with psychotic control subjects, psychotic suicide completers were more likely to have currently (previous six months) met diagnostic criteria for a depressive disorder not otherwise specified and to have had two or more comorbid axis I disorders. The psychotic suicide completers were also more likely to have been currently experiencing moderate to severe psychotic symptoms and to have exhibited lower levels of negative symptoms. With regard to axis II diagnoses and symptoms, the data indicated that the psychotic suicide completers were characterized by lower levels of cluster A and cluster C symptoms.

According to the authors, the present study suggests that behavioral mediators of suicide risk, such as impulsive-aggressive behaviors, do not play a role in completed suicide among schizophrenics and persons with other types of chronic psychoses; this is contrary to findings in other clinical populations and implies that there is heterogeneity in the predisposing mechanisms involved in suicide. The current data also indicate that cluster A and cluster C personality traits appear to have a protective effect against suicide in individuals with schizophrenia and other chronic psychoses. (68 References) EAF
ADOLESCENT SUICIDAL IDEATION AS PREDICTIVE OF PSYCHOPATHOLOGY, SUICIDAL BEHAVIOR, AND COMPROMISED FUNCTIONING AT AGE 30

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AM J PSYCHIATRY, 163:1226-32, July 2006

The importance of suicidal ideation, particularly in adolescence, and its relationship to psychiatric morbidity and completed suicide continue to be subjects of debate. In spite of clinical concern and research interest, there have been few prospective studies of the relationship between suicidal ideation in adolescence and developmental outcomes in adulthood. The purpose of the present investigation was to determine whether suicidal ideation in adolescence is merely a manifestation of adolescent angst or is predictive of psychopathology, suicidal behavior, and compromised functioning in adulthood.

The study sample was composed of 346 participants (166 males, 180 females; 98% Caucasian) who were part of a single-age cohort from a working-class community and whose development had been traced from age 5 to age 30. Subjects with suicidal ideation at age 15 (N=76) were compared with those without suicidal ideation at age 15 (N=270) on measures of psychopathology, suicidal ideation and behavior, problem behavior, and adult functioning at age 30. Gender differences were assessed across all domains. The results showed that in most domains examined, at age 30, both male and female adolescents with suicidal ideation were markedly different from their counterparts without suicidal ideation. The subjects with suicidal ideation were twice as likely to have an axis I disorder and nearly 12 times more likely to have attempted suicide by age 30; they were also 15 times more likely to have expressed suicidal thoughts over the previous four years. Subjects with suicidal ideation had more problem behaviors and poorer overall functioning as assessed by multiple informants. Their self-perceptions of coping ability, self-esteem, and interpersonal relations were also lower. Although both male and female subjects with suicidal ideation had higher levels of psychopathology, suicidal ideation and behavior, and problem behaviors at age 30, male subjects with suicidal ideation had lower salaries, were of lower socioeconomic status, and were less likely to have achieved residential independence.

The current findings underscore the need for identification and treatment of adolescent suicidal ideation in order to alleviate immediate distress and forestall future negative consequences. (43 References)
CHARACTERIZATION OF IMPULSIVITY IN SUICIDE COMPLETERS: CLINICAL, BEHAVIORAL AND PSYCHOSOCIAL DIMENSIONS

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Suicide is a major public health problem that ranks among the top 10 causes of death for individuals of all age groups in several countries. Impulsivity is usually conceptualized as the inability to resist a drive or stimulus, or a behavior that occurs without reflection or consideration of its consequences. Impulsivity has attracted a great deal of interest in suicide research over the past few years, since it is thought to be a familial trait that predisposes individuals to act out their suicidal thoughts. The purpose of the present investigation was to better understand the clinical, behavioral, and psychosocial correlates of impulsivity in suicide completers.

The authors evaluated the cases of 164 suicide completers for whom valid impulsivity scores were available (as measured by the Barratt Impulsivity Scale [BIS]). Those subjects whose BIS scores were equal to or above the 70th percentile (N=50) were designated as the impulsive suicide group and those whose BIS scores were equal to or below the 30th percentile (N=50) were designated as the non-impulsive suicide group. These two groups were compared on a variety of clinical, behavioral, and psychosocial suicide risk factors that were assessed by means of structured psychological autopsy methods with best informants. The Temperament and Character Inventory (TCI) was used to measure four temperament and three character dimensions. Compared with the non-impulsive suicide completers, the impulsive suicide completers were significantly younger, had a lower personal income, had completed fewer years of schooling, had worked for fewer years, and were less likely to have been major income providers. The impulsive suicide completers also were characterized by higher levels of aggressive behavior, a higher lifetime prevalence of substance abuse/dependence, and high levels of axis I and axis II diagnostic comorbidity. They were more likely to have a cluster B diagnosis and differed significantly from their non-impulsive counterparts on all subscales of the TCI except Harm Avoidance and Reward Dependence. The impulsive suicide completers also were more likely to have had a history of childhood abuse and to have experienced a triggering life event at some time during the week preceding the suicide.

According to the authors, most of the known risk factors commonly associated with suicide appear to be particularly valid for impulsive suicide completers. Furthermore, precipitating and/or adverse life events seem to play a primary role in impulsive suicide. (66 References)
INDIRECT SELF-DESTRUCTIVE BEHAVIOR AND OVERT SUICIDALITY IN PATIENTS WITH COMPLICATED GRIEF

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J CLIN PSYCHIATRY, 67:233-9, February 2006

The risk of suicide is known to be higher during bereavement, with reports indicating that this risk is greatest during the first two years of bereavement but remains elevated throughout the fifth year after the loss. Complicated grief is diagnosed six months or longer after the death of a loved one and is characterized by intense and persistent yearning for the person who died; preoccupation with thoughts and images of the deceased; disbelief and inability to accept the death; bitterness or anger about the death; and avoidance of reminders of the lost loved one. While complicated grief has been found to be associated with increased suicidal ideation in samples of bereaved persons, suicidal behavior has not been assessed in these individuals. In the present study, the authors examined rates and correlates of suicide attempts and indirect self-destructive behaviors in a group of 149 help-seeking patients (35 men, 114 women; mean age, 46.9 years) who met criteria for complicated grief (Inventory of Complicated Grief score of 25 or higher) and completed suicidality assessments prior to beginning treatment.

Of the 149 participants, 97 (65%) reported thoughts of wanting to die following the death of their loved one. Among these 97 patients, 56 (38% of the study sample) reported engaging in suicidal behavior; this included 13 (9%) who reported suicide attempts and 43 (29%) who reported indirect self-destructive behaviors (e.g., not eating, not taking medications). When asked about the period prior to the loss, 57 participants (38%) reported a wish to die, and 21 (14%) reported making at least one suicide attempt. Although only four of those who reported a suicide attempt before the loss made an attempt after the death, twice this number engaged in indirect self-destructive behavior. Thus, 57% (12/21) of those who attempted suicide before their loss engaged in suicidal behavior after the death of their loved one. A multiple logistic regression model indicated that only high levels of complicated grief and pre-loss suicidality were significantly associated with post-loss suicidal behavior.

The current findings provide further support for previous reports that have found an association between complicated grief and endorsement of a wish to die. These data also suggest that among bereaved individuals with complicated grief, there is an associated risk for suicidal behavior, especially indirect self-destructive behavior. (28 References)
SUICIDE RISK DURING ANTIDEPRESSANT TREATMENT

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AM J PSYCHIATRY, 163:41-7, January 2006

In March 2004, the U.S. Food and Drug Administration (FDA) issued a public health advisory that warned physicians and patients about the possibility of an increased suicide risk in those being treated with 10 newer antidepressant drugs (bupropion, citalopram, fluoxetine, fluvoxamine, mirtazapine, nefazodone, paroxetine, sertraline, escitalopram, and venlafaxine). However, available data leave considerable uncertainty with regard to the actual risk of attempted and completed suicide during antidepressant treatment. In the investigation presented here, the authors used population-based data to evaluate the risk of serious suicide attempt and completed suicide in relation to the initiation of antidepressant treatment.

Computerized health plan records were used to identify 82,285 episodes of antidepressant treatment among 65,103 patients (19,856 males and 45,247 females) between January 1, 1992, and June 30, 2003. Death by suicide was identified through the use of national and state death certificate data. A serious suicide attempt, defined as a suicide attempt that led to hospitalization, was identified through the use of hospital discharge data. The researchers identified 31 deaths by suicide (40 per 100,000 treatment episodes) and 76 serious suicide attempts (93 per 100,00 treatment episodes) that occurred in the six-month period following the index antidepressant prescription. The risk of a serious suicide attempt was 314 per 100,000 in children and adolescents and 78 per 100,000 in adults. The risk of death by suicide was not significantly higher in the month immediately after beginning antidepressant treatment than it was in subsequent months. The risk of making a serious suicide attempt was highest in the month prior to the initiation of antidepressant therapy, and this risk progressively declined after medication was started. When the 10 newer antidepressants included in the FDA advisory were compared with older drugs, an increase in the risk of attempted and completed suicide was observed only for the older antidepressants.

The current results indicate that the risk of suicide during the acute phase of antidepressant therapy is approximately one in 3,000 treatment episodes, and the risk of a serious suicide attempt is approximately one in 1,000. The available data, the authors conclude, do not indicate a significant increase in the risk of suicide or a serious suicide attempt after the initiation of treatment with newer antidepressant drugs. (34 References)
THE RISK OF SUICIDE WITH SELECTIVE SEROTONIN REUPTAKE INHIBITORS IN THE ELDERLY

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AM J PSYCHIATRY, 163:813-21, May 2006

Selective serotonin reuptake inhibitors (SSRIs) have become increasingly popular for the treatment of depression. While several anecdotal reports have described the emergence of intense suicidality during the initial phase of SSRI therapy, it is difficult to separate the role of depression from a possible adverse effect of treatment. The authors of the present investigation explored the relationship between the initiation of SSRI antidepressant therapy and the subsequent risk of completed suicide in elderly patients.

The researchers linked population-based coroner’s records with patient-level prescription data, physician billing claims, and hospitalization data for more than 1.2 million elderly Ontario residents (66 years of age or older). Consecutive cases of suicide that occurred among these residents over a nine-year period (January 1, 1992, to December 31, 2000) were identified. For each person who had committed suicide, four closely matched comparison subjects were selected from the general population through the use of propensity score methods. The odds ratios for suicide with SSRI therapy and suicide with other antidepressant treatment were determined, calculated at discrete monthly intervals from the beginning of treatment. Of 1,329 suicide victims, 191 (14%) had propensity scores that were too high to permit propensity-based matching with four comparison subjects. Thus, the matched analyses included 1,138 suicide victims and 4,552 comparison subjects with comparable demographic characteristics and antecedent patterns of illness. During the first month of therapy, SSRIs were associated with a nearly fivefold higher relative risk of completed suicide than other antidepressants. The risk was independent of a recent diagnosis of depression or the receipt of psychiatric care, and suicides of a violent nature were distinctly more common during SSRI therapy. Numerous sensitivity analyses yielded consistent results. No disproportionate suicide risk was seen during the second and subsequent months of treatment with SSRIs, and the absolute risk of suicide with all antidepressants was low.

The current findings appear to mirror the clinical observation that the vast majority of patients treated with SSRI antidepressants do not attempt suicide, but that in rare instances these drugs do seem to incite suicidal ideation during the first weeks of therapy. (87 References)
PROBLEMS IN PSYCHOTHERAPY
WITH SUICIDAL PATIENTS

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AM J PSYCHIATRY, 163:67-72, January 2006

Considerable evidence points to the complexity of the psychotherapeutic treatment of suicidal patients. It appears that many clinicians who treat suicidal patients employ a relatively open-ended, eclectic therapeutic approach that incorporates cognitive behavior therapy and interpersonal techniques, along with varying degrees of reliance on psychodynamic principles. The present authors studied recurrent problems in psychotherapy with suicidal patients by retrospectively examining the cases of patients who died by suicide while receiving open-ended psychotherapy and medication.

The therapists of 36 patients who had committed suicide while in treatment filled out semistructured questionnaires dealing with the patient’s background, clinical history, medication history, affective state, and psychodynamic phenomena related to the suicide. They also provided information on their reactions to the patient’s suicide and prepared detailed case narratives. Two therapists at a time then met with project investigators at an all-day workshop to review the cases and identify critical problems. Of the 36 therapists who participated, 25 were men and 11 were women. Twenty-nine were psychiatrists, five were psychologists, and two were social workers. All the psychiatrists provided both psychotherapy and medication management. In the seven cases in which psychotherapy was provided by a psychologist or a social worker, medications were managed by a psychiatrist. None of the 36 therapists followed a structured treatment protocol. Six recurrent problem areas were identified in these cases: (1) poor communication with another therapist involved in the case; (2) permitting patients or their relatives to control the therapy; (3) avoidance of issues related to sexuality; (4) ineffective or coercive actions resulting from the therapist’s anxiety about a patient’s potential suicide; (5) not recognizing the meanings of patients’ communications; and (6) untreated or under-treated symptoms.

Persons who kill themselves while in psychotherapy are not representative of all who commit suicide. In the most obvious respect, the current authors state, occurrences within the treatment process itself frequently become factors in driving patients’ suicides. Yet the suicidal patients who enter therapy are the ones clinicians have the greatest opportunity to help. Examining problems encountered in psychotherapy with suicidal patients should help to improve the effectiveness of their treatment. (26 References)
Suicidal behavior is a broad description that includes death by suicide as well as intentional, nonfatal, self-injurious acts committed with or without an intent to die. Borderline personality disorder (BPD) is one of only two DSM-IV diagnoses for which suicidal behavior is a criterion. Dialectical behavior therapy (DBT) is a treatment for suicidal behavior and BPD with well-documented efficacy. To evaluate the hypothesis that unique aspects of DBT are more efficacious than treatment offered by non-behavioral psychotherapy experts, the authors conducted a two-year randomized controlled study of these interventions (one year of DBT or community treatment by experts [CTBE] plus one year of posttreatment follow-up). CTBE was designed to maximize internal validity by controlling for therapist sex, availability, expertise, allegiance, training and experience, consultation availability, and institutional prestige.

In all, 101 clinically referred women (age range, 18 to 45 years) who met criteria for BPD and who had engaged in recent suicidal and self-injurious behavior were matched to treatment condition with regard to age, suicide attempt history, negative prognostic indication, and number of lifetime intentional self-injuries and psychiatric hospitalizations; 52 were randomized to DBT and 49 to CTBE. The main outcome measures were trimester assessments of suicidal behavior, emergency services use, and general psychological functioning. In the intent-to-treat analysis, DBT was found to be associated with better outcomes than CTBE in most target areas over the two-year study. Subjects receiving DBT were half as likely to make a suicide attempt, required less hospitalization for suicide ideation, and had a lower medical risk across all suicide attempts and self-injurious acts combined. Those receiving DBT also were less likely to drop out of treatment and had fewer psychiatric hospitalizations and psychiatric emergency department visits.

The current findings replicate those of previous studies and suggest that the effectiveness of DBT cannot reasonably be attributed to general factors associated with expert psychotherapy. DBT appears to be uniquely effective in reducing suicide attempts. (54 References)
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PREVALENCE, HERITABILITY, AND PROSPECTIVE RISK FACTORS FOR ANOREXIA NERVOSA

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ARCH GEN PSYCHIATRY, 63:305-12, March 2006

Anorexia nervosa (AN) is a perplexing psychiatric illness that primarily strikes females and is associated with the highest mortality rate of any mental disorder. AN is familial, with family members being at significantly elevated risk for AN, bulimia nervosa, and eating disorders not otherwise specified. In the present study, the authors explored the prevalence, heritability, and prospectively assessed risk factors for AN in a large population-based cohort of Swedish twins.

During a four-year period ending in 2002, all living, contactable, interviewable, and consenting twins in the Swedish Twin Registry (N=31,406) born between January 1, 1935, and December 31, 1958, underwent screening for a range of disorders, including AN. Information collected systematically from 1972 to 1973, before the onset of AN, was used to examine prospective risk factors for AN. AN subjects were identified as those individuals who met full DSM-IV criteria by means of clinical interview (Screening Across the Lifespan of Twins), those who had a hospital discharge diagnosis of AN, or those who had a cause-of-death certificate that included an AN diagnosis. The overall prevalence of AN was 1.20% and 0.29% for female and male participants, respectively. The prevalence of AN in both sexes was greater in those individuals born after 1945. Individuals with lifetime AN reported lower body mass index, greater physical activity, and better health satisfaction than those without lifetime AN. AN was inversely associated with the later development of overweight status (odds ratio, 0.29; 95% confidence interval [CI], 0.16-0.54). The heritability of narrowly defined DSM-IV AN (additive genetic effects) was estimated to be $\alpha^2=0.56$ (95% CI, 0.00-0.87), with the remaining variance being attributed to shared environment ($c^2=0.05$; 95% CI, 0.00-0.64) and unique environment ($e^2=0.38$; 95% CI, 0.13-0.84). Neuroticism measured approximately three decades before the diagnostic assessment was significantly associated with the later development of AN (odds ratio, 1.62; 95% CI, 1.27-2.05).

According to the authors, individuals who survive AN and who no longer have a body mass index in the AN range appear to be at lower risk for becoming overweight later in life. The researchers conclude that AN seems to be a moderately heritable psychiatric disorder that may be predicted by the presence of early neuroticism. (77 References)
BINGE-EATING DISORDER AS A DISTINCT FAMILIAL PHENOTYPE IN OBESE INDIVIDUALS

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ARCH GEN PSYCHIATRY, 63:313-9, March 2006

Obesity is a global epidemic with profound medical and social consequences, but its complex causes remain incompletely understood. Binge-eating disorder (BED), a syndrome that only recently has attracted scientific attention, is often seen in obese individuals, especially those with severe obesity. However, it remains unclear whether BED represents an etiologically distinct behavioral phenotype of obesity or whether it is simply a nonspecific eating pattern sometimes seen in obese individuals. In the present study, the authors attempted to determine whether BED aggregates in families independently of obesity, and if it does, whether familial factors for BED also independently increase the risk of obesity.

Between October 2002 and July 2004, the researchers conducted a blinded family interview study of 300 overweight or obese probands (150 subjects with BED and 150 age- and sex-matched subjects without BED) and 888 of their first-degree relatives (431 relatives of probands with BED and 457 relatives of probands without BED). The main outcome measures were lifetime diagnosis of BED and current and highest lifetime body mass index (calculated as the weight in kilograms divided by the square of the height in meters). A lifetime diagnosis of BED was found in 87 (20.2%) of the relatives of the probands with BED and in 44 (9.6%) of the relatives of the probands without BED. BED aggregated strongly in families independently of obesity (odds ratio, 2.2; 95% confidence interval, 1.4-3.6; \( P < .001 \)). Compared with relatives of probands without BED, relatives of probands with BED displayed a markedly higher prevalence of severe obesity in adulthood (body mass index \( \geq 40 \)), even when body mass index of the probands was controlled (odds ratio, 2.5; 95% confidence interval, 1.4-4.4; \( P = .002 \)).

The authors conclude that BED is a familial disorder caused partly by factors distinct from other familial factors for obesity. Furthermore, these BED-specific familial factors may independently increase the risk of obesity, especially severe obesity. It follows, the researchers state, that targeted interventions capable of preventing or treating traits influenced by these BED-specific familial factors could reduce the public health burden of obesity. (48 References)
PERINATAL FACTORS AND THE RISK OF DEVELOPING ANOREXIA NERVOSA AND BULIMIA NERVOSA

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ARCH GEN PSYCHIATRY, 63:82-8, January 2006

Eating disorders are considered to be psychiatric disturbances with complex etiologies, and it has been hypothesized that their development is influenced by the interaction of several genetic and environmental factors. The aim of the present investigation was to explore the role of obstetric complications in the development of anorexia nervosa and bulimia nervosa.

The authors conducted a blind analysis of the obstetric records of individuals with and without eating disorders. All of the study subjects were female, white, belonged to the same population birth cohort, and were born in the two obstetric wards of Padua Hospital, Padua, Italy, between January 17, 1971, and December 30, 1979. Part of the eating-disordered sample and all of the individuals without eating disorders (normal controls) took part in a prevalence study carried out in two randomly selected areas of Padua. Also included was a group of eating-disordered subjects who were from the same birth cohort and who had been referred to an outpatient eating disorders unit. The final sample was composed of 114 subjects with anorexia nervosa, 73 subjects with bulimia nervosa, and 554 normal control subjects. Several complications, such as maternal anemia, diabetes mellitus, preeclampsia, placental infarction, neonatal cardiac problems, and neonatal hyporeactivity were found to be significant independent predictors of the development of anorexia nervosa. The risk of developing anorexia nervosa increased with the total number of obstetric complications. In addition, an increasing number of complications anticipated the age at onset of anorexia nervosa. Obstetric complications found to be significantly associated with the development of bulimia nervosa were placental infarction, neonatal hyporeactivity, early eating difficulties, and a low birth weight for gestational age. Being shorter for gestational age significantly differentiated the subjects with bulimia nervosa from both the subjects with anorexia nervosa and the normal control subjects.

In the present investigation, the researchers found a significant relationship between the occurrence of specific types of obstetric complications and the development of an eating disorder. These results highlight the importance of perinatal factors in the pathogenesis of eating disorders. The authors conclude that an impairment in neurodevelopment could be implicated in the pathogenesis of eating disorders. (35 References)
IDENTIFYING DIETERS WHO WILL DEVELOP AN EATING DISORDER: 
A PROSPECTIVE, POPULATION-BASED STUDY

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AM J PSYCHIATRY, 162:2249-55, December 2005

Eating disorders are a major source of physical and psychosocial morbidity among young women. In the present study, the authors attempted to identify the characteristics of young female dieters most at risk for the subsequent development of eating disorders and to evaluate the feasibility of using a brief questionnaire to identify such dieters in advance.

A general population cohort of young women (N=2,992) who were dieting but did not have an eating disorder were asked to complete a validated measure of eating disorders features. On four occasions over the subsequent two-year period, these women were recontacted and asked to complete additional copies of the same measure. At each occasion, the women whose responses suggested that they had developed an eating disorder were interviewed to confirm their diagnostic status. The initial questionnaires of the participants who had and had not developed an eating disorder were compared for the purpose of identifying features that would predict future case status. Over the course of the two-year follow-up, 104 of the dieters developed an eating disorder of clinical severity; 10 (9.6%) developed anorexia nervosa, 19 (18.3%) developed bulimia nervosa, and 75 (72.1%) developed an eating disorder not otherwise specified. Of those who developed an eating disorder, nearly 40% did so within the first six months of follow-up, with the rates slowly decreasing over the remaining 18 months of the study (23%, 20%, and 17%, respectively). The baseline questionnaire scores of dieters who developed eating disorders differed in several respects from the scores of those who did not develop eating disorders. Items associated with developing an eating disorder were selected through the use of three different statistical methods (Cox proportional hazards regression analysis, linear discriminant function analysis, and signal detection analysis). A simple case-predicting instrument based on one of five items scoring above an optimal cut point had a sensitivity of 71% and a specificity of 72% (overall efficiency=72%)

According to the authors, young women who are dieting and who will develop an eating disorder within the next two years appear to have distinctive characteristics. It may be possible to identify these women in advance by means of a brief, case-predicting questionnaire. Such a questionnaire could be incorporated into routine health assessments and thereby aid in identifying those at high risk for developing eating disorders. (32 References)
POSTREMISSION PREDICTORS OF RELAPSE
IN WOMEN WITH EATING DISORDERS

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AM J PSYCHIATRY, 162:2263-8, December 2005

Relapse is a significant problem for eating-disordered individuals, with outcome studies of anorexia nervosa and bulimia nervosa reporting relapse rates ranging from 22% to 51%. Identification of predictors of postremission relapse could reveal key targets for the prevention of future episodes of illness. Using a prospective, longitudinal design, the authors of the present investigation attempted to evaluate patterns and predictors of relapse in a cohort of women with anorexia nervosa or bulimia nervosa.

The study sample was composed of 246 women who were prospectively followed for nine years. Interviews were conducted every six to 12 months to assess symptoms of eating disorders, axis I disorders, treatment, and psychosocial functioning. At intake, 136 (55%) women met diagnostic criteria for anorexia nervosa, and 110 (45%) met criteria for bulimia nervosa. Most participants (96%) received some form of treatment during follow-up, with 37% receiving inpatient treatment. At the final follow-up, 229 (93%) subjects were still participating in the study. Of the 136 women with intake diagnoses of anorexia nervosa, 42 (31%) achieved remission during the course of follow-up; of these 42, 15 relapsed (representing 36% of those whose illness remitted or 11% of the total group). Of the 110 women with intake diagnoses of bulimia nervosa, 83 (75%) attained remission during follow-up; of these 83, 29 relapsed (representing 35% of those whose illness remitted or 26% of the total group). Women with intake diagnoses of anorexia nervosa, restricting subtype, tended to develop bulimic symptoms during relapse, whereas women with intake diagnoses of anorexia nervosa, binge-purge subtype, or bulimia nervosa tended to return to bulimic patterns during relapse. Greater body image disturbance contributed to the risk of relapse in women with anorexia nervosa as well as in those with bulimia nervosa, and poorer psychosocial functioning increased the risk of relapse in women with bulimia nervosa.

According to the authors, the current data may help to explain the long-term efficacy of interpersonal therapy for bulimia nervosa. The present findings also suggest that focused body image work during relapse prevention may enhance long-term recovery from eating disorders. (36 References)
NORMAL BRAIN TISSUE VOLUMES AFTER LONG-TERM RECOVERY IN ANOREXIA AND BULIMIA NERVOSA

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BIOL PSYCHIATRY, 59:291-3, February 1, 2006

Individuals who are ill with anorexia nervosa (AN) or bulimia nervosa (BN) often exhibit increased cerebrospinal fluid (CSF) volumes and decreased total gray matter (GM) and total white matter (WM) volumes. However, it is not clear whether these brain abnormalities persist after recovery from AN or BN, or whether they are partially or fully reversible. The goal of the present study was to assess brain tissue abnormalities in a large sample of women who were considered to be in long-term recovery from eating disorders (EDs).

The authors recruited 40 recovered ED subjects and 31 healthy control women. To be considered “recovered,” the ED subjects had to have met the following criteria over the previous year: (1) maintained a weight above 85% of average body weight; (2) had regular menstrual cycles; (3) not binged, purged, restricted food intake, or exercised excessively; and (4) not used psychoactive medications. Of the women who had recovered from EDs, 14 met criteria for restricting type AN, 16 for binge/purging type AN, and 10 for BN. All the study subjects underwent magnetic resonance imaging, and voxel-based morphometry was used for data analysis. The recovered subjects and the control women were of similar age and body mass index (BMI). The recovered AN and BN subgroups were similar to the control group in terms of total CSF volume as well as in total and regional GM and WM volume. There was a small but nonsignificant decline in total GM volume with age, while all recovered subjects showed a small but nonsignificant increase in total WM volume and total CSF volume. The results remained the same when the researchers covaried for age, BMI, total brain volume and length of recovery (recovered subjects). However, the BN subgroup showed an increase in GM insula volume when age was included as a nuisance variable. No relationship was found between total or regional GM volume, WM volume, or CSF and comorbid diagnoses.

According to the authors, the findings of the current investigation suggest that structural brain abnormalities may be reversible after long-term recovery from an eating disorder. (25 References)
BINGE EATING DISORDER AND NIGHT EATING SYNDROME:  
A COMPARATIVE STUDY OF DISORDERED EATING

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J CONSULT CLIN PSYCHOL, 73:1107-15, December 2005

Two forms of disordered eating have been described in overweight and obese  
individuals: binge eating disorder (BED) and night eating syndrome (NES). The  
authors of the present investigation examined eating patterns, disordered eating,  
features of eating disorders, and psychological distress (depressive symptoms) in  
persons with BED, individuals with NES, and overweight participants without  
BED or NES (comparison group). For purposes of this study, NES was defined by  
the following criteria: eating 25% or more of one’s daily total caloric intake after  
the evening meal and/or experiencing awakenings with nocturnal ingestions three  
or more times per week.

The study sample was composed of 177 participants with BED (37 males,  
140 females), 68 participants with NES (21 males, 47 females), and 45  
overweight comparison subjects (15 males, 30 females). The majority were well-  
educated, with 86.3% of the BED group, 76.4% of the NES group, and 77.8% of  
the comparison group having at least some college education. All the  
participants completed semistructured interviews and other assessment  
measures, including the Eating Disorder Examination Interview, the Three-  
Factor Eating Questionnaire/Eating Inventory, and the Beck Depression  
Inventory (BDI). As measured by the BDI, depressive symptoms were found to be  
significantly higher in the BED and NES groups than in the comparison group.  
The number of objective bulimic episodes and days differed significantly across  
the three groups. The BED group had significantly more objective bulimic  
episodes in total and more days on which they occurred than the NES group,  
with the latter having them more often than the comparison group. Similarly,  
the number of objective overeating episodes in total and days on which they  
ocurred were more frequent in the BED group than in the NES or comparison  
groups, while the latter two did not differ from each other. NES subjects ate  
fewer meals during the day and more during the night than BED and  
comparison subjects, while BED subjects ate more during the day than  
comparison subjects. Individuals in the BED group reported more shape/weight  
commisns, disinhibition, and hunger than those in the NES and comparison  
groups. Participants in the NES group reported more eating pathology than  
those in the comparison group.

According to the authors, the current findings provide strong evidence that  
BED and NES are different constructs, with each one representing strikingly  
different eating patterns and psychological characteristics. (55 References)  
EAF
A RANDOMIZED, PLACEBO-CONTROLLED TRIAL OF SERTRALINE IN THE TREATMENT OF NIGHT EATING SYNDROME

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AM J PSYCHIATRY, 163:893-8, May 2006

Night eating syndrome is an eating disorder that is associated with both obesity and psychological distress. It is characterized by morning anorexia, evening hyperphagia, and insomnia, with awakenings followed by nocturnal ingestions. Food intake is lower in the first half of the day and greater in the evening and nighttime, with sleep often being disrupted in the service of food ingestion. In the present investigation, the authors assessed the efficacy of sertraline in the treatment of night eating syndrome.

In an eight-week, double-blind, flexible-dose (50-200 mg/day) trial, 34 outpatients with a diagnosis of night eating syndrome were randomly assigned to receive either sertraline (N=17) or placebo (N=17). The researchers used a mixed effects linear regression model to analyze changes in the primary outcome measure, which was the Clinical Global Impression (CGI) improvement rating. Secondary outcome measures included changes in night eating symptoms, number of nocturnal awakenings and ingestions, total daily caloric intake after the evening meal, CGI severity ratings, quality of life ratings, and weight. The results indicated that sertraline was associated with significantly greater improvement than placebo. The CGI improvement ratings classified 12 (71%) of the subjects in the sertraline group as having responded (much or very much improved); seven of these 12 achieved remission or complete resolution of night eating syndrome symptoms. Only three (18%) of the subjects in the placebo group were classified as having responded. The sertraline group also showed significant improvements with regard to night eating symptoms, CGI severity ratings, quality of life ratings, frequency of nocturnal awakenings and ingestions, and caloric intake after the evening meal. Compared with overweight and obese subjects in the placebo group (N=14), overweight and obese subjects in the sertraline group (N=14) had lost a significant amount of weight by week 8 of the trial. Sertraline was well tolerated, and no subject withdrew because of adverse events. Common side effects were mild in intensity and included dry mouth, fatigue, diminished libido, and sweating.

The authors conclude that in the current eight-week trial, sertraline proved to be effective in the treatment of night eating syndrome. (18 References) EAF
TREATING DISTURBANCES IN THE RELATIONSHIP BETWEEN MOTHERS WITH BULIMIC EATING DISORDERS AND THEIR INFANTS: A RANDOMIZED, CONTROLLED TRIAL OF VIDEO FEEDBACK

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AM J PSYCHIATRY, 163:899-906, May 2006

Maternal psychiatric disorders (including eating disorders) that occur during the postnatal period may adversely affect mother-infant interaction and child development. The authors attempted to determine whether video feedback treatment that specifically targeted mother-child interaction would be superior to supportive counseling in improving mother-infant interaction, especially with regard to mealtime conflict, infant weight, and infant autonomy.

The sample was composed of 80 mothers who were diagnosed with bulimia nervosa or a similar eating disorder, who were attending routine baby clinics, and whose infants were between the ages of four and six months. They were randomly assigned to video-feedback interactional treatment (N=40) or supportive counseling (N=40, control condition). Thirteen one-hour treatment sessions were offered in the mothers’ homes, beginning when the infants were between four and six months old and ending by the time the infants were 12 months old. Both groups also received guided cognitive behavioral self-help for their eating disorders. The primary outcome measure was mealtime conflict; secondary outcome measures were other aspects of mother-infant interaction, infant weight, and infant autonomy. Seventy-seven mothers (38 from the video-feedback group and 39 from the supportive counseling group) were followed up when their infants were 13 months old. The group that received video feedback exhibited significantly less mealtime conflict than the group that received supportive counseling. Episodes of marked or severe conflict were demonstrated by 23.7% of the mother-infant pairs in the video-feedback group and by 53.8% of those in the control group. Video feedback produced significant improvement in several other interaction measures as well as greater infant autonomy. Both groups maintained adequate infant weight, with no significant differences being found between them. Maternal eating disorder psychopathology was reduced in both groups.

The authors conclude that a targeted treatment conducted in the community during the postnatal period may have significant benefits for eating-disordered mothers and their infants. (20 References)
A SINGLE-CENTER, DOUBLE-BLIND, PLACEBO-CONTROLLED EVALUATION OF LAMOTRIGINE IN THE TREATMENT OF OBESITY IN ADULTS

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J CLIN PSYCHIATRY, 67:258-62, February 2006

Obesity is a common disorder, affecting over 97 million adults in the United States. Unlike many other medications used to treat mood disorders, lamotrigine has not been shown to be associated with weight gain. The purpose of the present investigation was to evaluate the safety and efficacy of lamotrigine as a monotherapy for weight loss in obese adults.

Healthy adult volunteers (over the age of 18 years) were eligible to participate in the study if they had a diagnosis of obesity as calculated by a body mass index (BMI) of 30 or higher but lower than 40. Of 57 subjects screened, 40 (33 women, seven men; age range, 23 to 65 years) met entry criteria and were randomly assigned to receive lamotrigine 200 mg/day (N=20) or placebo (N=20) for a period of 26 weeks. The primary efficacy endpoint was defined as the change in body weight (in pounds) from baseline to endpoint (week 26). Secondary endpoints included change from baseline to endpoint in BMI, percent body fat, subject satisfaction with treatment, subject quality of life, and blood lipid and glycosylated hemoglobin values. Of the 40 subjects who were initially randomized to treatment, 28 completed the 26-week trial (17 in the lamotrigine group and 11 in the placebo group). The mean change in body weight from baseline to endpoint (last observation carried forward) was –6.4 pounds in the lamotrigine group and –1.2 pounds in the placebo group. The mean baseline body weight was slightly different in the two treatment groups, with that of the lamotrigine group being 207.9 pounds and that of the placebo group being 225 pounds. There was a significant difference between the two groups in mean change in BMI from baseline to endpoint (–1.5 for the lamotrigine group and –0.1 for the placebo group). The subjects expressed more satisfaction with lamotrigine therapy than with placebo. There were no significant differences between treatment groups in terms of other secondary endpoints. Lamotrigine was well tolerated, and side effects were generally mild and transient. The most frequently reported adverse event was mild-to-moderate headache, which was reported by 15% of the lamotrigine group and 15% of the placebo group.

According to the author, the results of this preliminary investigation indicate that lamotrigine, unlike many pharmacologic treatments for bipolar disorder, is not associated with weight gain and may have some weight-reduction properties in obese individuals. (16 References)
BOOKS RECEIVED FOR REVIEW


DIGEST of NEUROLOGY and PSYCHIATRY

Abstracts and Reviews of Selected Literature in Psychiatry, Neurology, and their Allied Fields

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A defining characteristic of attention deficit hyperactivity disorder (ADHD) is ineffective control of behavior in cognitive, emotional, and social domains. Cognitive control, the ability to voluntarily constrain actions in a goal-directed manner, comprises at least two operations: the inhibition of inappropriate but prepotent responses (response inhibition) and the suppression of interfering responses (interference suppression). In the present study, the authors examined the neural basis of both response inhibition and interference suppression in a group of preadolescent children.

The study sample was composed of 10 preadolescent children with combined-type ADHD (seven boys, three girls; mean age, 8.8 years) and 10 age- and gender-matched comparison subjects (mean age, 9.2 years). All underwent rapid event-related functional magnetic resonance imaging (fMRI) during performance of a modified flanker task. Functional maps were generated through group averaging and performance-based correlational analyses. Rapid event-related fMRI revealed that response inhibition and interference suppression were associated with different patterns of atypical brain activation in the ADHD children; they failed to suppress interference more often and exhibited reduced engagement of a frontal-striatal-temporal-parietal network that subserved healthy performance. They also showed reduced response inhibition relative to comparison children, and the two groups recruited different anterior brain regions (frontal cortex and caudate nucleus in the comparison subjects but not in the ADHD children) and different posterior brain regions (superior temporal cortex in ADHD children but not in comparison subjects).

According to the authors, the current data provide the first evidence for multiple, rather than unitary, patterns of functional neural abnormality in ADHD. The functional abnormalities observed in the present sample did not result from prolonged stimulant exposure, the authors conclude, since most of the ADHD children were medication-naïve. The researchers’ findings provide support for the view that the caudate nucleus is a region of functional abnormality related to ADHD rather than a specific task, because it was abnormal across two cognitive control operations within the same preadolescent ADHD children. (30 References)
PREDICTORS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER WITHIN 6 MONTHS AFTER PEDIATRIC TRAUMATIC BRAIN INJURY

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 44:1032-40, October 2005

The authors of the present investigation attempted to assess the phenomenology and predictive factors involved in the development of attention-deficit/hyperactivity disorder (ADHD) after traumatic brain injury (TBI), also referred to as secondary ADHD (SADHD). The researchers hypothesized (1) that SADHD in children and adolescents with moderate to severe TBIs would be significantly associated with severity of injury and preinjury adverse psychosocial factors; and (2) that SADHD would be significantly associated with lesions of the basal ganglia and the orbitofrontal gyrus.

The study subjects were recruited from five trauma centers. In all, 143 children (93 males, 50 females; age range, 5-14 years) with TBIs but without preinjury ADHD were followed prospectively for six months and evaluated at baseline and six-month follow-up by means of semistructured psychiatric interviews. Standardized instruments were used to assess injury severity; lesion characteristics; and preinjury variables, including psychiatric disorder, family psychiatric history, family history of ADHD, family functioning, socioeconomic status, psychosocial adversity, and adaptive functioning. Of the original sample of 143 children, 115 (73 males, 42 females) returned for the six-month psychiatric assessment. Among these 115, SADHD was found to occur in 16% (10 males, eight females). The children presented with the following subtypes: inattentive (N=8), not otherwise specified (N=6), combined (N=3), and hyperactive/impulsive (N=1). New-onset personality changes due to TBI were found in eight (44%) of the 18 children with SADHD as opposed to 16 (17%) of the 97 without SADHD. New-onset oppositional defiant disorder/conduct disorder/disruptive behavior disorders were present in six of 18 children with SADHD versus two of those without SADHD. There was a trend for children with greater psychosocial adversity to develop SADHD. Socioeconomic status and the presence of orbitofrontal gyrus lesions were found to be significantly and independently associated with the development of SADHD.

According to the authors, the occurrence of TBI in children and adolescents is a major public health problem. SADHD is a relatively common and important complication of TBI in children and adolescents during the first six months after injury. In addition, SADHD is typically found to be comorbid with other functionally disruptive psychiatric disorders. (29 References)
PREDICTORS OF SECONDARY ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS 6 TO 24 MONTHS AFTER TRAUMATIC BRAIN INJURY

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 44:1041-9, October 2005

Attention-deficit/hyperactivity disorder (ADHD) that occurs after pediatric traumatic brain injury (TBI) is referred to as secondary ADHD (SADHD). To investigate further the phenomenology and predictive factors involved in the development of SADHD, the authors of the present report extended the outcome assessment of their earlier study (Max et al., 2005) beyond six months after injury to two years postinjury.

The study subjects were recruited from five trauma centers. In all, 143 children (age range, 5-14 years) with TBIs but without preinjury ADHD were observed prospectively from six to 12 months postinjury and from 12 to 24 months postinjury and were assessed at 12 months and 24 months postinjury by means of semistructured psychiatric interviews. Injury and preinjury psychosocial variables were also evaluated. SADHD occurred in 15 (15%) of 103 children who returned for the 12-month assessment. Of these 15, seven presented with the inattentive subtype (including one resolved and one in partial remission), five presented with SADHD not otherwise specified (NOS), one presented with the combined subtype, and two with the hyperactive/impulsive subtype. Eighty-two children returned for the 24-month assessment. SADHD occurred in 17 (21%) of them at some point between the 12- and 24-month assessments. Of these 17, 10 presented with the inattentive subtype (including two resolved and one in partial remission by 24 months postinjury), four presented with SADHD NOS, one presented with the combined subtype, and two with the hyperactive/impulsive subtype (including one in partial remission by 24 months postinjury). SADHD was found to be significantly comorbid with personality change due to TBI and with new-onset disruptive behavior disorders. Preinjury adaptive functioning was a consistent predictor of SADHD. Regression analyses revealed that preinjury psychosocial adversity was an independent predictor of SADHD in the second year after injury. Neither severity of injury nor lesion location predicted SADHD from six to 24 months postinjury.

According to the authors, in children with TBIs, determination of preinjury psychosocial adversity and preinjury functioning, if carried out during index hospitalization, might serve to improve the identification of those children at highest risk for the development of SADHD. (23 References)
Attention-deficit/hyperactivity disorder (ADHD) often presents with concurrent mood and anxiety disorders. To assess the tolerability and safety of atomoxetine combined with fluoxetine as well as the value of atomoxetine as a monotherapy for ADHD in the presence of depression or anxiety, the authors conducted a multisite study in which they evaluated atomoxetine alone or in combination with fluoxetine in the treatment of children with ADHD and comorbid mood or anxiety symptoms. The researchers hypothesized that atomoxetine would be safe and well tolerated when coadministered with fluoxetine and that atomoxetine alone and in combination with fluoxetine not only would reduce ADHD symptoms but also would alleviate symptoms of anxiety and depression.

The sample was composed of pediatric patients (age range, seven to 17 years) with DSM-IV-defined ADHD (any subtype) and comorbid depressive or anxiety symptoms that met minimum severity criteria. At study entry, patients were randomly assigned to receive either fluoxetine (N=127) or placebo (N=46) under double-blind conditions. After approximately three weeks, atomoxetine was added to each patient’s regimen for the final five weeks of treatment, and the atomoxetine/fluoxetine (A/F) group was compared with the atomoxetine/placebo (A/P) group. At end point, both groups showed marked improvement in symptoms of ADHD and depression as well as improvement in anxiety symptoms. Some differences between the treatment groups for depressive symptoms were significant, but the magnitudes of the differences were small and likely of limited clinical importance. Completion rates for the two groups were similar (83.5% [106/127] for the A/F group and 80.4% [37/46] for the A/P group), as were discontinuation rates due to adverse events (2.4% [3/127] for the A/F group and 2.2% [1/46] for the A/P group). The A/F group experienced greater increases in blood pressure and pulse than the A/P group.

The magnitude of the changes in ADHD, mood, and anxiety symptoms and the similar degree of improvement in the two groups observed in the present study suggest that most ADHD patients who have comorbid depressive or anxiety symptoms and who are treated with atomoxetine will benefit across all these symptom domains. (36 References)
ADHD TREATMENT WITH ONCE-DAILY OROS METHYLPHENIDATE: FINAL RESULTS FROM A LONG-TERM OPEN-LABEL STUDY

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 44:1015-23, October 2005

Attention-deficit/hyperactivity disorder (ADHD) is one of the most prevalent childhood psychiatric disorders, affecting between 8% and 10% of children. Stimulant medications such as methylphenidate (MPH) are among the first-line agents in the pharmacotherapy of ADHD. However, few studies have assessed the effectiveness and tolerability of stimulants when they are administered over prolonged periods of time in the treatment of children with ADHD. OROS® MPH (CONCERTA®) is a once-daily, osmotic, controlled-release formulation of MPH. In the current report, the authors present the final results of a multisite, long-term, open-label study of OROS MPH.

A total of 407 children with ADHD (age range, six to 13 years) were enrolled in the trial, with the subjects receiving OROS MPH for up to 24 months. They were initially assigned to one of three dosing levels (18, 36, or 54 mg once daily). Throughout the course of the trial, doses were adjusted upward or downward in 18-mg increments on the basis of clinical response and occurrence of adverse events. Multiple measures of ADHD symptoms, vital signs, weight, height, and laboratory results were assessed throughout the study. Of the 407 subjects who received medication, 289 completed 12 months of treatment. Of these 289 children, 278 enrolled in the second year of the trial, and 229 received treatment up to the 21/24-month endpoint. Parent and investigator assessments indicated that the effectiveness of OROS MPH therapy was maintained throughout the study period. Over the course of the trial, there was a 26% increase in mean daily dose (from 35.2 mg at baseline to 44.2 mg at endpoint), with most of the increase occurring during the first year of the study. In general, treatment was well tolerated, with only 31 subjects discontinuing treatment because of adverse events. Over the course of the study, only minimal effects on growth in height and weight were observed, and no clinically significant effects on vital signs or laboratory test parameters were seen.

According to the authors, the results of the present open-label study add to the body of literature demonstrating the continued effectiveness and tolerability of an extended-release preparation of MPH for up to two years. Thus, the researchers conclude, the effectiveness of stimulant therapy appears to be maintained over time, although dosage increases may be necessary to sustain the therapeutic effect. (29 References)
RELATIONSHIP BETWEEN RESPONSE TO METHYLPHENIDATE TREATMENT IN CHILDREN WITH ADHD AND PSYCHOPATHOLOGY IN THEIR FAMILIES

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 45:47-53, January 2006

Methylphenidate (MPH), a psychostimulant, is one of the most commonly prescribed medications for the treatment of attention-deficit/hyperactivity disorder (ADHD). However, not all patients respond equally to MPH. Several studies have suggested a link between family psychopathology and ADHD. In the investigation presented here, the authors compared the pattern of familial aggregation of psychopathology in ADHD children who were considered to be good responders (GR) to MPH with that in ADHD children who were deemed to be poor responders (PR) to this medication.

Between 1999 and 2004, 118 clinically referred children (103 boys, 15 girls; age range, six to 12 years) who were diagnosed with ADHD participated in a double-blind, placebo-controlled, randomized, two-week crossover trial of MPH. The children received daily placebo or 0.5 mg/kg of MPH (adjusted to body weight and administered in two equal doses) during the first week of the study and were crossed over during the second week. Family history was obtained by interviewing at least one key historian relative of each subject by means of the Family Interview for Genetic Studies. Information was collected on 342 first-degree relatives and 1,151 second-degree relatives of the ADHD children. Compared with placebo, MPH produced no improvement or a mild response in 44 subjects (PR) and significant improvement in 74 subjects (GR). First-degree relatives of the GR subjects were found to be at significantly higher risk for ADHD than relatives of PR subjects. Compared with the relatives of the PR children, second-degree relatives of the GR children were found to be at significantly higher risk for antisocial personality disorder.

According to the authors, the differential pattern of familial aggregation of ADHD-related disorders in GR and PR patients suggests that these two groups may suffer from two types of disorders that are at least partially different in terms of pathogenesis. Because good responsiveness to MPH is associated with higher familial loading, the researchers conclude, it is possible that the genes involved in increasing the risk of this subform of ADHD are also involved in treatment response or interact with those genes implicated in therapeutic response to MPH. (33 References)
THE GENETIC AND ENVIRONMENTAL CONTRIBUTIONS TO ATTENTION DEFICIT HYPERACTIVITY DISORDER AS MEASURED BY THE CONNERS’ RATING SCALES—REVISED

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AM J PSYCHIATRY, 162:1614-20, September 2005

The majority of the published reports on twin studies of attention deficit hyperactivity disorder (ADHD) have indicated robust additive genetic influences and unique environmental influences. These studies typically evaluated DSM ADHD symptoms that were collected by telephone surveys or interviews with mothers of ADHD children. The purpose of the present investigation was to test the genetic architecture of ADHD by using the ADHD index from Conners’ Rating Scales—Revised (2001). This is a 12-item index that Conners and his colleagues found to be the most likely to identify children at risk for DSM-IV ADHD. Scores are provided that allow the clinician to compare a raw score to a gender- and age-specific T score for the purposes of determining whether an individual child meets DSM-IV criteria for ADHD.

The study sample was composed of 1,595 seven-year-old twin pairs (1,530 boys, 1,591 girls) from the Netherlands Twin Registry. Information was collected from their mothers by means of the ADHD index of Conners’ Rating Scales—Revised. The data were analyzed to determine (1) the percentage of children (by sex) who met criteria for clinical deviance according to the ADHD index; and (2) estimates of genetic (additive and dominant) and environmental contributions to ADHD as defined by the ADHD index. These data were tested in gender-genetic models to estimate whether gender, rater bias or sibling interaction, or dominance contributed to individual differences in scores on the ADHD index. According to the mothers’ reports, the prevalence of ADHD across the sample was approximately 4%, consistent with other reported rates of ADHD. However, when the authors used the gender-specific norms provided with the ADHD index, they found slightly higher rates of ADHD in girls than had been previously reported. Genetic analyses yielded a model that included genetic dominance (48%), additive genetic factors (30%), and unique environmental factors (22%).

According to the authors, the ADHD index from Conners’ Rating Scales—Revised identified an appropriate percentage of children from the current epidemiological twin sample as being at risk for ADHD. The results of the genetic analyses, the researchers state, are consistent with previous reports indicating that ADHD is influenced predominantly by genetic factors that are both dominant and additive in nature. (18 References)
COST-EFFECTIVENESS OF ADHD TREATMENTS: FINDINGS FROM THE MULTIMODAL TREATMENT STUDY OF CHILDREN WITH ADHD

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AM J PSYCHIATRY, 162:1628-36, September 2005

Attention deficit hyperactivity disorder (ADHD) is the most prevalent behavioral disorder in children and represents a costly public health problem. The authors of the present report examined the cost-effectiveness of the different treatment modalities used in the six-site National Institute of Mental Health Multimodal Treatment Study of Children with ADHD (MTA Study).

In all, 579 children (age range, 7 to 9.9 years) with ADHD (combined type) were assigned to 14 months of medication management (titration followed by monthly half-hour visits; N=144); intensive behavioral treatment (parent, school, and child components, with therapist involvement gradually reduced over time; N=144); combined medical management and behavioral treatment (N=145); or routine community care (treatment by community providers; N=146). Services, including medication, health care visits, behavioral treatments, and rental costs, were tallied throughout the study. Provider specialty, total time, and number of visits with providers were used to calculate costs, which were adjusted to FY 2000 dollars by means of the consumer price index. Treatment costs were found to vary fourfold. Medication management was the least expensive, followed by behavioral treatment (at over five times the cost of medication) and combined medical management and behavioral treatment (at over six times the cost of medication alone). Lower costs of medication treatment were found in the community care group, reflecting the less intensive (and less effective) nature of community-delivered treatment. Medical management was more effective (but more costly) than community care and was more cost-effective than combination treatment or behavioral treatment alone. In some instances, combination treatment was somewhat more cost-effective, as demonstrated by lower costs per additional child “normalized” among those with multiple comorbid disorders.

It appears that medical management, although not as effective as combined medication and behavioral treatment, is likely to be more cost-effective in the routine treatment of children with ADHD, particularly those without comorbid disorders. For some children with comorbid disorders, it may be cost-effective to provide combination treatment. (32 References)
Attention deficit hyperactivity disorder (ADHD) is a highly heritable neurodevelopmental syndrome with a significant lifetime risk for functional impairment. The authors of the present report examined ADHD and comorbid psychopathology in a group of adults identified through a genetic study of families characterized by the presence of more than one ADHD child.

The sample was composed of 435 parents (208 fathers, 227 mothers) of ADHD children ascertained through 230 families recruited through sampling of affected sibling pairs. Rates and mean ages of onset of comorbid psychopathology were assessed in parents with lifetime ADHD, parents with persistent ADHD, and parents without ADHD. Age-adjusted rates of comorbidity were compared with Kaplan-Meier survival curves. Logistic regression was used to assess additional risk factors for conditions found more frequently in ADHD parents. Of the 435 parents, 152 (35%) had lifetime ADHD, while 283 (65%) were unaffected by ADHD. Of the 152 subjects with lifetime ADHD, 79 (52%) were diagnosed with persistent ADHD. The parents with ADHD were significantly more likely to be unskilled workers and were less likely to have a college degree. The ADHD parents had more lifetime psychopathology, with 87% having at least one other psychiatric disorder and 56% having at least two other psychiatric disorders; comparable rates for the non-ADHD parents were 64% and 27%, respectively. Subjects with lifetime ADHD showed significantly higher rates of major depressive disorder, multiple anxiety disorders, oppositional defiant disorder, conduct disorder, and substance use disorders. Parents with ADHD had earlier onsets of oppositional defiant disorder, major depressive disorder, dysthymia, and conduct disorder. Group differences in frequencies of comorbid disorders according to Kaplan-Meier age-corrected risks were consistent with those presented for raw frequency distributions. Male sex contributed to the risk for disruptive behavior disorders. Female sex and oppositional defiant disorder contributed to the risk for depression and anxiety. ADHD was not a significant risk factor for substance use disorders when male sex, disruptive behavior disorders, and socioeconomic status were controlled.

According to the authors, the current data indicate that adult ADHD is associated with significant lifetime psychiatric comorbidity that cannot be explained by clinical referral bias. (29 References)
ASSOCIATION BETWEEN SMOKING AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS IN A POPULATION-BASED SAMPLE OF YOUNG ADULTS

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ARCH GEN PSYCHIATRY, 62:1142-7, October 2005

Attention-deficit/hyperactivity disorder (ADHD) has been associated with an increased risk for smoking, and there is some evidence to suggest that specific problems with inattention and related deficits in executive functioning may underlie this risk. To date, studies examining the relationship between ADHD symptoms and smoking have focused primarily on clinical or high-risk samples. The objective of the present investigation was to evaluate the relationship between smoking-related variables and number of retrospectively reported ADHD inattentive (IN) and hyperactive/impulsive (HI) symptoms in a population-based sample of young adults.

The subjects were drawn from wave III of the National Longitudinal Study of Adolescent Health, a nationally representative sample of adolescents followed from 1995 (mean age, 15.65 years) to 2002 (mean age, 22.96 years). Logistic regression was used to examine the association between self-reported ADHD symptoms and the lifetime likelihood of being a regular smoker (having ever smoked at least one cigarette a day for 30 days). The authors also examined the extent to which ADHD symptoms predicted age at onset of regular smoking and number of cigarettes smoked in those who reported regular smoking. Complete data on ADHD and tobacco use were available for 13,850 of 15,197 eligible participants. Subjects who reported ever having smoked at least one cigarette a day for 30 days were classified as “ever-regular smokers” (N=5,344). All others were classified as “never-regular smokers” (N=8,506). Reporting higher numbers of conduct disorder (CD) symptoms, being Caucasian, and reporting six or more IN and/or HI symptoms were all significantly associated with a greater likelihood of ever having been a regular smoker. When demographic variables and CD symptoms were controlled, significant relations were seen between number of self-reported ADHD symptoms and smoking outcome measures. These relationships were largely linear, with each additional symptom typically conferring additional risk of regular smoking. HI symptoms were found to be better predictors of lifetime regular smoking than IN symptoms. Among regular smokers, more ADHD symptoms were associated with earlier regular smoking and greater cigarette consumption (again in a largely linear manner).

Here, self-reported ADHD symptoms were found to be associated with adult smoking outcomes, providing further evidence of a likely link between symptoms of ADHD and risk for tobacco use. (37 References)
Digest of Neurology and Psychiatry

Abstracts and Reviews of Selected Literature in Psychiatry, Neurology, and their Allied Fields

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PATHWAYS TO PTSD, PART I: CHILDREN WITH BURNS

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AM J PSYCHIATRY, 162:1299-1304, July 2005

Fire is a leading cause of unintentional injuries in children. In an earlier study of the prevalence of psychiatric diagnoses in burned children, it was found that 30% of children interviewed more than six months after suffering a severe burn had met DSM-III criteria for posttraumatic stress disorder (PTSD) at some point after being burned. The aim of the present investigation was to develop a model of risk factors for PTSD in a group of acutely burned children. The authors attempted to evaluate the ways in which pretrauma variables, trauma characteristics, and reactions in the immediate aftermath of a trauma are related to subsequent PTSD symptoms.

The study sample was composed of 72 children (48 boys, 24 girls; age range, 7 to 17 years; mean age, 11.2 years) who had been hospitalized for treatment of an acute burn. Written informed consent was obtained from the children and their parents. Assessments were conducted shortly after hospital admission and again three months later. Measures included the Child PTSD Reaction Index, the Multidimensional Anxiety Scale for Children, the Colored Analogue Pain Scale, and the Child Stress Disorders Checklist. A path analytic strategy was used to build a model of risk factors for PTSD. Variables were divided as follows: 1) PTSD symptoms (main dependent variable, derived from Child PTSD Reaction Index); 2) posttraumatic (variables assessed at three-month follow-up); 3) peritraumatic (variables assessed shortly after the trauma); 4) trauma exposure (percentage of body surface area burned); and 5) pretrauma (variables related to the child or his/her family prior to the trauma). Two pathways to PTSD were found: (1) from the size of the burn and the level of pain following the burn to the child’s level of acute separation anxiety, and then to PTSD; and (2) from the size of the burn to the child’s level of acute dissociation following the burn, and then to PTSD. Together these pathways accounted for almost 60% of the variance in PTSD symptoms and constituted a model with excellent fit indices.

According to the authors, the current findings support a model of complex etiology for childhood PTSD in which two independent pathways may be mediated by different biobehavioral systems. In the present investigation, one pathway was mediated by acute separation anxiety and the other, by acute dissociative responses. (45 References)
PATHWAYS TO PTSD, PART II: SEXUALLY ABUSED CHILDREN

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AM J PSYCHIATRY, 162:1305-10, July 2005

Child sexual abuse is an all too common event in the lives of children and can produce severe psychological damage in victims both at the time of the abuse and years later. Many researchers have identified posttraumatic stress disorder (PTSD) as a core manifestation of sexual abuse trauma because of the high frequency with which this disorder and related symptoms appear in sexually abused children. The authors of the current investigation used path analytic techniques to evaluate the ways in which pretrauma vulnerabilities, trauma characteristics, and stress reactions upon disclosure of sexual abuse are related to later symptoms of PTSD in children.

The study sample consisted of 156 children (27 boys, 129 girls; age range, 8 to 13 years; mean age, 10.7 years) who had been referred to a treatment facility that offered services to children considered to be possible victims of sexual abuse. All were medically examined, interviewed, and videotaped for forensic purposes. Abuse was rated as confirmed for 54% of the participants, probable for 18%, and suspicious for 28%. At time 1 (initial interview), several measures (e.g., clinicians' written reports, videotapes, Trauma Symptom Checklist for Children) were used to assess pretrauma variables, trauma variables, and stress reactions upon disclosure of sexual abuse. At time 2 (seven to 36 months following the initial interview), the children were assessed for the presence of PTSD symptoms. A path analysis involving a series of hierarchically nested ordinary least squares multiple regression analyses indicated three direct paths to PTSD: avoidant coping, anxiety/arousal, and dissociation (all measured during or immediately after disclosure of sexual abuse). In addition, age and gender predicted avoidant coping, while life stress and age at onset of abuse predicted symptoms of anxiety/arousal. Taken together, these pathways accounted for approximately 57% of the variance in PTSD symptoms.

According to the authors, the current results demonstrate that symptoms measured at the time of disclosure constitute direct, independent pathways by which sexually abused children are likely to develop subsequent symptoms of PTSD. These findings speak to the importance of assessing children during the disclosure of sexual abuse in order to identify those who appear to be most at risk for developing PTSD symptoms. (51 References)
LONGITUDINAL COURSE OF POSTTRAUMATIC STRESS DISORDER AND POSTTRAUMATIC STRESS DISORDER SYMPTOMS IN A COMMUNITY SAMPLE OF ADOLESCENTS AND YOUNG ADULTS

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AM J PSYCHIATRY, 162:1320-7, July 2005

Posttraumatic stress disorder (PTSD) is a disorder for which overall community lifetime prevalence estimates range from a minimum of 1% in earlier reports to a maximum of 12.3% in more recent surveys. Few studies have focused on the natural course of PTSD and its determinants in the general population. In the present investigation, the authors examined determinants of PTSD remission and chronicity as well as its association with other disorders in a large community sample.

The data were drawn from a prospective, longitudinal, epidemiological survey of adolescents and young adults (N=2,548) who were between the ages of 14 and 24 years at baseline. The course of PTSD from baseline to follow-up (34 to 50 months later) was examined in 125 respondents who met full DSM-IV criteria for PTSD at baseline (N=24) or who were considered to have subthreshold PTSD at baseline (N=101). During the follow-up period, 52% (N=65) reported remission of PTSD symptoms. The remaining 48% (N=60) reported experiencing full or subthreshold PTSD or PTSD symptoms during follow-up and were classified as having a chronic course of illness. Compared with the respondents who experienced remission of PTSD, those with a chronic course of the disorder were more likely to experience new traumatic events during follow-up, to have higher rates of avoidant symptoms at baseline, and to report more help seeking. In addition, rates of incident somatoform disorders and other anxiety disorders were found to be significantly associated with a chronic course of PTSD.

The authors conclude that the current results confirm that PTSD is often a persistent and chronic disorder. In adolescents and young adults, exposure to new traumatic events and seeking help for PTSD symptoms (which could be an indicator either of severity or of coping ability) are associated with poorer outcomes. Efforts to prevent persons from being exposed to new traumas during the course of PTSD could lessen the chronicity of this disorder. Prevention might be achieved through the implementation of therapies that include techniques for teaching individuals how to seek safe living environments and nonabusive social and romantic relationships. (35 References)
THE RELATIONSHIP OF GENDER AND TRAUMA CHARACTERISTICS TO POSTTRAUMATIC STRESS DISORDER IN A COMMUNITY SAMPLE OF TRAUMATIZED NORTHERN PLAINS AMERICAN INDIAN ADOLESCENTS AND YOUNG ADULTS

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J CLIN PSYCHIATRY, 66:1176-83, September 2005

Previous studies have identified a high prevalence (25%-80%) of trauma among American Indian and non-American Indian adolescents and adults. However, only a fraction of traumatized individuals develop posttraumatic stress disorder (PTSD). In the present investigation, the authors examined the prevalence and correlates of PTSD in a community sample of American Indian adolescents and young adults who had experienced at least one traumatic event in their lifetime. The objective was to quantify the relative relationships of female gender, type of trauma, number of traumas, and age at first traumatic experience to the development of PTSD in traumatized individuals.

Complete data were collected from 349 American Indians (151 males, 198 females; age range, 15 to 24 years; mean age, 21 years) who participated in a cross-sectional community-based study from July 1997 to December 1999 and reported experiencing at least one traumatic event. Traumatic events and PTSD were assessed by means of a version of the Composite International Diagnostic Interview. Logistic regression was used to determine the relationships of gender, trauma type, age at first trauma, and number of traumas (independent variables) to the development of PTSD (dependent variable). Of the 349 participants who had experienced at least one traumatic event, 42 (nine males, 33 females) or 12% met criteria for lifetime PTSD. While all four of the independent variables studied demonstrated univariate associations with PTSD, multivariate logistic regression analyses indicated that only having experienced a sexual trauma and having experienced six or more traumatic events were independent predictors of the development of PTSD.

The current data indicate that traumatic experiences are common among American Indian adolescents and young adults and that females who experience sexual trauma and both males and females who experience multiple traumas may be at particularly high risk for developing PTSD. (45 References)
POSTTRAUMATIC STRESS DISORDER AMONG ISRAELI EX-PRISONERS OF WAR 18 AND 30 YEARS AFTER RELEASE

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J CLIN PSYCHIATRY, 66:1031-7, August 2005

War captivity is one of the most traumatic events perpetrated by human beings. Most prisoners of war (POWs) are held in solitary confinement; are incarcerated in small and filthy cells; are sometimes blindfolded and handcuffed; and are subjected to deliberate and systematic acts of violence, including physical torture, deprivation of basic needs, and deliberate humiliation. Rates of posttraumatic stress disorder (PTSD) found among ex-POWs approximately two to five decades after captivity vary along a wide spectrum, ranging from 5% to 88%. Empirical research on POWs has consistently found that captivity produces long-lasting psychological, somatic, and functional injuries. In the present study, the psychological responses to captivity were examined in a sample of former POWs 18 and 30 years after their release from captivity.

Using a prospective, longitudinal design, the researchers evaluated 209 Israeli veterans of the 1973 Yom Kippur War (103 ex-POWs and 106 controls) who were assessed in 1991 and again in 2003. Self-report questionnaires were administered at both assessments. The present study measured current rates of PTSD; changes in PTSD over time; and the contribution of the following variables to the prediction of long-term posttraumatic sequelae: sociodemographic factors, severity of captivity (subjective and objective), and psychological appraisal and coping with captivity. Significantly more ex-POWs than non-POW controls met DSM-IV symptom criteria for PTSD 30 years after the Yom Kippur War (23.2% versus 3.8%, respectively). The ex-POWs were ten times more likely than the controls to experience deterioration in their psychological condition in the 12-year interval between the 18- and 30-year assessments. Almost 20% of the ex-POWs who did not meet PTSD criteria 18 years after their release did meet criteria for PTSD at the 30-year assessment, as compared with less than 1% of the controls. Current PTSD, 30 years after the Yom Kippur War, was predicted by younger age at the time of captivity, by loss of emotional control and higher subjective appraisal of suffering in captivity, and by a greater number of PTSD symptoms at the 1991 assessment.

According to the authors, the current data highlight the importance of following up and offering treatment to former POWs. The researchers recommend that special attention be paid to those ex-POWs who lost emotional control in captivity as well as to those former POWs who felt that the conditions of their captivity were severe. (39 References)
PTSD FOLLOWING TERRORIST ATTACKS: 
A PROSPECTIVE EVALUATION

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AM J PSYCHIATRY, 162:1188-91, June 2005

Recent events have focused the world’s attention on the psychological effects of terrorism. Elevated rates of posttraumatic stress disorder (PTSD) symptoms have been observed in the aftermath of major terrorist attacks in the United States. While such symptoms tend to subside over time, a significant minority of individuals initially affected may develop chronic PTSD. In the study presented here, the authors prospectively evaluated the incidence of PTSD in survivors of terrorist attacks and survivors of motor vehicle accidents. They also compared the progressive attenuation of early PTSD symptoms during a period of continuous terrorist threat with that seen during years of sporadic terrorism.

The study sample consisted of 39 survivors of terrorist attacks (19 males, 20 females) and 354 survivors of motor vehicle accidents (179 males, 175 females). All were evaluated upon admission to a general hospital emergency room and again one week and four months later. Heart rate was measured at the time of emergency room admission. Peritraumatic dissociation was assessed one week later. Symptoms of PTSD, anxiety, and depression were measured one week and four months after the traumatic event. The Clinician-Administered PTSD Scale was used to confer a diagnosis of PTSD at the four-month mark. To examine the effect of a higher frequency of terrorism on the course of early PTSD symptoms, 137 survivors whose trauma occurred during an era of frequent terrorist attacks were compared with 256 survivors whose trauma occurred during years of relative calm. Four months after the traumatic event, survivors of terrorist attacks had higher rates of PTSD than survivors of motor vehicle accidents; 14 survivors of terrorist attacks (36%) met DSM-IV diagnostic criteria for PTSD, as compared with 65 survivors of motor vehicle accidents (18%). Heart rate (measured at emergency room admission), peritraumatic dissociation, and early PTSD symptoms were predictors of the development of PTSD; however, type of traumatic event (terrorist attack versus motor vehicle accident) did not contribute to the prediction of PTSD. The longitudinal course of early PTSD symptoms was not affected by the fact that the trauma had occurred during a period of frequent terrorism as opposed to a time of sporadic terrorism.

The authors conclude that early symptoms are reliable risk indicators of PTSD across events and circumstances. Converging effects of terror-induced fear, adjustment, and resiliency might explain the lack of effect of intense terrorism on the course of PTSD symptoms. (14 References)
COMORBID PTSD AND SOCIAL PHOBIA IN A TREATMENT-SEEKING POPULATION
An Exploratory Study

Claudia Zayfert, PhD (Department of Psychiatry, Dartmouth Hitchcock Medical Center, One Medical Center Drive, Lebanon, NH 03756-0001); Jason C. DeViva, PhD; and Stefan G. Hofmann, PhD
J NERV MENT DIS, 193:93-101, February 2005

The lifetime co-occurrence of posttraumatic stress disorder (PTSD) and social phobia (SP) has been documented in studies of both veteran and civilian populations. Although the lifetime association between these two disorders may be relevant to understanding their etiology, research on current comorbidity is of greater interest to clinicians who face the challenge of treating two simultaneous problems, each of which can substantially impair functioning. In the present investigation, the authors attempted to determine the following: (1) whether the prevalence of comorbid SP in patients with a principal diagnosis of PTSD would differ from the rate of comorbid PTSD in patients with a principal diagnosis of SP; and (2) whether patients with comorbid PTSD and SP would be more impaired than those with either disorder alone or than those with either disorder accompanied by anxiety comorbidity.

The study participants were drawn from a sample of 443 patients (mean age, 38.1 years) who had been evaluated at an anxiety disorders clinic and assigned a principal or comorbid diagnosis of PTSD or SP. Assessment tools included the Anxiety Disorders Interview Schedule-Revised, the Beck Depression Inventory, the Medical Outcomes Study 36 Item Short-Form Health Survey, and the Social Interaction Self-Statement Test. Of the 443 patients, 240 were assigned a principal diagnosis of PTSD, and 57 were assigned a principal diagnosis of SP. Of the 240 patients with a principal diagnosis of PTSD, 103 (43%) had comorbid SP. Of the 57 patients with a principal diagnosis of SP, only four (7%) were found to have comorbid PTSD. Compared with participants with only PTSD or SP, patients with principal PTSD and comorbid SP were more likely to meet diagnostic criteria for major depression and other anxiety disorders and to report more severe depression and anxiety and poorer physical, mental, and social functioning, regardless of the presence or absence of other anxiety comorbidity. PTSD patients with comorbid SP reported more trauma-related guilt and a greater frequency of childhood abuse than those without SP.

In the current study, the proportion of patients with a principal diagnosis of PTSD who had comorbid SP was significantly higher than the proportion of patients with a principal diagnosis of SP who had comorbid PTSD. The authors suggest that when both PTSD and SP are present, PTSD is usually associated with greater functional interference and distress and may be the disorder for which treatment is sought. (46 References)
PTSD AND TREATMENT ADHERENCE
The Role of Health Beliefs

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J NERV MENT DIS, 193:515-22, August 2005

Although the role of health beliefs in treatment decisions has been amply demonstrated in various medical conditions, only recently have health beliefs become a focus of study in mental health treatment decisions. Information on treatment adherence in patients with posttraumatic stress disorder (PTSD) is limited; however, available evidence suggests that PTSD is associated with an increased likelihood of missed appointments, underuse of medication for medical conditions, and abuse of prescribed psychoactive drugs. In the present study, the authors examined the health beliefs and treatment behavior of a group of veterans who had PTSD and who were receiving disability compensation for their condition from the Department of Veteran Affairs.

Using standard survey methodology, the researchers assessed beliefs about the cause of PTSD, expected duration and controllability of symptoms, and life consequences of the disorder (i.e., degree of negative impact). In addition, treatment participation and medication compliance were evaluated, as were such common treatment correlates as patient-provider relationships, dosing frequency, side effect severity, number of prescribed medications, and use of alcohol or drugs to control PTSD symptoms. Of 145 potentially eligible subjects, 84 returned usable surveys, yielding a response rate of 58%. With regard to an explanatory model of PTSD, psychosocial causation was endorsed more frequently than biological causation. Most subjects viewed PTSD as a chronic illness that they would have for the rest of their lives, and symptoms were largely seen as difficult to control. Some 65% of the respondents were taking medication to treat their PTSD symptoms; 43% were participating in psychotherapy, and 26% acknowledged that they used alcohol or illicit drugs at least once a week as a means of coping with their PTSD symptoms. Explanatory models of PTSD, perceived controllability, and use of benzodiazepines were found to be predictive of psychiatric medication use. Negative life consequences of PTSD were found to be associated with participation in psychotherapy.

According to the authors, the results of the present investigation demonstrate that individuals with PTSD hold a variety of cognitive representations with regard to their illness and that some of these cognitive representations are associated with treatment behavior. (28 References)
RISPERIDONE IN PSYCHOTIC COMBAT-RELATED POSTTRAUMATIC STRESS DISORDER: AN OPEN TRIAL

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J CLIN PSYCHIATRY, 66:922-7, July 2005

Psychotic combat-related posttraumatic stress disorder (PTSD) is a severe form of the illness. PTSD is usually treated pharmacologically with antidepressants, adrenergic and antianxiety agents, and mood stabilizers; however, the presence of psychotic symptoms in individuals with PTSD is often associated with treatment resistance and requires additional pharmacologic strategies, such as the use of neuroleptics or atypical antipsychotics. The authors of the present study hypothesized that war veterans who were diagnosed with psychotic PTSD and who were resistant to prior antidepressant therapy would respond well to six weeks of treatment with the atypical antipsychotic risperidone, administered as a monotherapy.

Twenty-six white Croatian male war veterans (mean age, 36.9 years) who met diagnostic criteria for psychotic PTSD completed six weeks of inpatient treatment with risperidone (2-4 mg/day) between November 1999 and December 2002. The primary outcome measure was change from baseline to endpoint (six weeks) in Positive and Negative Syndrome Scale (PANSS) total and subscale scores. Secondary outcome measures were changes in PTSD Interview (PTSD-I) and Clinical Global Impressions-Severity of Illness (CGI-S) total and subscale scores. Clinical improvement was assessed by means of the CGI-S, CGI-Improvement scale, and Patient Global Impression of Improvement scale. Adverse events were recorded with the Drug-Induced Extrapyramidal Symptoms Scale. Three or six weeks of risperidone therapy was found to be associated with significant reductions (decline in baseline scores of 44%-70%) in total and subscale scores on the PANSS, the PTSD-I, and the CGI-S. Analyses of variance revealed that total and subscale scores on positive, negative, general psychopathology, and supplementary items of the PANSS; total and subscale scores on trauma re-experiencing, avoidance, and hyperarousal on the PTSD-I; and total scores on the CGI-S were all significantly lower after three and six weeks of risperidone treatment. Reported side effects included akathisia, psychomotor agitation, and rigor; sedation; anxiety; increased appetite; and weight gain. These effects were generally mild in nature and did not lead to any dropouts.

According to the authors, the current findings support the use of the atypical antipsychotics as effective monotherapies in the treatment of antidepressant-resistant war veterans with psychotic PTSD. (44 References) EAF
MAINTENANCE THERAPY WITH FLUOXETINE IN POSTTRAUMATIC STRESS DISORDER
A Placebo-Controlled Discontinuation Study

Jonathan R. T. Davidson, MD (Anxiety and Traumatic Stress Program, Department of Psychiatry and Behavioral Sciences, Box 3812, Duke University Medical Center, Durham, NC 27710; e-mail: Jonathan.Davidson@duke.edu); Kathryn M. Connor, MD; Michael A. Hertzberg, MD; Richard H. Weisler, MD; William H. Wilson, PhD; and Victoria M. Payne, MD
J CLIN PSYCHOPHARMACOL, 25:166-9, April 2005

Active posttraumatic stress disorder (PTSD) symptoms may persist for as long as 20 years. In some treatment studies, PTSD patients have reported experiencing symptoms for more than 10 years. Consequently, it is important to determine the efficacy of long-term pharmacotherapy for this disorder. In the present investigation, the authors conducted a one-year, single-center trial in which subjects with PTSD received open-label fluoxetine (FLU) therapy for six months, followed by double-blind, randomized treatment with FLU or placebo (PBO) for an additional six months.

One hundred twenty-three subjects who fulfilled diagnostic criteria for PTSD entered the open-label phase of treatment; of these, 114 (53 men, 61 women) returned for at least one visit. Of 63 subjects who completed 24 weeks of treatment and demonstrated clinical improvement, 62 decided to enter the double-blind phase of the study and were randomly assigned to remain on FLU (N=30) or be switched to PBO (N=32). Of these 62 individuals, 57 (27 in the FLU group and 30 in the PBO group) returned at least once and were subject to analysis. During the open-label phase, the daily dose of FLU ranged from 10 mg to 60 mg; at randomization, mean daily doses were 48.6 mg and 42.1 mg for the FLU and PBO groups, respectively. Outcome measures included the Clinical Global Improvement Scale, the Clinical Global Impressions of Severity scale, the Short PTSD Rating Interview, and the Davidson Trauma Scale. The results showed that the rate of relapse was significantly higher in the PBO group (50%) than in the FLU group (22.2%), and time to relapse was longer in the FLU subjects than in the PBO subjects. The estimated relative risk of relapse was 1.55 for those on PBO and 0.44 for those on FLU. The odds ratio for relapse on PBO relative to FLU was 3.50. FLU was well-tolerated during the double-blind phase, with nightmares (N=5) and insomnia (N=5) being the most commonly reported adverse events. In the PBO group, the most commonly reported side effects were nightmares (N=6), insomnia (N=5), akathisia (N=4), racing heart (N=7), headache (N=7), increased appetite (N=7), and weight gain (N=6).

The current data support the efficacy of FLU maintenance therapy in protecting those with PTSD against relapse. (12 References)
BOOKS RECEIVED FOR REVIEW


Abstracts and Reviews of Selected Literature in Psychiatry, Neurology, and their Allied Fields

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THE IMPACT OF PERSONALITY ON SYMPTOM EXPRESSION IN OBSESSIVE-COMPULSIVE DISORDER

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J NERV MENT DIS, 193:231-6, April, 2005

Earlier research on personality dimensions in obsessive-compulsive disorder (OCD) has focused on the role of neuroticism and extraversion as vulnerability markers for the disorder. More recent research has also begun to examine the broad domains and more narrow lower-order facets of the five-factor model (FFM) of personality in OCD. The FFM comprises the broad personality trait domains of neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness. In turn, each of these broad personality domains is composed of six lower-order correlated traits or facets. For example, neuroticism encompasses the predisposition to experience negative affectivity such as anxiety, depression, anger, guilt, and disgust. Extraversion includes sociability, cheerfulness, and liveliness. Openness to experience consists of esthetic sensitivity, intellectual curiosity, and need for variety. Agreeableness incorporates trust, altruism, and sympathy. Finally, conscientiousness includes a strict adherence to principles and a desire to achieve goals. The authors of the present study explored the relationship between the domains and facets of the FFM and the severity of obsessive-compulsive symptoms.

The sample was composed of 56 psychiatric outpatients (mean age, 35.6 years) who had a primary DSM-IV diagnosis of OCD. All the participants completed the Revised NEO Personality Inventory, the Yale-Brown Obsessive Compulsive Scale, and the Beck Depression Inventory. The facets of neuroticism, extraversion, and agreeableness were not found to be associated with the severity of obsessive-compulsive symptoms. However, the researchers found that facets of openness were significantly associated with obsession and compulsion symptom severity, even after they accounted for depression severity. More specifically, patients with a trait disposition to be low in openness to actions reported comparatively greater clinical compulsions, whereas patients with a stable tendency to be low in openness to new and unconventional ideas reported experiencing more severe obsessions.

As opposed to past reports that emphasized the association between neuroticism and extraversion and dimensionally rated obsessive-compulsive symptoms, the current study demonstrated specific relationships between selective facets of openness and clinical obsessions and compulsions. Facets of openness, the authors conclude, may influence the particular expression and severity of obsessive-compulsive symptoms. (40 References)
WHITE MATTER ABNORMALITIES IN OBSESSIVE-COMPULSIVE DISORDER
A Diffusion Tensor Imaging Study

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ARCH GEN PSYCHIATRY, 62:782-90, July, 2005

Obsessive-compulsive disorder (OCD) has a prevalence rate of 2% to 3% and is often chronically disabling, with concomitant impairments in interpersonal and occupational functioning. Several neurobiological models of OCD posit a primary role for dysfunction of the anterior cingulate gyrus. Both functional and structural neuroimaging studies have implicated anterior cingulate gray matter abnormalities in the pathophysiology of OCD, but very few have investigated the role of anterior cingulate white matter. The authors of the present report hypothesized that the integrity of anterior cingulate white matter microstructure seen in patients with OCD would differ from that seen in healthy volunteers (as inferred from diffusion tensor imaging). The researchers also examined group differences in white matter integrity across the entire brain.

The study sample was composed of 15 adult outpatients with a DSM-IV diagnosis of OCD and 15 healthy volunteers matched for age, sex, and handedness. All underwent diffusion tensor imaging (DTI) and structural magnetic resonance imaging (MRI) examinations. DTI represents an in vivo MRI technique that can be used to examine white matter microstructure in humans. Fractional anisotropy (FA), a robust intravoxel measure of water self-diffusion, was compared between groups on a voxel-by-voxel basis in the anterior cingulate white matter after standardization in Talairach space. All subjects were clinically assessed by means of the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), the 17-item Hamilton Depression Rating Scale, and the Hamilton Anxiety Rating Scale. Compared with healthy volunteers, OCD patients demonstrated significantly lower FA bilaterally in three areas of anterior cingulate gyrus white matter. Additional analyses conducted across the rest of the brain white matter revealed several additional areas of decreased FA in the OCD patients; they demonstrated lower FA bilaterally in the parietal region (supramarginal gyri), right posterior cingulate gyrus, and left occipital lobe (lingual gyrus). No areas of significantly higher FA were observed in patients as compared with volunteers. A significant correlation was found between lower FA in the parietal region and higher Y-BOCS scores.

According to the authors, the preliminary findings presented here provide evidence of white matter abnormalities in the pathogenesis of OCD at the microstructural level. (94 References)
NEUROPSYCHOLOGICAL FUNCTIONING IN EARLY- AND LATE-ONSET OBSESSIVE-COMPULSIVE DISORDER

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J NEUROPSYCHIATRY CLIN NEUROSCI, 17:208-13, Spring, 2005

Childhood or adolescent onset is reported by approximately one third to one half of adults with obsessive-compulsive disorder (OCD). Presently, it is unclear whether early- and late-onset OCD represent different subtypes of the illness or are parts of a developmental continuum. Significant relationships have been found between age of onset and demographics, clinical characteristics, and cerebral metabolic activity in OCD. In the present study, the authors examined several domains of neuropsychological functioning in patients with early- and late-onset OCD. OCD was defined as late onset if symptoms of the disorder first occurred when the patient was 13 years of age or older.

The study sample consisted of 21 OCD outpatients (eight males, 13 females) who reported onset of the disorder at 12 years of age or younger (early-onset group), 17 OCD outpatients (nine males, eight females) with a reported onset at age 13 years or older (late-onset group), and 27 healthy comparison subjects (16 males, 11 females). Neuropsychological tests and self-reported mood measures were administered in a fixed order in a single session lasting approximately three and a half hours. Neuropsychological domains evaluated included executive functions, verbal memory, visual memory, and motor skills. There were no significant group differences in terms of age, sex composition, or handedness. However, the OCD patients were significantly more depressed and anxious than the comparison subjects. The early- and late-onset OCD groups did not differ with respect to symptom severity (as measured by the Yale-Brown Obsessive Compulsive Scale), percentage of patients with comorbid depressive or anxiety disorders, or percentage of patients receiving psychotropic medications. The results revealed that the late-onset OCD group obtained poorer scores on measures of executive function and auditory attention than the early-onset OCD group. The late-onset OCD patients also exhibited poorer visual memory than the healthy comparison subjects.

According to the authors, the findings of the current investigation suggest that early- and late-onset OCD may be the result of at least partially differing neurobiological mechanisms. The researchers note that positron emission tomography and functional magnetic resonance imaging carried out during the performance of cognitive tasks could be helpful in directly evaluating the relationship between cognitive functioning and underlying neural circuitry in early- and late-onset OCD. (36 References)
FAMILIAL AND SPORADIC SUBTYPES OF EARLY-ONSET OBSESSIVE-COMPULSIVE DISORDER

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BIOL PSYCHIATRY, 57:895-900, April 15, 2005

Obsessive-compulsive disorder (OCD) is a heterogeneous illness of unknown etiology that has been subtyped according to age at onset of obsessive-compulsive (OC) symptoms. Family studies of OCD indicate that there is substantial heterogeneity in the familiality of the disorder. In the present investigation, the authors attempted to determine whether there are differences between familial and sporadic (nonfamilial) probands with early-onset OCD in terms of OC symptom categories and comorbid psychiatric diagnoses.

Fifty OCD probands (33 males, 17 females; age range, 10 to 19 years) with an onset of OC symptoms before the age of 15 years were directly assessed by means of semistructured diagnostic interviews; 186 first- and second-degree relatives also were directly interviewed, and family history information was collected on an additional 302 first- and second-degree relatives. An OCD proband was classified as familial if a first-degree relative was diagnosed with definite or subthreshold OCD on the basis of direct interview or detailed clinical records. An OCD proband was classified as sporadic if direct interview or family informant data revealed no evidence of OCD in any first-degree relatives. Logistic regression was used to examine significant differences in categorical data while controlling for age, gender, and age at onset of OC symptoms. Using all available sources of information, the researchers determined that 33 of the 50 probands had familial OCD, and 17 had sporadic OCD. In the familial subgroup, the three most common types of compulsions were washing, repeating, and ordering. In the sporadic subgroup, washing, repeating, and checking were the three most commonly reported compulsions. Ordering and arranging compulsions were significantly more common in the familial OCD probands. Aberrant grooming behaviors (hair pulling, nail biting, and skin picking) occurred significantly more frequently in the familial subgroup than in the sporadic subgroup, with skin picking contributing significantly to this difference. Anxiety disorders other than OCD were found to occur significantly more frequently in the familial subgroup than in the sporadic subgroup, with phobic disorders contributing significantly to this difference.

The current results indicate that familial and sporadic forms of early-onset OCD may be differentiated by ordering compulsions, aberrant grooming behaviors, and anxiety disorders other than OCD. (45 References)
ADAPTIVE, EMOTIONAL, AND FAMILY FUNCTIONING OF CHILDREN WITH OBSESSIVE-COMPULSIVE DISORDER AND COMORBID ATTENTION DEFICIT HYPERACTIVITY DISORDER

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AM J PSYCHIATRY, 162:1125-32, June, 2005

Obsessive-compulsive disorder (OCD) is characterized by distressing and intrusive thoughts, impulses, or images (obsessions) and repetitive overt or covert behaviors (compulsions) performed to reduce distress. Clinical accounts often reflect that OCD children are impaired in their daily routine, emotional adjustment, family and peer relationships, and academic performance. The purpose of the present study was to examine adaptive, emotional, and family functioning in a well-characterized group of children and adolescents with OCD and to evaluate the influence of comorbid attention deficit hyperactivity disorder (ADHD) on levels of impairment in various functional domains.

The study sample comprised 287 children and adolescents (191 boys, 96 girls; age range, seven to 18 years; mean age, 11.5 years). Of these subjects, 56 had OCD only, 43 had both OCD and ADHD, 95 had ADHD only, and 93 were unaffected comparison children. Best-estimate DSM-IV diagnoses were assigned on the basis of structured interviews and clinical ratings. The subjects’ functioning was evaluated with a comprehensive battery of well-established standardized measures, including the Vineland Adaptive Behavior Scales, parents’ ratings of social and family functioning, and children’s self-reports of emotional adjustment. Children with OCD only were more impaired than unaffected comparison children in multiple areas of adaptive functioning and emotional adjustment. The group with OCD and ADHD was similar to the ADHD-only group in all areas of functional impairment. Children with OCD and ADHD were more impaired than children with OCD only in school and social functioning. Having a diagnosis of either OCD or ADHD contributed to impaired social functioning, school problems, and self-reported depression. Impairment in daily living skills, reduced number of activities, and self-reported anxiety were uniquely associated with a diagnosis of OCD. Family dysfunction was associated with ADHD but not with OCD.

The authors conclude that children and adolescents with OCD are impaired in multiple domains of adaptive and emotional functioning. When comorbid ADHD is present, there is an additional burden on social, school, and family functioning. (44 References)
A NATURALISTIC STUDY OF REFERRED CHILDREN AND ADOLESCENTS WITH OBSESSIVE-COMPULSIVE DISORDER

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Obsessive-compulsive disorder (OCD) in children and adolescents is a fluctuating, often chronic illness. In the present study, the authors describe the symptomatology, pattern of comorbidity, and response to pharmacotherapy in children and adolescents with OCD, all of whom were followed naturalistically and treated with serotonin reuptake inhibitors (SRIs).

The sample was composed of 94 patients (65 males, 29 females; age range, eight to 18 years; mean age, 13.6 years) who had been referred to the pediatric psychopharmacology service of a research hospital and who were diagnosed as having current OCD through the use of historical information, clinical interview (Diagnostic Interview for Children and Adolescents-Revised), and DSM-IV criteria. The patients were followed for an average of 10 months (range, three to 24 months). Of the 94 patients, 81 showed significant clinical impairment that derived from one prevalent symptom dimension. Symmetry obsessions and/or ordering, counting, and repeating compulsions were reported in 30 patients; aggressive, sexual, religious, and/or somatic obsessions and checking compulsions in 21; contamination obsessions and/or cleaning compulsions in 23; and hoarding obsessions and/or hoarding/collecting compulsions in seven. Subjects with contamination obsessions and washing rituals showed less need for atypical antipsychotics. Subjects with aggressive, sexual, and religious obsessions and checking rituals as well as patients with symmetry obsessions and ordering or repeating rituals had higher rates of comorbid tic disorders. Forty-seven patients received SRI monotherapy, while the other 47 received SRIs and adjunctive medications. Those receiving SRIs alone were less severely impaired; were younger at the time of hospital visit; had higher rates of depression and anxiety; and had lower rates of bipolar disorder, tic disorder, oppositional defiant disorder, and conduct disorder. On the basis of a Clinical Global Impressions-Improvement Scale score of 1 or 2, 63 patients were considered to be treatment responders, and 31 subjects were designated as nonresponders. Nonresponders were more severely impaired and had higher rates of bipolar disorder, oppositional defiant disorder, and conduct disorder.

The authors conclude that long-term naturalistic studies of pediatric OCD patients could prove to be valuable sources of information with regard to the effectiveness of a treatment over extended periods of time under ordinary clinical conditions. (30 References)
RANDOMIZED, PLACEBO-CONTROLLED TRIAL OF EXPOSURE AND RITUAL PREVENTION, CLOMIPRAMINE, AND THEIR COMBINATION IN THE TREATMENT OF OBSESSIVE-COMPULSIVE DISORDER

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While serotonin reuptake inhibitors (e.g., clomipramine) and cognitive behavior therapy by exposure and ritual prevention are both established therapeutic modalities for obsessive-compulsive disorder (OCD), their relative and combined efficacies have not been demonstrated conclusively. The purpose of the present double-blind, randomized, placebo-controlled trial was to test the relative and combined efficacies of clomipramine and exposure and ritual prevention in the treatment of adults with OCD. The study was conducted at three centers: one known for its expertise in exposure and ritual prevention, one with expertise in psychopharmacological treatment, and one experienced with both modalities.

One hundred twenty-two adult outpatients with OCD were randomly assigned to the following groups: exposure and ritual prevention (N=29); clomipramine (N=36); exposure and ritual prevention plus clomipramine (N=31); and pill placebo (N=26). Active interventions included intensive exposure and ritual prevention for four weeks, followed by eight weekly maintenance sessions, and/or clomipramine (maximum dose, 250 mg/day) administered for 12 weeks. Main outcome measures were the Yale-Brown Obsessive Compulsive Scale total score and response rates as determined by the Clinical Global Impression improvement scale. At week 12, the effects of all three active treatments were superior to that of placebo. The effect of exposure and ritual prevention did not differ from that of exposure and ritual prevention plus clomipramine, and both treatments were superior to clomipramine-only therapy. Treated and completer response rates were, respectively, 62% and 86% for exposure and ritual prevention; 42% and 48% for clomipramine alone; 70% and 79% for exposure and ritual prevention plus clomipramine; and 8% and 10% for placebo.

The authors conclude that clomipramine, exposure and ritual prevention, and their combination are all effective treatments for OCD. Intensive exposure and ritual prevention may be superior to clomipramine and, by implication, to monotherapy with other serotonin reuptake inhibitors. (49 References)
RISPERIDONE AND HALOPERIDOL AUGMENTATION OF SEROTONIN REUPTAKE INHIBITORS IN REFRACTORY OBSESSIVE-COMPULSIVE DISORDER: A CROSSOVER STUDY

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Although serotonin reuptake inhibitors (SRIs) are considered to be first-line agents for the treatment of obsessive-compulsive disorder (OCD), between 40% and 60% of OCD patients do not respond adequately to SRI monotherapy and require adjunctive treatment. The authors conducted a nine-week, double-blind, placebo-controlled study in which they compared the benefits of adjunctive risperidone, haloperidol, and placebo in OCD patients who continued to have severe symptoms despite being maintained on a stable dose of an SRI. To be eligible for the trial, patients had to have been receiving a therapeutic dose of an SRI for at least 12 weeks. At initial screening, they were required to have a score of 10 or higher on items 1-5 (obsession) of the Yale-Brown Obsessive Compulsive Scale (YBOCS) and a total score of 16 or higher on the YBOCS.

Sixteen patients (seven men, nine women; age range, 19 to 56 years) were enrolled, and 12 completed the study. Throughout the nine-week trial, subjects continued to take the same SRI at the same dose they were taking at screening. After a one-week, single-blind placebo period, each patient was randomly assigned to receive two weeks of placebo, risperidone (1 mg/day), or haloperidol (2 mg/day) in a crossover fashion, with a one-week placebo washout between each treatment. Assessment tools included the YBOCS, the 17-item Hamilton Rating Scale for Depression (HAM-D-17), the Hopkins Symptom Checklist 90-Revised (SCL-90R), and the Profile of Mood States (POMS). Compared with placebo, both risperidone and haloperidol significantly reduced the YBOCS obsession score. There was also a tendency for haloperidol and, to a lesser degree, risperidone to reduce the compulsion and total scores of the YBOCS. These results were accompanied by a reduction in SCL-90R anxiety scale scores. Risperidone, but not haloperidol, significantly improved depressed mood as assessed by the HAM-D-17, the SCL-90R, and the POMS. Neither risperidone nor haloperidol had a significant effect on neurocognitive functioning. Patients experienced substantially more serious side effects while receiving haloperidol than while receiving risperidone.

The effectiveness of both risperidone and haloperidol demonstrated in the present study supports the use of antipsychotics in the acute treatment of patients with SRI-refractory OCD. (41 References)
MIRTAZAPINE FOR OBSESSIVE-COMPULSIVE DISORDER:
AN OPEN TRIAL FOLLOWED BY DOUBLE-BLIND DISCONTINUATION

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Serotonin reuptake inhibitors (SRIs) are the only drugs approved by the United States Food and Drug Administration for the treatment of obsessive-compulsive disorder (OCD). However, a substantial proportion of OCD patients are unresponsive to SRIs. The antidepressant mirtazapine enhances serotonergic function by a mechanism distinct from reuptake inhibition. An earlier pilot study (Koran et al., 2001) pointed to the potential usefulness of mirtazapine in treating patients with OCD. To investigate further the efficacy of mirtazapine in both treatment-naïve and treatment-experienced patients with OCD, the authors conducted a larger, controlled trial.

Thirty adult outpatients (15 men, 15 women) were recruited for the study; 15 were treatment-naïve, and 15 were treatment-experienced. All had OCD (diagnosed according to DSM-IV criteria) for one year or longer, and all had a Yale-Brown Obsessive Compulsive Scale (YBOCS) score of 20 or higher at initial screening. The trial was conducted in two phases. In the 12-week, open-label phase, all subjects received mirtazapine (started at 30 mg/day and titrated over two weeks as tolerated to 60 mg/day). At the end of week 12, responders (those whose YBOCS scores decreased by more than 25%) were randomly assigned in a double-blind fashion to continue mirtazapine or switch to placebo; this eight-week discontinuation phase included a one-week, double-blind taper week for those assigned to placebo. During the open-label phase, the subjects’ mean YBOCS score fell from 28.3 to 20.3, a significant decrease. Medication side effects led five of the 30 subjects to discontinue participation in the trial. At the end of open-label treatment, 16 subjects (eight treatment-naïve and eight treatment-experienced) were considered to be responders. Response to mirtazapine was independent of comorbid mood disorders. Of the 16 responders, 15 agreed to enter the second phase of the study. During this double-blind discontinuation phase, the mirtazapine group’s mean YBOCS score fell an average of 2.6 points, while the placebo group’s mean YBOCS score rose an average of 9.1 points. All other outcome measures were consistent with mirtazapine’s superiority over placebo.

According to the authors, the findings of the present investigation indicate that mirtazapine may be as effective as SRIs in the treatment of patients with OCD. (46 References)
AN 11-TO 13-YEAR FOLLOW-UP OF 75 SUBJECTS WITH OBSESSIVE-COMPULSIVE DISORDER

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There is a paucity of data on the long-term course and outcome of obsessive-compulsive disorder (OCD), although demographic, epidemiologic, and clinical features have been well characterized. Available data indicate that the course of OCD is chronic and lifelong, with waxing and waning symptom severity. However, most previous studies have focused on severely ill patients who were often clinically referred and hospitalized. In the present investigation, the authors describe the long-term course and outcome of OCD in a group of patients who were, for the most part, drug-naive, self-referred, and seen on an outpatient basis.

Of 105 subjects who were initially seen at a major psychiatric hospital in India between 1991 and 1992 and who met DSM-IV diagnostic criteria for OCD, 75 (71%) were available for assessment 11 to 13 years after baseline evaluation; at the time of initial consultation, 63 (84%) were self-referred, 60 (80%) were outpatients, and 54 (72%) were drug-naive. None had received any kind of previous psychotherapeutic intervention. Follow-up evaluations were carried out by experienced clinicians using various scales and structured instruments. Course and outcome were determined according to predefined criteria. Multinomial logistic regression analysis was performed to identify potential predictors of outcome. The results indicated that a majority of the subjects (N=57, 76%) had been adequately treated with medications; 53 (71%) were not receiving any form of treatment at the time of follow-up evaluation. Only 18 (24%) of the 75 subjects were considered to have clinical OCD at follow-up. In all, 57 subjects (76%) were judged to have had a favorable outcome; of these, 32 (43%) had no OCD and 25 (33%) had subclinical OCD. The mixed subtype of OCD and any Axis I lifetime comorbidity were found to be predictive of a “clinical OCD” outcome at follow-up.

The authors conclude that the course and outcome of OCD appear to be better than generally assumed. The current findings offer a new perspective on the long-term outcome of OCD. According to the researchers, the poor outcomes found in earlier studies may have been due to the inclusion of severely and chronically ill patients. The prognosis of OCD may be more favorable in moderately ill OCD patients. (24 References)
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BOOKS RECEIVED FOR REVIEW
SUBTHRESHOLD DEPRESSION IN ADOLESCENCE AND
MENTAL HEALTH OUTCOMES IN ADULTHOOD

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ARCH GEN PSYCHIATRY, 62:66-72, January, 2005

Individuals with subthreshold depression have clinically relevant symptoms of major depression (MD) but do not meet the full criteria for MD. There is a growing body of evidence that suggests that individuals with subthreshold depression have an increased risk of subsequently developing MD and other disorders. Using data gathered on a New Zealand birth cohort of more than 1,000 young people who were studied up to the age of 25 years (the Christchurch Health and Development Study), the authors conducted a seven-year prospective study of the linkages between subthreshold depression in adolescence (17-18 years) and subsequent mental health in young adulthood (18-25 years). Analyses were based on a sample of 1,006 individuals who were assessed on measures of depression at age 18 and on mental health outcomes at age 21 or 25 years. This sample represented 80% of the original cohort, which was composed of 1,265 members (635 males, 630 females).

At the age of 18 years, more than a quarter of the sample reported at least one core DSM-IV symptom of MD; 18.4% met diagnostic criteria for MD, and 7.3% met criteria for subthreshold depression. Significant associations were found between the extent of depression at ages 17 to 18 years and rates of subsequent depressive symptoms, MD, treatment for depression, anxiety disorders, treatment for anxiety disorders, suicidal ideation, and suicide attempts. After adjustments were made for confounding factors (child, family, social, and related life history measures; comorbid mental disorder at age 18; and MD, anxiety disorders, an suicidal behaviors prior to age 17), the extent of depression at ages 17 to 18 years remained associated with later depression and suicidal tendencies. Planned comparisons showed that the risks of future adverse outcomes for individuals with subthreshold depression were similar to the risks experienced by those who met criteria for MD.

According to the authors, the present findings indicate that individuals with subthreshold depression clearly form a population that is at a significantly increased risk for later depression and suicidal behaviors. Current diagnostic procedures, which classify people with subthreshold depression into complex discrete groups, might obscure the fact that depressive symptoms are dimensional and range from none to severe. (36 References)
REDUCED HIPPOCAMPAL VOLUMES AND MEMORY LOSS IN PATIENTS WITH EARLY- AND LATE-ONSET DEPRESSION

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BR J PSYCHIATRY, 186:197-202, March, 2005

The hippocampus plays a key role in the regulation of mood and cognition and has come under increased scrutiny in people with mood disorders. To date, structural imaging studies of hippocampal volumes have yielded mixed results. The present authors examined the interrelationships between hippocampal volume changes; visual and verbal memory function; and key clinical, vascular, and genetic risk factors in older persons with major depression.

The study sample was composed of 66 individuals with primary major depressive disorder (mean age, 53.5 years; range, 28-82 years) and 20 healthy controls (mean age, 55.8 years; range, 40-74 years). All underwent magnetic resonance imaging and clinical assessment, which included measures of depression severity, psychomotor retardation, verbal and visual memory, and vascular and specific genetic risk factors. On the basis of DSM-IV criteria, 47 of the depressed subjects were classified as melancholic, and 19 were considered to be nonmelancholic. Those who experienced their first episode of depression prior to age 50 were designated as having “early-onset” depression (N=49), while those who first experienced depression at age 50 or older were classified as having “late-onset” depression (N=17). The mean lifetime duration of illness was 19.3 years for those with early-onset depression and 3.5 years for those with late-onset depression. Late-onset depressives were significantly older (mean age, 63.7 years) than early-onset depressives (mean age, 50.1 years). The depressed subjects demonstrated reduced whole-brain and left and right hippocampal volumes; impaired verbal and visual memory; and an increased number of clinical risk factors for vascular disease. Reductions in hippocampal volumes in these depressed individuals (but not in controls) were correlated with age, age of illness onset, and general cognitive and memory decrements. Although reductions in hippocampal volumes were more significant in older patients, in those with late-onset depression, and in those with melancholia, patients with early-onset depression also had smaller hippocampal volumes. Hippocampal volume reduction was not predicted by specific genetic risk factors for neurodegeneration or by clinical or genetic risk factors for vascular disease.

According to the authors, hippocampal volume changes may explain how depression emerges as a risk factor for dementia. (31 References)
TACHYPHYLAXIS IN UNIPOLAR MAJOR DEPRESSIVE DISORDER

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J CLIN PSYCHIATRY, 66:283-90, March, 2005

Major depressive disorder is usually a recurring illness, with each episode increasing the probability of yet another. Treatment guidelines suggest the use of maintenance therapy to forestall or prevent these recurrences. Despite the use of full doses of maintenance medication, however, patients sometimes experience a recurrence of major depression, which is termed tachyphylaxis. In the present observational study, the authors provide additional data on tachyphylaxis and identify risk factors associated with this phenomenon.

The study sample consisted of 103 subjects (42 males, 61 females) who participated in the National Institute of Mental Health-Collaborative Program on the Psychobiology of Depression. Subjects diagnosed with unipolar major depressive disorder were enrolled from 1978 to 1981 and prospectively followed for up to 20 years. Treatment was recorded but not controlled by anyone connected with the study. Subjects were selected for the present study if at some point during follow-up they received antidepressant medication for treatment of an episode of major depressive disorder, recovered from that episode, and subsequently received maintenance pharmacotherapy. Some were successfully treated for multiple episodes of major depression and received maintenance medication after each of these episodes, resulting in multiple maintenance treatment intervals. Among the 103 subjects, there were 171 maintenance treatment intervals during which a subject received maintenance pharmacotherapy after having recovered from a major depressive episode. The median duration of maintenance treatment was 20 weeks. Tachyphylaxis occurred during 43 (25%) of the 171 maintenance treatment intervals. Of the 103 subjects, 28 (27%) accounted for all the episodes of tachyphylaxis. The median time to recurrence for these episodes of tachyphylaxis was 31 weeks; 25% occurred within 14 weeks; and 75%, within 75 weeks. Having melancholic (endogenous) major depression significantly elevated the risk of developing tachyphylaxis during the subsequent maintenance treatment interval.

Despite the use of maintenance pharmacotherapy, the authors conclude, major depression recurs in a considerable number of patients. Improved prophylaxis for these patients requires treatment strategies that are based on a greater understanding of recurrence. (34 References)
CHRONIC DEPRESSION
Medication (Nefazodone) or Psychotherapy (CBASP) Is Effective When the Other Is Not

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ARCH GEN PSYCHIATRY, 62:513-20, May, 2005

A substantial proportion of patients treated for depression do not respond to the initial trial of either antidepressant medication or depression-targeted psychotherapy. Although various strategies are available to manage these nonresponders to initial treatment, no controlled trials have addressed the utility of switching from an antidepressant medication to a course of psychotherapy or vice versa. In the present controlled, rater-blinded, crossover study, the authors compared the responses of 140 chronically depressed outpatients (48 males, 92 females; mean age, 43.1 years) who were initially nonresponsive to 12 weeks of either nefazodone therapy or a cognitive behavioral analysis system of psychotherapy (CBASP) and who were then switched to the alternate treatment. In all, 61 patients were switched from nefazodone to CBASP, and 79 CBASP nonresponders were switched to nefazodone. Treatment lasted 12 weeks. The dosage of nefazodone ranged from 100 to 600 mg/day. CBASP was provided twice weekly during weeks 1 through 4 and weekly thereafter. Thirty patients dropped out of the study prematurely, 22 in the nefazodone group and eight in the CBASP group.

Analysis of the intent-to-treat sample revealed that both the switch from nefazodone to CBASP and the switch from CBASP to nefazodone resulted in clinically and statistically significant improvements in symptoms. Neither the rates of response nor the rates of remission were significantly different when the groups of completers were compared. However, the switch to CBASP from nefazodone was associated with significantly less attrition due to adverse events, a finding which could serve to explain the higher intent-to-treat response rate in those switched to CBASP (57% vs 42% in those switched to nefazodone).

For chronically depressed individuals, the current data provide a strong basis for switching to CBASP after a medication does not produce a response and, conversely, for switching to medication after patients do not respond to an adequate trial of psychotherapy. (28 References)
PAIN PREDICTS LONGER TIME TO REMISSION DURING TREATMENT OF RECURRENT DEPRESSION

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J CLIN PSYCHIATRY, 66:591-7, May, 2005

Pain and depression are mutually exacerbating. While it has been reported that each of these syndromes predicts the future occurrence of the other, it is not known whether the presence of pain slows the effect of treatment for depression. The authors of the present investigation hypothesized that in a well-characterized sample of adults with recurrent depression, higher levels of reported bodily pain at baseline would predict a delayed time to remission in response to treatment with imipramine and interpersonal psychotherapy (IPT). To test this hypothesis, they performed secondary data analyses of an archived study (Frank et al, 1990).

The subjects were 230 individuals (50 men, 180 women) who were between 21 and 65 years of age and who were enrolled in a study of maintenance treatment for recurrent unipolar depression. The patients had to meet Research Diagnostic Criteria (RDC) for a major depressive episode and historical requirements for at least three prior episodes and clear remissions (according to RDC). They were also required to have a minimum score of 15 on the Hamilton Rating Scale for Depression and a minimum score of 7 on the Raskin Severity of Depression Scale. The current report focuses on the acute treatment phase, during which all subjects received combination therapy that consisted of imipramine hydrochloride (150 to 300 mg) and IPT. Pain and somatization were assessed by means of the Hopkins Symptom Checklist. The data indicated that higher levels of both pain and somatization predicted a longer time to remission from depression. After controlling for baseline severity of depression, the researchers found that only pain continued to be significant in predicting a longer time to remission. Headache and muscle soreness were the two variables from the pain index whose presence independently predicted a slower remission. Both pain and somatization improved during the acute treatment phase. When the severity of depression was controlled, it was found that subjects with more pain and somatization also reported more suicidality. Women were more likely than men to report pain.

The authors conclude that pain may be a marker of a more difficult-to-treat depressive disorder. They recommend that adults who suffer from recurrent depression be screened for the presence of pain prior to the initiation of treatment. (62 References)
PREVALENCE AND CLINICAL CORRELATES OF IRRITABILITY IN MAJOR DEPRESSIVE DISORDER: A PRELIMINARY REPORT FROM THE SEQUENCED TREATMENT ALTERNATIVES TO RELIEVE DEPRESSION STUDY

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J CLIN PSYCHIATRY, 66:159-66, February, 2005

Although irritability appears to be a common feature of major depressive disorder (MDD), it is not included in the DSM-IV diagnostic criteria for adult MDD, and most standard rating scales of depressive symptom severity do not specifically measure irritability. Irritability, with or without depression, has been found to be associated with risk for suicide, violence, and cardiovascular disease. To better understand the prevalence and possible clinical relevance of irritability in MDD, the authors examined a simple clinical rating of irritable depression, and its sociodemographic and clinical correlates, in a large MDD cohort.

The prevalence of significant levels of irritability was assessed in the first 1,456 outpatients who entered the Sequenced Treatment Alternatives to Relieve Depression Study and who were considered to have nonpsychotic MDD. Sociodemographic and clinical features were compared in participants who did and did not report experiencing irritability at least 50% of the time during the week preceding entry into the study. Of the 1,456 evaluable subjects, 582 (40%) reported irritability more than half the time (high irritability group), and 874 either reported irritability less than half the time or denied experiencing irritability (low irritability group). Compared with subjects in the low irritability group, those in the high irritability group were more likely to be female, to be younger, to be unemployed, and to report a history of at least one suicide attempt. Functional status and quality of life were also poorer in the high irritability group. Irritability was correlated with overall severity of depression, an association that accounted for many of the clinical differences observed. An association was found between the presence of significant irritability and vascular disease, evident only after the researchers controlled for differences in sex, age, and overall severity of depression.

The results of the current study indicate that substantial levels of irritability are commonly found in adult outpatients with MDD. According to the authors, irritable depression, defined as MDD accompanied by frequent irritable mood, may not represent a distinct depressive subtype per se, but rather a variant of MDD that is associated with greater severity of depression as well as with vascular morbidity. (106 References)
SUBSTANCE USE DISORDER COMORBIDITY IN MAJOR DEPRESSIVE DISORDER: AN EXPLORATORY ANALYSIS OF THE SEQUENCED TREATMENT ALTERNATIVES TO RELIEVE DEPRESSION COHORT

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COMPR PSYCHIATRY, 46:81-9, March/April, 2005

Patients with major depressive disorder (MDD) often present for treatment with concurrent substance use disorders (SUD) involving alcohol and/or illicit drugs. The SUD may be readily apparent or may remain undiagnosed, depending on clinician inquiry and/or the readiness of the patient to admit the problem. The authors of the present investigation attempted to determine whether depressed patients with SUD differ meaningfully from depressed patients without SUD in terms of sociodemographic characteristics, medical and psychiatric comorbidities, course of depressive illness, and presenting depressive symptoms. The first 1,500 outpatients who were consecutively enrolled in the Sequenced Treatment Alternatives to Relieve Depression Study and who had a diagnosis of nonpsychotic MDD were divided into those with and without concurrent SUD symptoms as ascertained by means of a self-report instrument, the Psychiatric Diagnostic Screening Questionnaire (PDSQ).

Of the 1,484 MDD patients with a completed baseline PDSQ, 419 (28%) were identified as having symptoms consistent with a concurrent SUD. Among these individuals with concurrent SUD symptoms, 66% had symptoms indicative of an alcohol use disorder, 16% had symptoms of an illicit drug use disorder, and 18% had symptoms consistent with both an alcohol and drug use disorder. Compared with patients without SUD symptoms, those with concurrent SUD symptoms were more likely to be men, to be either divorced or never married, to have a younger age of onset of depression, and to have a higher rate of previous suicide attempts. Patients who had symptoms consistent with SUD also endorsed greater functional impairment attributable to their illness than those without concurrent SUD symptoms. The presence of SUD symptoms did not alter the overall depressive symptom pattern of presentation. However, the MDD patients with SUD symptoms reported higher levels of hypersomnia, anxious mood, and suicidal ideation than those without SUD symptoms.

The authors conclude that gender, marital status, age of onset of major depression, functional impairment, and suicide risk factors differ in depressed patients with and without SUD comorbidity. (32 References)
DEHYDROEPIANDROSTERONE MONOTHERAPY IN MIDLIFE-ONSET MAJOR AND MINOR DEPRESSION

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Midlife in both men and women is characterized by a decline in the production of the adrenal androgen and neurosteroid dehydroepiandrosterone (DHEA). DHEA is available as an over-the-counter hormonal therapy and has been reported to have antidepressant-like effects. Since alternative and over-the-counter medications have become increasingly popular choices for many patients who prefer not to take traditional antidepressants, the authors of the present study attempted to evaluate the efficacy of DHEA as a monotherapy for individuals with midlife-onset depression. They conducted a randomized, placebo-controlled, double-blind trial in which 46 outpatients (23 men, 23 women; age range, 45 to 65 years) with midlife-onset major or minor depression received six weeks of DHEA therapy (90 mg/day for three weeks and 450 mg/day for three weeks) and six weeks of placebo treatment. None of the subjects received concurrent antidepressant medications. Outcome measures included the 17-item Hamilton Depression Rating Scale (HDRS-17), the Center for Epidemiologic Studies Depression Scale, and the Derogatis Interview for Sexual Functioning. Results were analyzed by means of repeated-measures analysis of variance and post hoc Bonferroni t tests.

Compared with ratings obtained at baseline and after six weeks of placebo treatment, scores on the HDRS-17 and the Center for Epidemiologic Studies Depression Scale after six weeks of DHEA administration were indicative of significant improvement. A 50% or greater reduction in baseline HDRS-17 scores was observed in 23 subjects after DHEA therapy and in 13 subjects after placebo treatment. DHEA treatment increased plasma free T levels in both men and women. Six weeks of DHEA treatment also was associated with significant improvements in Derogatis Interview for Sexual Functioning scores relative to baseline and placebo conditions. Despite initial suggestions of a sexual dimorphism in the therapeutic actions of DHEA, the response to DHEA did not differ between men and women.

According to the authors, DHEA appears to be an effective monotherapy for the treatment of both major and minor depression of moderate severity occurring at midlife in men and women. (65 References)
COGNITIVE THERAPY VS MEDICATIONS IN THE TREATMENT OF MODERATE TO SEVERE DEPRESSION

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ARCH GEN PSYCHIATRY, 62:409-16, April, 2005

There is substantial evidence to indicate that antidepressant medications (ADMs) are effective in the treatment of individuals with moderate to severe depression. Cognitive therapy (CT) has also shown promise in the treatment of those with major depressive disorder (MDD); however, there are less data available regarding the effects of CT in this population. The authors conducted a large, two-site (University of Pennsylvania, Philadelphia and Vanderbilt University, Nashville, Tennessee), placebo-controlled, randomized trial to test the relative efficacy of ADM and CT in outpatients with moderate to severe MDD.

In all, 240 depressed outpatients (age range, 18 to 70 years) were randomly assigned to one of the following treatment conditions: 16 weeks of ADM (N=120), 16 weeks of individual CT (N=60), or eight weeks of pill placebo (N=60). Those in the ADM group received paroxetine (up to 50 mg/day), which was augmented with lithium carbonate and desipramine hydrochloride if necessary. The primary outcome measure was the modified 17-item Hamilton Depression Rating Scale, which provided continuous severity scores and allowed for designations of response and remission. At eight weeks, the response rates of the ADM group (50%) and the CT group (43%) were both superior to that of the placebo group (25%). Analyses based on continuous scores at eight weeks indicated an advantage for each of the active treatments over placebo. The advantage was significant for ADM relative to placebo, and there was a nonsignificant trend in favor of CT relative to placebo. At 16 weeks, response rates were 58% in each of the active treatment conditions; the remission rate was 46% in the ADM group and 40% in the CT group. Follow-up tests of a site by treatment interaction indicated a significant difference only at Vanderbilt University, where ADM proved to be superior to CT. Site differences in patient characteristics and in the relative experience levels of the cognitive therapists each appeared to have contributed to this interaction.

The authors conclude that cognitive therapy can be as effective as pharmacotherapy for the initial treatment of moderate to severe major depression; however, this degree of effectiveness may depend on a high level of therapist experience or expertise. (34 References)
PREVENTION OF RELAPSE FOLLOWING COGNITIVE THERAPY VS MEDICATIONS IN MODERATE TO SEVERE DEPRESSION

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ARCH GEN PSYCHIATRY, 62:417-22, April, 2005

Antidepressant medication (ADM) is effective in the treatment of moderate and severe depression, and it prevents the return of depressive symptoms, but only as long as treatment is continued. There is some evidence to indicate that cognitive therapy (CT) has an enduring effect that reduces the risk of relapse following successful treatment. The aim of the present investigation was to determine whether CT has an enduring effect and to compare this effect with that produced by continued ADM.

The subjects were recruited from outpatient psychiatric clinics at two different sites and initially were diagnosed with moderate to severe unipolar depression. Of 180 patients who had been randomly assigned to 16 weeks of CT (N=60) or ADM (N=120), 104 (57.8%) responded to treatment and were enrolled in the 12-month continuation phase of the study. CT responders (N=35) were withdrawn from treatment and compared with ADM responders who had been randomly assigned to either continuation medication (N=34) or placebo withdrawal (N=35). Patients withdrawn from CT were allowed no more than three booster sessions during the continuation phase; patients assigned to continuation medication were kept at full dosage levels. Patients who completed the continuation phase without relapse were withdrawn from all treatment and observed across a subsequent 12-month naturalistic follow-up. Relapse was defined as a return (for at least two weeks) of symptoms sufficient to meet criteria for major depression or Hamilton Depression Rating Scale scores of 14 or higher during the continuation phase. Recurrence was defined in a similar fashion during the subsequent naturalistic follow-up. The results showed that patients withdrawn from CT were significantly less likely to relapse during the continuation phase than patients withdrawn from medication (30.8% vs 76.2%, respectively). Patients withdrawn from CT were no more likely to relapse than patients who were assigned to continuation medication (30.8% vs 47.2%, respectively). There were also indications that the effect of CT extended to the prevention of recurrence.

The authors conclude that cognitive therapy has an enduring effect that extends beyond the end of treatment. Moreover, it appears to be as effective as keeping patients on medication. (24 References)
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**BOOKS RECEIVED FOR REVIEW**
Early Signs in Schizophrenia Spectrum Disorders

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J NERV MENT DIS, 193:17-23, January 2005

In schizophrenia spectrum disorders, the onset of psychotic symptoms such as hallucinations and delusions is often preceded by relatively nonspecific changes in behavior and emotional state. Recent studies have suggested that sleep disturbance, anxiety, anger/irritability, depressed mood, deterioration in functioning, social withdrawal, poor concentration, suspiciousness, loss of motivation/drive, and low energy are among the signs and symptoms most commonly seen during the prepsychotic phase of schizophrenia spectrum disorders. In the investigation presented here, the authors examined the frequency of various early signs of illness in first-episode patients suffering from a schizophrenia spectrum disorder. A factor analysis of these early signs of illness was performed, and each of the dimensions identified was evaluated in terms of its relationship to symptoms of psychosis at presentation for treatment and after one year of treatment.

The study sample (N=96) was composed of 70 males and 26 females. Seventy were given a diagnosis of schizophrenia, 23 had a schizoaffective disorder, and three were considered to have a schizophreniform disorder. Mean age at study entry was 26.2 years (range, 16.3 to 51 years), and mean age at illness onset was 24.5 years (range, 12 to 50.7 years). More than 80% of the subjects were single, over 50% had completed high school, and 33.4% had attended a college or university. Among these patients, the most common early signs in the prepsychotic period primarily reflected changes in social functioning; mood changes; psychobiological changes in appetite, sleep, energy, and restlessness; and changes reflecting odd ideas and perceptual experiences that had not reached threshold as clear psychotic symptoms. Exploratory factor analysis suggested the existence of the following five primary dimensions: emotional dysphoria and odd perceptual and cognitive content, impaired functioning, changes related to psychobiological or vegetative functioning, suspiciousness accompanied by difficulties with concentration, and irritability/aggression.

Impaired functioning in the prepsychotic period was associated with higher levels of negative symptoms at presentation for treatment. Higher levels of psychobiological changes in the early stage of illness were associated with greater improvement in positive symptoms after one year of treatment. The possible association between psychobiological changes in the prepsychotic phase and a more emotionally reactive form of schizophrenia warrants further study, the authors conclude. (34 References)
THALAMUS SIZE AND OUTCOME IN SCHIZOPHRENIA

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SCHIZOPHR RES, 71:473-84, December 1, 2004

The thalamus has extensive and reciprocal connections to the striatum and the cortex. Its association nuclei, including the medial dorsal nucleus and the pulvinar, are involved in maintaining attention and modulation of sensory input. The disturbance of these functions in schizophrenia, taken together with evidence from postmortem and neuroimaging studies of volume reduction and functional abnormalities, has implicated the thalamus as a nexus of defective circuits in schizophrenia. Schizophrenic patients with more severe symptoms and poorer social and occupational functioning (i.e., poor-outcome or “Kraepelinian” patients) seem to be especially likely to exhibit thalamic volume loss. In the investigation presented here, the authors used high-resolution magnetic resonance imaging to examine the size of the thalamus in 106 schizophrenic patients (52 good-outcome, 54 poor-outcome) and 42 normal controls. The thalamus was traced at five axial levels proportionately spaced from dorsal to ventral directions.

Compared with the normal controls, the schizophrenic patients did not exhibit overall reduced absolute or relative thalamic size. However, the schizophrenic patients did have significantly smaller thalamic areas at more ventral levels. Thalamic size was positively associated with frontal lobe and temporal lobe size. As a group, the schizophrenic patients had slightly larger thalami at more dorsal levels than the normal controls, and this effect appeared to be mostly driven by the poor-outcome patients. Poor-outcome patients had significantly smaller absolute thalami and significantly smaller absolute and relative ventral aspects of the thalamus than good-outcome patients. Among the schizophrenic patients, thalamic size was found to be positively associated with measures of positive psychopathology in dorsal and ventral areas and with general psychopathology in ventral levels.

Taken together with other recent reports, the current data provide further evidence of thalamic volumetric deficits in schizophrenia and suggest that poorer outcome may be associated with more ventral thalamic volume loss. The authors suggest that variability in reports of thalamic volume loss may be related to the volume loss that is restricted to pulvinar, medial dorsal, and ventrolateral posterior regions. (51 References)
STABILITY OF COGNITIVE PERFORMANCE IN OLDER PATIENTS WITH SCHIZOPHRENIA: AN 8-WEEK TEST-RETEST STUDY

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AM J PSYCHIATRY, 162:110-7, January 2005

Previous research has focused on cognitive enhancement in schizophrenia. One of the most salient methodological issues that must be considered in interpreting apparent improvements in cognitive test performance is whether such changes actually reflect improved cognitive ability or simply result from improved test performance without improvement in underlying cognitive ability. The purpose of the present study was threefold: (1) to examine practice effects over a test-retest interval similar to a clinical trial; (2) to develop norms for evaluating cognitive changes in middle-aged and older psychotic patients treated with conventional antipsychotic medications; and (3) to identify the width of the prediction intervals for defining “unusual” changes that would be unlikely to be the result of either measurement errors or practice effects. The authors also attempted to determine whether retest stability and prediction intervals varied as a function of baseline levels of cognitive impairment.

The study sample was composed of 45 middle-aged and older schizophrenic outpatients (36 men, nine women; age range, 45 to 77 years; mean age, 59.4 years) who were receiving clinically appropriate and stable doses of conventional antipsychotic medications. All participants completed the Aged Schizophrenia Assessment Schedule-Cognitive Battery at baseline and again at an eight-week follow-up evaluation. The results indicated that performance on all cognitive measures was stable over time, as demonstrated by significant test-retest correlations. Practice effects on most of the 22 neuropsychological test scores were absent or minimal. Tests administered with alternate forms were no more temporally stable than tests administered twice with the same form. In only a very few individual cases was there evidence of substantial variation at retest across the 22 test scores. Drawing on these data and using the reliable change index method, the authors developed “norms for evaluating change.”

The results of the current study suggest that older schizophrenic patients who are receiving conventional antipsychotic treatment manifest quite stable cognitive performances across time, showing little evidence of practice effects or wide scatter retest performance across subjects. However, the authors note, there are test-by-test variations in performance that indicate that clinically significant differences across tests may differ. Also there may be interindividual differences in retest variance in test scores. (35 References)
OSTEOPOROSIS IN PATIENTS WITH SCHIZOPHRENIA

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Despite the fact that treatment with prolactin-increasing antipsychotic medications is regularly mentioned as a risk factor for osteoporosis, little is known about the prevalence and the degree of loss of bone mineral density in patients suffering from schizophrenia. The cumulative effect of several disease- and medication-related processes renders a higher risk of osteoporosis plausible in schizophrenic patients. In the present cross-sectional study, the authors investigated the association, if any, between schizophrenia and a decrease in bone mineral density.

The study sample was composed of 75 schizophrenic patients (57 men, 18 women). All had been treated with antipsychotics for at least one year. To exclude patients with age-related idiopathic osteoporosis, only those between the ages of 19 and 50 years were evaluated. Dual x-ray absorptiometry was used to determine bone mineral density. According to World Health Organization guidelines, osteopenia was defined as bone mineral density more than one standard deviation (SD) below the young adult mean but less than 2.5 SDs below this value. Osteoporosis was defined as bone mineral density 2.5 SDs or more below the young adult mean. In all, 33.3% of the women were found to suffer from osteopenia in the lumbar region and in the right proximal femur. In the lumbar region, osteopenia was found in 45.6% of the men, and osteoporosis was seen in 10.5% of the men. In the right proximal femur, osteopenia was seen in 19.3% of the men, and osteoporosis was found in 3.5% of the men. Bone mineral density in men, but not women, was significantly lower than normal in the lumbar region. This phenomenon was not found in the femurs of either male or female patients. A comparison of loss of bone mineral density in male and female patients showed significant differences between the sexes. In male patients, bone mineral density was negatively correlated with negative symptoms and Positive and Negative Syndrome scale total scores but was positively correlated with 25-hydroxy-vitamin D3 levels and body mass index. In female patients, a positive correlation was found between bone mineral density and body mass index. Exposure to prolactin-increasing antipsychotic medications was not found to be related to bone mineral density.

The authors conclude that patients with schizophrenia may suffer from low bone density. They recommend that more attention be paid to bone metabolism in schizophrenic patients. (35 References)
EFFECTS OF BEHAVIORAL THERAPY ON WEIGHT LOSS IN OVERWEIGHT AND OBESE PATIENTS WITH SCHIZOPHRENIA OR SCHIZOAFFECTIVE DISORDER

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J CLIN PSYCHIATRY, 66:205-12, February 2005

Weight management for patients with schizophrenia is seldom emphasized and remains a poorly researched area, despite the high rates of obesity and associated medical comorbidity documented in this population. The authors conducted a 14-week, multicenter, open-label, rater-blinded, randomized study designed to evaluate the effects of a group-based behavioral treatment (BT) on weight loss in overweight and obese patients who met DSM-IV criteria for schizophrenia or schizoaffective disorder and whose medication had been switched from olanzapine to risperidone.

In all, 72 patients were randomly assigned to receive BT (N=35) or usual clinical care (UC, N=37). BT included 20 sessions during which patients were taught various techniques for reducing caloric intake. Patients in the UC group were encouraged to lose weight but received no special advice about weight reduction. The primary outcome measure was change in body weight. Weight was measured at baseline and at weeks 4, 8, and 14 of the study. One patient in the BT group withdrew consent, did not receive study medication, and was removed from all analyses. An attendee analysis included all patients who received at least one dose of study medication and attended at least one BT session. Post hoc analysis also assessed a completer population, which included attendee patients for whom week 14 weight data were available. Statistically significant weight loss was reported at endpoint in both treatment groups. At endpoint, nine patients (26.5%) in the BT group and four (10.8%) in the UC group had lost 5% or more of their baseline body weight. Post hoc analysis of the attendee population showed that significantly more patients in the BT group than in the UC group had lost 5% or more of their body weight at endpoint (32.1% [9/28] and 10.8% [4/37], respectively) and at week 14 (completer population; 40.9% [9/22] and 14.3% [4/28], respectively).

The current data indicate that BT can reduce weight gain in obese schizophrenic patients who are receiving atypical antipsychotic medications. However, the weight reduction seen in the present study was modest; thus, the importance of choosing an antipsychotic agent with a low propensity for inducing weight gain remains undiminished. (50 References)
CLOzapine: Its Impact on Aggressive Behavior Among Children and Adolescents with Schizophrenia

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 44:55-63, January 2005

Early-onset schizophrenia (onset of psychotic symptoms by age 18) is a severe form of the disorder that is associated with long-term disability and poor outcome. Aggression is a frequent precipitant of hospitalization among young people with schizophrenia. While previous reports have suggested that clozapine has anti-aggressive effects in schizophrenic adults, there is little evidence regarding the effects of clozapine on aggression in youths with serious mental disorders. The authors of the present study evaluated the impact of clozapine on aggressive behaviors in a sample of 20 children and adolescents (14 males, six females; age range, 8.5 to 18 years) who were considered to have treatment-refractory schizophrenia and who were started on clozapine therapy between November 1997 and August 2001 at Bronx Children’s Psychiatric Center.

Clozapine was administered in an open-label fashion through use of a flexible titration schedule. Using a mirror-image study design, the researchers compared the frequency of aggressive behaviors during clozapine treatment with the frequency of aggressive behaviors during an equivalent period of previous antipsychotic treatment. The primary outcome measures were administration of emergency oral medications, administration of emergency injectable medications, and episodes of seclusion. Incident data were collected for the three-month period immediately prior to clozapine treatment (to establish a baseline) and for the period ranging from 12 to 24 weeks after the initiation of clozapine therapy (to allow sufficient time for patients to respond to clozapine given its slower titration schedule in children). A statistically significant decrease in the frequency of the administration of emergency oral medications, the administration of emergency injectable medications, and seclusion events was found in these patients during weeks 12 to 24 of clozapine treatment as compared with their baseline condition before clozapine initiation.

According to the authors, the current preliminary data suggest that in children and adolescents with schizophrenic disorders, treatment with clozapine may diminish violence and aggression and may hasten discharge to a less restrictive setting. (21 References)
REDUCING VIOLENCE RISK IN PERSONS WITH SCHIZOPHRENIA: 
OLANZAPINE VERSUS RISPERIDONE

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J CLIN PSYCHIATRY, 65:1666-73, December 2004

Although violent behavior in the community is generally uncommon among 
schizophrenics, an increased risk for violence has been found in some patients 
who have comorbid substance abuse problems and are not treatment-compliant 
as well as in those with a history of frequent relapses that result in 
hospitalization or arrest. Although atypical antipsychotics (including clozapine, 
risperidone, olanzapine, quetiapine, and ziprasidone) in general appear to reduce 
violece in schizophrenic individuals, little is known about whether this effect is 
equivalent across these medications. For example, while olanzapine and 
risperidone have been shown to ameliorate hostility in schizophrenia, these two 
medications have distinct psychopharmacological profiles, have different 
influences on cognitive functioning, and are characterized by dissimilar levels of 
patient compliance. The authors conducted a longitudinal, observational study 
of violent behavior among schizophrenic individuals under “usual care” 
conditions in the community. They compared olanzapine with risperidone in 
terms of their effectiveness in reducing violence risk over time.

The participants were 124 adults (69 men, 55 women; mean age, 46.1 years; 
age range, 20 to 77) who met DSM-IV criteria for schizophrenia spectrum 
disorders and who were receiving treatment in a public mental health services 
system. After enrollment (1997-1999), subjects were followed for three years, 
with assessments being conducted every six months. The incidence of violence 
over six six-month periods was modeled through the use of general linear 
regression analysis for repeated measures, with the probability of violence 
estimated prospectively as a function of medication type in the previous periods 
(controlling for salient clinical and demographic variables). The authors found 
that remaining on olanzapine for one year or longer resulted in a significantly 
lower violence risk when compared with the probability of violent behavior 
occurring during the first switch period (first six months of follow-up after initial 
switch to olanzapine). No significant change in violence risk was found for 
subjects who remained on risperidone for one year or longer. Adherence with 
prescribed medication was found to mediate the association between olanzapine 
treatment and reduced violent behavior.

In the complex “real world” settings where persons with schizophrenia reside, 
long-term treatment with olanzapine appears to confer some advantage over 
risperidone in reducing violence risk. (66 References)
OLANZAPINE TREATMENT OF RESIDUAL
POSITIVE AND NEGATIVE SYMPTOMS

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PhD; and William T. Carpenter, Jr., MD
AM J PSYCHIATRY, 162:124-9, January 2005

Olanzapine is a new-generation antipsychotic that has been hypothesized to exhibit superior efficacy in patients with treatment-resistant schizophrenia. In the present study, the authors examined the comparative efficacy and safety of olanzapine and haloperidol in 63 schizophrenic outpatients (46 men, 17 women) who were required to meet retrospective and prospective criteria for partial response to conventional antipsychotics. Retrospective criteria were: (1) a history of residual positive and/or negative symptoms after at least two six-week trials of therapeutic doses of conventional antipsychotics from at least two different classes; and (2) a minimum level of positive and/or negative symptoms at the time of evaluation for participation in the study.

Of the 63 patients who entered the 16-week, double-blind, parallel-groups comparison of olanzapine and haloperidol, 29 (22 men, seven women) were randomly assigned to receive olanzapine and 34 (24 men, 10 women), to receive haloperidol. There were three noncompleters in each treatment group. In the olanzapine group, two patients met criteria for a clinically significant worsening of symptoms, and one was withdrawn because of alcohol abuse. In the haloperidol group, the three noncompleters all met criteria for a clinically significant worsening of symptoms. The results showed that there were no significant differences between olanzapine and haloperidol with regard to their effect on positive or negative symptoms. There were no significant differences between the two treatment groups on measures of social and functional outcome. Patients treated with olanzapine experienced a significantly greater reduction in extrapyramidal symptoms than patients treated with haloperidol. On the Side Effect Checklist, olanzapine-treated patients reported significantly greater reductions in stiffness and dry mouth than haloperidol-treated patients. Patients in the olanzapine group exhibited significantly greater increases in systolic blood pressure and weight than patients in the haloperidol group.

The authors conclude that olanzapine has limited differential benefit for either positive or negative symptoms in patients with treatment-resistant schizophrenia. Although olanzapine is associated with fewer extrapyramidal symptoms, other side effects may offset this benefit. (27 References) EAF
CLOZAPINE AUGMENTED WITH RISPERIDONE IN THE TREATMENT OF SCHIZOPHRENIA: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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AM J PSYCHIATRY, 162:130-6, January 2005

Clozapine has been established as the treatment of choice for severely ill schizophrenic patients whose psychotic symptoms are refractory to conventional antipsychotic therapy. However, there are still a considerable number of patients who are only partially responsive to clozapine or who are totally nonresponsive to the drug. A limited number of case reports and small studies have described the effects of clozapine when augmented with other antipsychotic medications. To date, risperidone has been the most extensively documented clozapine augmentation agent. The authors of the present investigation evaluated the efficacy and safety of augmenting clozapine with risperidone in a group of patients with treatment-refractory schizophrenia.

In a randomized, double-blind, placebo-controlled, 12-week trial, 40 schizophrenic patients who were unresponsive or partially responsive to clozapine monotherapy received a steady dose of clozapine in combination either with placebo (N= 20) or with risperidone (N=20). Patient psychopathology was assessed at two-week intervals with the Brief Psychiatric Rating Scale (BPRS), the Scale for the Assessment of Negative Symptoms (SANS), and other measures. Movement disorders were assessed with the Simpson-Angus Rating Scale. From baseline to week 6 and week 12, mean BPRS total and positive symptom subscale scores were significantly reduced in both treatment groups, but the reductions were significantly greater in the clozapine/risperidone group. Reductions in SANS scores also were significantly greater with clozapine/risperidone treatment than with clozapine/placebo therapy. The adverse event profile of the clozapine/risperidone group was similar to that of the clozapine/placebo group. Simpson-Angus Rating Scale scores were lower in the clozapine/risperidone group throughout the trial, although they increased to approach those in the clozapine/placebo group by week 12. Compared with clozapine/placebo therapy, clozapine/risperidone treatment did not induce additional weight gain, agranulocytosis, or seizures.

Augmentation with risperidone may benefit patients who are partially responsive or nonresponsive to clozapine monotherapy. (36 References)
EFFICACY AND TOLERABILITY OF ZIPRASIDONE VERSUS RISPERIDONE IN PATIENTS WITH ACUTE EXACERBATION OF SCHIZOPHRENIA OR SCHIZOAFFECTIVE DISORDER: AN 8-WEEK, DOUBLE-BLIND, MULTICENTER TRIAL

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J CLIN PSYCHIATRY, 65:1624-33, December 2004

Atypical antipsychotics are now considered first-line agents in the treatment of schizophrenia. More head-to-head comparisons of these drugs are needed not only to examine their relative efficacy but also to evaluate their safety and tolerability profiles. The primary aim of the present eight-week, multicenter, double-blind, randomized, parallel-group study was to demonstrate the equivalence of efficacy of flexible-dose ziprasidone and risperidone in the treatment of patients who were experiencing an acute exacerbation of schizophrenia or schizoaffective disorder.

In all, 296 patients (215 men, 81 women) were randomly assigned to an eight-week regimen of ziprasidone 40 to 80 mg twice daily (N=149) or risperidone 3 to 5 mg twice daily (N=147). Primary efficacy measures included the Positive and Negative Syndrome Scale (PANSS) total score and the Clinical Global Impressions-Severity of Illness scale (CGI-S) score; secondary measures included scores on the PANSS negative subscale, the CGI Improvement scale (CGI-I), and the PANSS-derived Brief Psychiatric Rating Scale (BPRSd) total and core item scores. Safety assessments included movement disorder evaluations, laboratory tests, electrocardiography, vital signs, and body weight. Efficacy analyses employed a prospectively defined Evaluable Patients cohort. Treatment equivalence was conferred if the lower limit of the 95% confidence interval of the ziprasidone/risperidone ratio of least-squares mean change from baseline was greater than 0.60. Data were gathered from August 1995 to January 1997. Equivalence was demonstrated in PANSS total scores, CGI-S scores, PANSS negative subscale scores, BPRSd total and core item scores, and PANSS total and CGI-I responder rates. Both agents were well tolerated. Risperidone yielded a significantly higher Movement Disorder Burden score and higher incidences of prolactin elevation and clinically relevant weight gain. However, the authors note, compared with current recommendations, study dosing may have been high for some risperidone-treated patients (mean dose, 7.4 mg/day) and low for some ziprasidone-treated patients (mean dose, 114.2 mg/day).

The authors conclude that ziprasidone and risperidone were equally effective in reducing psychotic symptoms. (40 References)
BOOKS RECEIVED FOR REVIEW


Abstracts and Reviews of Selected Literature in Psychiatry, Neurology, and their Allied Fields

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PERINATAL FACTORS AND THE DEVELOPMENT OF AUTISM
A Population Study

Emma J. Glasson, BPsysch, BSchons, PhD (School of Population Health, Univ. of Western Australia, 35 Stirling Hwy., Crawley WA 6009, Australia; e-mail: emma.glasson@health.wa.gov.au); Carol Bower, MBBS, MSc, PhD, FAFPHM, DLSHTM; Beverly Petterson, MSc, PhD; Nick de Klerk, BSc, MSc, PhD; Gervase Chaney, MBBS, FRACP; and Joachim F. Hallmayer, MD
ARCH GEN PSYCHIATRY, 61:618-27, June 2004

Autism is a developmental disorder characterized by severe impairment in social interaction and communication and by the presence of stereotypical behavior. Autism is part of a spectrum of disorders that includes Asperger syndrome and pervasive developmental disorder not otherwise specified (PDD-NOS). Autism is considered to have a genetic basis; however, some studies have reported an association between obstetric complications and the development of autism, although findings have been inconclusive. To examine the association between obstetric factors and the development of autism spectrum disorders in a large population-based sample drawn from a single geographical area, the authors of the present investigation used obstetric data contained in a statutory database and collected at the time of birth.

In all, 465 subjects born in Western Australia between 1980 and 1995 and diagnosed with an autism spectrum disorder by 1999 were included in the study; 314 were diagnosed with autism, 67 with Asperger syndrome, and 84 with PDD-NOS. Siblings of the autistic subjects (N=481) and a random population-based group of control subjects (N=1,313) were compared with the autistic subjects with regard to obstetric information obtained from the Maternal and Child Health Research Database of Western Australia. The data revealed that the parents of the autistic subjects were significantly older than the parents of the control subjects. Compared with the controls, the autistic subjects were more likely to be firstborn. The mothers of the autistic subjects were characterized by higher frequencies of threatened abortion, epidural caudal anesthesia use, labor induction, and a labor duration of less than one hour. The autistic subjects were more likely to have experienced fetal distress, to have been delivered by means of elective or emergency cesarean section, and to have had an Apgar score of less than 6 at one minute. Among the autistic subjects, those with a diagnosis of autism had more complications than those with PDD-NOS or those with Asperger syndrome. Nonaffected siblings were more similar to their autistic siblings than to the control subjects in terms of their profile of complications.

According to the authors, autism is unlikely to be caused by a single obstetric factor. The increased prevalence of obstetric complications in autistic individuals is most likely due to underlying genetic factors or to the interaction between these factors and the environment. (90 References)
HIPPOCAMPUS AND AMYGDALA VOLUMES IN PARENTS OF CHILDREN WITH AUTISTIC DISORDER

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AM J PSYCHIATRY, 161:2038-44, November 2004

The neuroanatomical pathology of autism is still poorly understood. Several reports have described changes in the cerebellum, hippocampus, amygdala, basal ganglia, cerebral ventricles, and planum temporale, although some of these changes have not been replicated in follow-up studies. Medial temporal lobe structures such as the hippocampus and the amygdala have been of particular interest, because these limbic structures have been proposed to underlie key behavioral dysfunctions in autism. The authors of the present investigation examined hippocampus and amygdala volumes in clinically unaffected parents of children with autistic disorder, in adults with autistic disorder, and in adults with no personal or familial history of autism. The researchers hypothesized that a volumetric difference in autism would be most pronounced in the affected adults and somewhat less pronounced in the unaffected parents of the autistic children, relative to those with no personal or familial history of autism.

Magnetic resonance imaging (MRI) scans were obtained from 17 biological parents of children with a DSM-IV diagnosis of autistic disorder. These MRI scans were compared with scans obtained from 15 adults with autistic disorder and 17 age-matched healthy comparison subjects with no personal or familial history of autism. Volumes of hippocampus, amygdala, and total brain were measured in all the participants. The results showed that the volume of the left hippocampus was larger both in the parents of autistic children and in the autistic adults, relative to that of the comparison subjects. The hippocampus was found to be significantly larger in the adults with autistic disorder than in the parents of children with autistic disorder. The left amygdala was smaller in the adults with autistic disorder than in either of the other two groups. No differences in total brain volume were found among the three groups.

According to the authors, their finding of a larger hippocampal volume in autistic individuals could be indicative of abnormal early neurodevelopmental processes; however, this finding is partly consistent with data from only one previous study and contradicts the results of several other investigations. The finding of a larger hippocampal volume in the parental group is suggestive of a potential genetic basis for the hippocampal abnormalities seen in individuals with autistic disorder. (44 References)
LINKAGE AND ASSOCIATION OF THE MITOCHONDRIAL ASPARTATE/GLUTAMATE CARRIER SLC25A12 GENE WITH AUTISM

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AM J PSYCHIATRY, 161:662-9, April 2004

Autism or autistic disorder (MIM number 209850) is a neurodevelopmental disorder characterized by deficits in verbal and nonverbal communication, impairments in reciprocal social interactions, and patterns of repetitive or stereotyped behaviors and interests. Autism appears to be the most highly genetic of the psychiatric disorders; however, it does not follow a simple Mendelian mode of transmission (i.e., dominant or recessive transmission), but is rather a polygenic disease. The authors recently mapped a susceptibility locus for autism to chromosome region 2q24-q33 (MIM number 606053). In the present investigation, genes across the 2q24-q33 interval were analyzed to identify an autism susceptibility gene in this region.

Mutation screening of positional candidate genes was performed in two stages. The first stage involved identifying (in unrelated subjects showing linkage to 2q24-q33) genetic variants in exons and flanking sequences within candidate genes and comparing the frequency of the variants in autistic subjects with the frequency in unrelated nonautistic subjects. Two single nucleotide polymorphisms (SNPs) that showed evidence of divergent distribution between autistic and nonautistic subjects were identified, both within SLC25A12, a gene encoding the mitochondrial aspartate/glutamate carrier. In the second stage, the two SNPs in SLC25A12 were further genotyped in 411 autistic families, and linkage and association tests were carried out in the 197 informative families. Linkage and association were observed between autistic disorder and the two SNPs (rs2056202 and rs2292813) found in SLC25A12. Whether the authors used a single affected subject per family or all affected subjects, evidence for excess transmission was found by the Transmission Disequilibrium Test for rs2056202, rs2292813, and a two-locus G*G haplotype. Similar results were seen when TRANSMIT was used for the analyses. Evidence for linkage was supported by linkage analysis with the two SNPs, with a maximal multipoint nonparametric linkage score of 1.57 and a maximal multipoint heterogeneity lod score of 2.11. Genotype relative risk was estimated to be between 2.4 and 4.8 for persons homozygous at these loci.

The current study demonstrated a strong association between autism and SNPs within the SLC25A12 gene. Further studies are needed to confirm this association, the authors conclude. (38 References)
NEUROANATOMIC VARIATION IN MONOZYGOTIC TWIN PAIRS DISCORDANT FOR THE NARROW PHENOTYPE FOR AUTISM

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AM J PSYCHIATRY, 161:539-46, March 2004

Autism is a behaviorally defined neurodevelopmental disorder that includes persistent deficits in communication, social interaction, and play. Over the past two decades, family and twin studies have found evidence to indicate that there is a significant genetic component in autism. For example, the risk for autism in siblings of autistic probands is approximately 45 times greater than the risk in the general population. The broader phenotype for autism includes relatives of autistic individuals who display social and language deficits that are qualitatively similar to those of autistic probands but that are milder in severity. In previous studies of monozygotic twins discordant for autism, more than 75% of the twins without autism displayed the broader phenotype. Differences in neuroanatomy between discordant monozygotic twins could be associated with the narrow and broader behavioral phenotypes. The authors of the present investigation attempted to determine the extent to which twin pair differences in clinical phenotype were associated with differences in neuroanatomic phenotype.

The study sample was composed of 48 children, including 16 pairs of monozygotic twins (N=32) and 16 age- and gender-matched unaffected peers. Fourteen of the twin pairs and their matched comparison subjects were boys. The mean age of the twin pairs was 8.4 years (range, 5.3 to 13.8); that of the comparison group was 8.3 years (range, 5.4 to 13.9). After magnetic resonance imaging was performed, a semiautomated procedure was applied to images in which the brain tissue was subdivided into neurofunctional regions and segmented into gray, white, and ventricular compartments. Seven of the twin pairs were found to be clinically concordant for the narrow phenotype for autism, while the remaining nine twin pairs were clinically discordant for strictly defined autism. Both the concordant and discordant twin pairs exhibited concordance in cerebral gray and white matter volumes. However, only the clinically concordant pairs exhibited concordance in cerebellar gray and white matter volumes. Within the discordant twin pairs, both the twins with autism and their co-twins exhibited frontal, temporal, and occipital white matter volumes that were lower than those found in the comparison subjects.

According to the authors, the current findings support the role and the limits of genetic liability in autism. (51 References)
INVESTIGATION OF NEUROANATOMICAL DIFFERENCES BETWEEN AUTISM AND ASPERGER SYNDROME

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ARCH GEN PSYCHIATRY, 61:291-8, March 2004

Autism and Asperger syndrome (ASP) are neurobiological conditions with overlapping behavioral symptoms and unknown etiologies. Results from previous autism neuroimaging studies have been difficult to replicate, possibly because of site differences in subject samples, scanning procedures, and image-processing methods. The authors attempted to determine whether low-functioning autism (LFA; IQ<70), high-functioning autism (HFA; IQ≥70), and ASP constitute distinct biological entities as evidenced by neuroanatomical measures. They also sought to examine similarities and differences in subject populations and neuroimaging data between two sites that used the same subject recruitment strategies, scanning protocols, and data measurement procedures.

The study sample consisted of four age-matched groups of volunteer boys who were between the ages of 7.8 and 17.9 years (13 boys with LFA, 18 patients with HFA, 21 boys with ASP, and 21 controls). Participants were recruited from two different academic medicine departments. All underwent brain scanning by means of magnetic resonance imaging (MRI). Coronally oriented 124-section spoiled gradient echo images were acquired on three MRI systems and processed by BrainImage 5.X. For purposes of neuroimaging reliability, the researchers used images from three volunteer adults who underwent scanning with the three MRI systems over a 10-month period. Main outcome measures included volumetric measures of total, white, and gray matter for cerebral and cerebellar tissues. Intersite differences were seen for subject age, IQ, and cerebellum measures. Cerebral gray matter volume was enlarged in both the HFA and LFA groups, as compared with that in the control group. Cerebral gray matter volume in the ASP group was intermediate between that of the HFA and control groups, but was nonsignificant. Exploratory analysis revealed a negative correlation between cerebral gray matter volume and performance IQ within the HFA but not the ASP group. A positive correlation between cerebral white matter volume and performance IQ was observed within the ASP but not the HFA group.

The authors conclude that lack of replication between earlier MRI studies could be due to intersite differences in MRI systems and subjects’ ages and IQs. Cerebral gray tissue findings suggest that ASP is on the mild end of the autism spectrum. (71 References)
OUTCOME CLASSIFICATION OF PRESCHOOL CHILDREN WITH AUTISM SPECTRUM DISORDERS USING MRI BRAIN MEASURES

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Autism is a neurodevelopmental disorder in which behavioral impairments and anomalies form the sole foundation for clinical diagnosis. While a number of brain abnormalities have been identified in postmortem and magnetic resonance imaging (MRI) studies of individuals with autism, commonalities across the clinical population have been difficult to identify. Although a clinical diagnosis of autism is often sensitive and stable over time in children younger than three years of age, stability increases when an autism spectrum approach is used; i.e., a proportion of children identified as having possible autism before age three do not meet criteria for autism at a later follow-up but are highly likely to meet criteria for pervasive developmental disorder-not otherwise specified (PDD-NOS). In the present investigation, the authors attempted to determine whether a combination of MRI measures obtained during early childhood would distinguish children with autism spectrum disorders (ASD) from typically developing children and whether these neuroanatomical characteristics would be associated with diagnostic and functional outcome ascertained after age five.

Quantitative MRI technology was used to measure gray and white matter volumes (cerebrum and cerebellum), total brain volume, and the area of the cerebellar vermis in 52 boys with a provisional diagnosis of autism (ASD group; age range, 1.9 to 5.2 years) and 15 typically developing boys (control group; age range, 1.7 to 5.2 years). Diagnostic confirmation and cognitive outcome data were obtained after the children reached five years of age. At the completion of the final diagnostic procedure, 42 (81%) of the ASD group were diagnosed with autism and 10 (19%) were diagnosed with PDD-NOS. On the basis of intellectual ability, the 42 autistic children were further designated as lower functioning (N=30) or higher functioning (N=12). A discriminant function analysis of the MRI brain measures (cerebellar white and gray matter volumes, area of the anterior and posterior cerebellar vermis, and cerebral white and gray matter volumes) correctly classified 95.8% of the ASD cases and 92.3% of the control cases. This set of variables also correctly classified 85% of the ASD cases as lower functioning and 68% of the ASD cases as higher functioning.

According to the authors, the current results indicate that variability in cerebellar and cerebral size is correlated with diagnostic and functional outcome in very young children with ASD. (42 References) EAF
SPEECH-IN-NOISE PERCEPTION IN HIGH-FUNCTIONING INDIVIDUALS WITH AUTISM OR ASPERGER’S SYNDROME

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The process of detecting speech in competing speech or everyday background sounds may be viewed as an example of “auditory scene analysis,” whereby information arising from several simultaneous sources is perceptually grouped into separate “auditory objects” or perceptual streams (Bregman, 1990). High-functioning individuals with autism (HFA) or Asperger’s syndrome (AS) commonly report difficulties understanding speech in situations in which background noise or speech is present. The objectives of the present study were as follows: (1) to verify the validity of these reported speech-in-noise problems; (2) to quantify the difficulties experienced; and (3) to propose possible mechanisms to explain the perceptual deficits described.

The study sample was composed of 11 high-functioning, normal-hearing adults and adolescents with confirmed diagnoses of autism or Asperger’s syndrome (HFA/AS) and nine normal-hearing, age/IQ-matched adult and adolescent control subjects. Speech-in-noise perception abilities were measured through the use of speech reception thresholds (SRTs), defined as the speech-to-noise ratio (SNR) at which approximately 50% of the speech is correctly identified. Using an adaptive procedure, the researchers measured SRTs in a non-reverberant, sound-attenuating chamber. The speech materials were standardized lists of everyday sentences spoken by a British male speaker. The background sounds were: (1) a single female talker; (2) a steady speech-shaped noise; (3) a speech-shaped noise with temporal dips; (4) a steady speech-shaped noise with regularly spaced spectral dips; and (5) a speech-shaped noise with temporal and spectral dips. Across the five background sounds, the SRTs of the HFA/AS group were generally higher (poorer) than those of the control group. However, statistically significant between-group differences in SRTs were found only for those background sounds that contained temporal or spectro-temporal dips. Whenever there were temporal dips in the background sound, HFA/AS individuals required a higher SNR to perform at the same level as controls.

According to the authors, the current results indicate that the speech-in-noise perception difficulties reported by autistic individuals are real and quantifiable. These difficulties may be due (at least, in part) to abnormal peripheral processing, specifically, to a reduced ability to exploit information about the target speech present during the spectral and temporal dips in the background. (42 References)
IMPAIRED DISENGAGEMENT OF ATTENTION IN YOUNG CHILDREN WITH AUTISM

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J CHILD PSYCHOL PSYCHIATRY, 45:1115-22, September 2004

Disengagement or distraction is thought to be a basic mechanism by which individuals regulate emotional upset. By implication, deficits in early-developing, general processes of visual attention may well underlie the restricted temperamental styles and contribute to the atypical social-communicative development characteristic of autism. In the present study, the authors examined the disengage and shift operations of visual attention in young children with autism. They hypothesized that young autistic children would have difficulty disengaging their attention when it was engaged on a particular stimulus/location in space.

The study sample consisted of 15 children with autism/pervasive developmental disorder, 13 children with Down syndrome, and 13 typically developing children. Each child was assessed individually in a quiet room, either at one of two local hospitals (the clinical groups) or at a day care facility (the typically developing group). The researchers used a simple visual orienting task that is thought to engage attention automatically. Once attention was first engaged on a central fixation stimulus, a second stimulus was presented on either side, either simultaneously or successively. Latency to begin an eye movement to the peripheral stimulus served as the main dependent measure. The two stimulus conditions (simultaneous and successive) provided independent measures of disengaging and shifting attention, respectively. The performance of the autistic children was compared with that of the children with Down syndrome and that of the normal children. Analyses of the mean eye movement latencies yielded group differences for the disengage but not the shift trials. Relative to both comparison groups, the autistic children were impaired in disengaging visual attention. There was essentially no overlap between groups; with two exceptions (both of whom pointed during the task), the individual mean disengage latencies for the autistic children all exceeded those of the typically developing children and the children with Down syndrome. On 20% of the trials, the children with autism remained fixated on the first of two competing stimuli for the entire eight-second duration of the trial.

According to the authors, the current findings on disengagement in children with autism parallel those reported in normal two-month old infants, in whom attention has been described as “obligatory.” (31 References)
Risperidone Treatment of Children with Autistic Disorder: Effectiveness, Tolerability, and Pharmacokinetic Implications

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J CHILD ADOLESC PSYCHOPHARMACOL, 14:39-47, Spring 2004

Recent evidence has indicated that atypical antipsychotics may represent a promising option for the treatment of autistic disorder. Risperidone in particular appears to be effective in treating aggressiveness, hyperactivity, irritability, stereotypies, social withdrawal, and lack of interests. The authors evaluated the effectiveness and tolerability of risperidone in children with autism and examined the correlation between plasma levels of risperidone, its active metabolite 9-hydroxyrisperidone (9-OH-risperidone), and clinical response.

Twenty children (14 boys, six girls; age range, three to 10 years; mean age, six years) who met DSM-IV criteria for autistic disorder were enrolled in the 24-week study. All were given risperidone at a starting dose of 0.25 mg/day, with the dose gradually being increased on the basis of individual response (final mean dose, 1.3 mg/day; range, 0.75 to 2.0 mg/day). Fourteen items selected from the Children’s Psychiatric Rating Scale (CPRS-14) and the Clinical Global Impression (CGI) scale were used for behavioral evaluation. Patients were classified as responders if they showed a 25% or greater decrease in CPRS-14 total score between baseline and final evaluation and if they had a final CGI rating of 1 (very much improved) or 2 (much improved). Blood samples for determination of risperidone and its active metabolite (9-OH-risperidone) were obtained after 12 weeks, and serum prolactin levels were measured on admission and at weeks 12 and 24. The mean CPRS-14 total score decreased significantly from 63.7 at baseline to 52.9 at week 12. At the end of 12 weeks of treatment, eight patients were considered to be responders, 10 were rated as slightly improved (CGI score of 3), and two showed no clinical improvement and did not participate in the next 12 weeks of treatment. Among the 18 patients who continued to receive risperidone for another 12 weeks, no further improvement was noted. There was no significant correlation between percent improvement in total CPRS-14 score and plasma levels of risperidone’s active fraction (sum of risperidone and 9-OH-risperidone concentrations). Weight gain and increased appetite were the most common adverse effects. In all children, serum prolactin levels increased significantly from baseline (166 UI/mL) to week 12 of treatment (504 UI/mL).

According to the authors, the current study provides further evidence of the beneficial effects of risperidone in autistic children. (47 References) EAF
Information on the long-term prognosis of autism is limited. Although the long-term outcome is known to be poor for autistic individuals with an IQ below 50, there have been few systematic studies of those with an IQ above this level. The authors of the present investigation addressed three questions. First, what is the long-term outcome, in terms of social, cognitive, linguistic, and behavioral functioning, for autistic individuals who, as children, had a performance IQ of at least 50? Second, how stable are childhood measures of IQ? Finally, how does early cognitive ability relate to prognosis in adulthood and what other factors, if any, are predictive of outcome?

Sixty-eight individuals (61 males, seven females) who met criteria for autism and who had a performance IQ of 50 or above in childhood were followed up in adulthood. When the subjects were first seen, their mean age was seven years (range, three to 15 years); at follow-up, their mean age was 29 years (range, 21 to 48 years). Outcome measures included standardized cognitive, language, and attainment tests. Information on social, communication, and behavioral problems was obtained by means of the Autism Diagnostic Interview. The results indicated that although a minority of the adults had achieved relatively high levels of independent functioning, most remained very dependent on their families or other support services. Few lived alone, had close friends, or were permanently employed. Communication generally was impaired, and reading and spelling abilities were poor. Stereotyped behaviors or interests frequently persisted into adulthood. Most of the adults were considered to have a “poor” (46%) or “very poor” (12%) outcome. Only 12% were rated as having a “very good” outcome, with 10% considered to have a “good” outcome, and 19%, a “fair” outcome. Correlations between childhood and adult IQs were highly significant; in many cases, actual IQ scores showed little change, and there were few significant differences in overall measures of either performance or verbal IQ over time. Individuals with a childhood performance IQ score of at least 70 had a significantly better outcome than those with an IQ below this level. However, within the normal IQ range, outcome varied greatly, and, on an individual level, neither verbal nor performance IQs were consistent prognostic indicators.

The authors conclude that the outcome for adults with autism has improved in recent years, with some being able to find work, live independently, and develop meaningful social relationships. Nevertheless, many remain highly dependent on others for support. (51 References)
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IMPACT OF CHILD SEXUAL ABUSE ON MENTAL HEALTH
Prospective Study in Males and Females

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BR J PSYCHIATRY, 184:416-21, May 2004

Methodologically, the most compelling evidence to date for an association between a history of childhood sexual abuse and adverse psychological and social outcomes is found in random community samples, birth cohorts, and twin samples. However, studies of these populations almost exclusively rely on the retrospective ascertainment of child sexual abuse and focus on female subjects. The authors of the present study used a prospective cohort design to examine the association between child sexual abuse in both boys and girls and subsequent treatment for mental illness.

The child sexual abuse cohort was composed of 1,612 subjects (285 males, 1,327 females) who were born prior to 1991 and after 1950 and who were determined to have been sexually abused after examination by forensic physicians. Their histories of mental health treatment were established by means of data linkage and compared with those of a general population control group of similar age (N=3,139,745; 1,566,972 males and 1,572,773 females). In both groups, the same specified period of time (July 1, 1991 to June 30, 2000) was examined for records of contact with mental health services. The results indicated that both male and female victims of sexual abuse had significantly higher rates of psychiatric treatment during the study period than general population controls (12.4% versus 3.6%). Male victims were significantly more likely to have had treatment than female victims (22.8% versus 10.2%). Compared with general population controls, sexual abuse victims had significantly higher rates of childhood mental disorders, personality disorders, anxiety disorders, and major affective disorders. For example, individuals in the child sexual abuse cohort were almost five times as likely to have a primary diagnosis of personality disorder, were more than three times as likely to be diagnosed with an anxiety disorder or an acute stress reaction, and were twice as likely to be diagnosed with a major affective disorder.

According to the authors of the current prospective study, their findings clearly demonstrate an association between child sexual abuse and a subsequent increase in rates of childhood and adult mental disorders. Male victims of child sexual abuse appear to be at least as likely as female abuse victims to show subsequent pathology. (22 References)
RETROSPECTIVE MEASURES OF CHILDHOOD ABUSE: CONCURRENT
VALIDITY AND RELIABILITY IN A NONCLINICAL SAMPLE
WITH BORDERLINE FEATURES

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J PERSONAL DISORD, 18:178-92, April 2004

Accurate assessment of childhood abuse is challenging yet essential for both clinical and research objectives. Current research suggests that both childhood physical abuse and childhood sexual abuse are linked to later adult psychopathology, including borderline personality disorder (BPD). Awareness of the potential impact of child abuse underscores the necessity of developing and identifying reliable, valid, and comprehensive measures of child abuse histories. In the study presented here, the authors evaluated the psychometric properties of retrospective reports of childhood sexual and physical abuse by comparing two assessment formats (interview and questionnaire) and by examining validity and test-retest reliability over a period of two years.

The nonclinical sample (composed of college students) was drawn from a study of the development of BPD features in young adults. Participants were asked to complete the Familial Experiences Interview (FEI; Ogata, 1988) and the Familial Experiences Questionnaire (FEQ; Wheelock et al., 1997) at age 18 (Time 1) and the FEQ again at age 20 (Time 2). Both the FEI and the FEQ are designed to assess childhood experiences that occurred before the age of 18, including physical and sexual abuse. The two instruments have similar formats and wording. At Time 1, 421 participants completed the FEI, with approximately half of them (N=206) also completing the FEQ. At Time 2, approximately two years later, 356 of the participants completed the FEQ. Cross-sectional analyses suggested that the questionnaire measure of childhood sexual abuse (FEQ) provided essentially the same information as did the interview-based measure of childhood sexual abuse (FEI). Although there was less agreement about the presence of childhood sexual abuse between the two assessment times (at age 18 and at age 20), individuals who did report childhood sexual abuse at both Time 1 and Time 2 were fairly consistent in characterizing the severity of the abuse. The consistency of the reports of childhood physical abuse was only fair cross-sectionally, across time (FEQ), and across time and assessment instrument.

According to the authors of the present study, their results suggest that reports of childhood abuse obtained through interviews are roughly equivalent to those obtained by means of questionnaires. (35 References)
**CHILDHOOD MALTREATMENT ASSOCIATED WITH ADULT PERSONALITY DISORDERS: FINDINGS FROM THE COLLABORATIVE LONGITUDINAL PERSONALITY DISORDERS STUDY**

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*J PERSONAL DISORD, 18:193-211, April 2004*

Personality disorders (PDs) are conceptualized as enduring, character-based patterns of pathology that first appear during adolescence or early adulthood. Although adverse childhood experiences such as abuse and neglect are frequently implicated in the development of PDs, relatively little empirical research has examined the role of childhood maltreatment in the majority of PDs. In the multisite study presented here, the authors addressed the following questions. What are the rates of childhood maltreatment in individuals with borderline PD (BPD), schizotypal PD (STPD), avoidant PD (AVPD), and obsessive-compulsive PD (OCPD)? How do these rates compare with those found in individuals with major depressive disorder (MDD) but no PD? Do individuals with BPD report more childhood maltreatment than those with other PD diagnoses? Finally, are particular types of childhood maltreatment associated with other, non-BPD diagnoses?

The study sample (N=600) comprised 517 individuals who were diagnosed with one or more of the targeted PDs (BPD, STPD, AVPD, and/or OCPD) and 83 comparison subjects who were diagnosed with MDD but no PD. Assessment instruments included the Diagnostic Interview for DSM-IV PDs, the Structured Clinical Interview for DSM-IV Axis I Disorders/Patient Version, and the Childhood Experiences Questionnaire-Revised. The results showed that a large proportion of the PD group reported exposure to abuse or neglect while growing up; 73% reported prior abuse, and 82% reported childhood neglect. Compared with individuals with MDD but no PD (who themselves reported relatively high rates of abuse [51%] and neglect [68%]), PD patients were significantly more likely to report several types of childhood maltreatment. When multiple PD diagnoses were examined concurrently, BPD was found to be the diagnosis most strongly associated with childhood maltreatment. Even when the authors controlled for the effect of BPD, other PD diagnoses were found to be associated with specific types of childhood maltreatment.

The current data provide support for the notion that childhood maltreatment plays a role in the development of BPD. *(42 References)*
CHILDHOOD MALTREATMENT AS A RISK FACTOR FOR ADULT CARDIOVASCULAR DISEASE AND DEPRESSION

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J CLIN PSYCHIATRY, 65:249-54, February 2004

It has been estimated that by the year 2020, disability worldwide will be determined largely by depression and heart disease. Several studies have shown a high rate of co-occurrence between these illnesses and have suggested that they may share common risk factors, such as life stress. The purpose of the current investigation was to determine whether early life stress, in the form of childhood maltreatment (defined as child sexual abuse, child physical abuse, or child neglect) is a risk factor for the development of depression and cardiovascular disease in adulthood. Because previous research has indicated that men and women respond differently to life stressors, the authors of the present report focused particularly on gender differences with regard to the relationships between maltreatment in childhood and the development of depression and/or cardiovascular disease in adulthood.

Data were drawn from Part 2 of the National Comorbidity Survey, which was designed to study the distribution, correlates, and consequences of psychiatric disorders in a nationally representative sample of the U.S. population. The weighted sample (N=5,393) was composed of 2,696 women (mean age, 33.4 years) and 2,697 men (mean age, 32.9 years). Relationships between childhood maltreatment (sexual abuse, physical abuse, neglect), DSM-III-R-diagnosed adult depression, and cardiovascular disease were examined by means of multiple logistic regression models, with specific emphasis being placed on the evaluation of sex differences. The results revealed that childhood maltreatment was associated with a significant increase (almost nine-fold) in cardiovascular disorders in women only and with a significant increase in lifetime depressive disorders in both men and women. A history of childhood maltreatment removed the natural protection against cardiovascular disease for women and depression for men. Although depression and cardiovascular disease were correlated, depression did not contribute to the prediction of cardiovascular disease in women when the authors controlled for history of childhood maltreatment.

The authors conclude that gender is important in evaluating the potential psychiatric and physical correlates of childhood maltreatment. Effective clinical assessment should recognize the role of childhood abuse and/or neglect in adult health and disease. (29 References)
IMPLICATIONS OF CHILDHOOD TRAUMA FOR DEPRESSED WOMEN:
AN ANALYSIS OF PATHWAYS FROM CHILDHOOD SEXUAL ABUSE TO DELIBERATE SELF-HARM AND REVICTIMIZATION

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AM J PSYCHIATRY, 161:1417-25, August 2004

Childhood sexual abuse is recognized as a key risk factor for depression, both during childhood and in adulthood. The severity of contact childhood sexual abuse has been found to be associated with higher rates of depression in adulthood, and a history of childhood sexual abuse often predicts a chronic course of depression in women. In the present investigation, the authors utilized information gathered from depressed women with and without a history of childhood sexual abuse to characterize clinical features that differentiated the two groups; they also examined the relationships among childhood sexual abuse, lifetime deliberate self-harm, and recent interpersonal violence.

The study sample was composed of 125 women with depressive disorders; all were interviewed and completed self-report questionnaires. Of the 125 women, 34 (mean age, 38.4 years) reported that they had experienced contact sexual abuse during childhood, and 91 (mean age, 36.4 years) reported no history of childhood sexual abuse. Compared with the women who had no history of childhood sexual abuse, those with a childhood sexual abuse history reported more childhood physical abuse, more childhood emotional abuse, and more parental conflict in the home. Although the two groups of women were similar in severity of depression, the women with a history of childhood sexual abuse were more likely to have attempted suicide and/or engaged in deliberate self-harm; they also became depressed earlier in life, were more likely to have a panic disorder, and were more likely to report a recent physical or sexual assault. Path analysis confirmed the contributory role of childhood sexual abuse to deliberate self-harm as well as the significance of childhood physical abuse with regard to recent interpersonal violence.

The authors conclude that childhood sexual abuse is an important risk factor to identify in women with depressive disorders. Depressed women with a history of childhood sexual abuse constitute a subgroup of patients who may require tailored interventions to combat both recurrences of depression and harmful and self-defeating coping strategies. (28 References)
A MULTISITE, RANDOMIZED CONTROLLED TRIAL FOR CHILDREN WITH SEXUAL ABUSE-RELATED PTSD SYMPTOMS

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 43:393-402, April 2004

Child sexual abuse (CSA) is associated with numerous negative sequelae during childhood, including depression, anxiety, behavior problems, and posttraumatic stress disorder (PTSD). There is evidence to support the theory that CSA and CSA-related PTSD place children at increased risk for suffering potential life-long difficulties. Therefore, it is critically important to identify therapeutic interventions that could prove to be effective in the treatment of children who suffer from PTSD and other sequelae of CSA. In the present investigation, the authors compared the efficacy of trauma-focused cognitive-behavioral therapy (TF-CBT) with that of child-centered therapy (CCT) for the treatment of PTSD and related emotional and behavioral problems in children who had been sexually abused.

In all, 229 children (age range, eight to 14 years) and their primary caretakers were randomly assigned to TF-CBT (114 children) or CCT (115 children). The children exhibited significant symptoms of PTSD, with 89% meeting full DSM-IV criteria for PTSD. More than 90% had experienced other traumas (e.g., sudden death of a loved one, community violence, natural disaster) in addition to sexual abuse. Of the original 229 children, five never returned for treatment, eight left after attending one session, and 13 left after attending two sessions. These 26 children and their parents were defined as dropouts. The remaining 203 children (102 assigned to TF-CBT and 101 assigned to CCT) attended at least three psychotherapy sessions; they constituted the final sample on which analyses of covariance were based. All 229 children were included in intent-to-treat analyses. Series analyses of variance indicated that children assigned to TF-CBT, when compared with those assigned to CCT, demonstrated significantly greater improvement with regard to PTSD, depression, behavior problems, shame, and abuse-related attributions. Similarly, parents assigned to TF-CBT showed greater improvement with respect to their own self-reported levels of depression, abuse-specific distress, support of the child, and effective parenting practices.

According to the authors, the results of the current multisite investigation empirically support the effectiveness of a short-term TF-CBT approach in the treatment of multiply traumatized, sexually abused children with PTSD and related difficulties. (35 References)
PARENT-CHILD INTERACTION THERAPY WITH PHYSICALLY ABUSIVE PARENTS: EFFICACY FOR REDUCING FUTURE ABUSE REPORTS

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J CONSULT CLIN PSYCHOL, 72:500-10, June 2004

Child physical abuse is the most prevalent form of abuse handled by child welfare systems. Despite the prevalence of physical abuse and the number of physically abusive parents receiving services, treatment interventions for these parents have received little research attention over the past two decades. The authors of the present study conducted a randomized trial that was designed to test the efficacy of parent-child interaction therapy (PCIT) in preventing re-reports of physical abuse among abusive parents. PCIT is a highly focused intervention whereby parents are treated with their children, parenting skills are behaviorally defined, and all skills are directly coached and practiced in dyadic parent-child sessions. Therapists observe parent-child interactions through a one-way mirror and coach the parent by means of a radio earphone.

Following a baseline assessment, 110 parent-child dyads (identified abusive parent and identified abused child) were randomly assigned to one of three parenting intervention conditions: PCIT, PCIT plus individualized enhanced services, or a standard community-based parenting group. All three conditions were structured and required approximately six months to complete. On the whole, the extent and duration of abusive behavior among the study participants was serious. Many parents had multiple prior child welfare system referrals and had engaged in documented serious parent-to-child violence. Over 62% of the participant households were considered to be living below the poverty line. Survival analysis revealed that over a median follow-up time of 850 days, a total of 37 participants (34%) had a future unduplicated physical abuse report not attributable to study surveillance effect. Among those who had a re-report of physical abuse, eight had been assigned to the PCIT condition, 12 to the enhanced PCIT condition, and 17 to the standard community group. Additional enhanced services did not appear to improve the efficacy of PCIT. The relative superiority of PCIT was mediated by greater reductions in negative parent-child interactions, which was consistent with the PCIT change model.

According to the authors, their findings support the efficacy of a PCIT-based behavioral parent training program with initial motivational enhancement orientation for reducing rates of future child physical abuse among physically abusive parents. (56 References)
PHYSICAL MALTREATMENT VICTIM TO ANTISOCIAL CHILD: EVIDENCE OF AN ENVIRONMENTALLY MEDIATED PROCESS

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J ABNORM PSYCHOL, 113:44-55, February 2004

In recent years, researchers who study how family functioning affects children’s outcomes have been faced with the assertions that the rearing environment created by parents exerts a relatively weak influence on their children’s development and that what matters most are the genetic characteristics transmitted by parents to their offspring. Well-designed, prospective studies of childhood physical maltreatment and children’s outcomes have found that being physically maltreated in childhood increases a person’s risk of exhibiting violent, antisocial behavior in adolescence and adulthood. The goal of the present investigation was to determine whether physical maltreatment leads to the development of antisocial behavior via an environmental causal process or via genetic transmission.

A representative sample (1,116 twin pairs and their families) was drawn from the Environmental Risk Longitudinal Twin Study, which investigates ways in which genetic and environmental factors shape children’s development. Assessments were conducted when the twins were five and seven years of age. Mothers reported on the children’s experience of physical maltreatment, and mothers and teachers reported on the children’s antisocial behavior. The results indicated that physical maltreatment prospectively predicted antisocial behavior; bore a dose-response relationship to antisocial outcome; and was followed by the emergence of new antisocial behavior. Children’s maltreatment victimization was not found to be influenced by genetic factors. When the authors controlled for parents’ history of antisocial behavior, the effects of physical maltreatment remained significant. After the researchers controlled for any genetic transmission of antisocial behavior, the effect of physical maltreatment was significant, although genetic factors did account for approximately half of the association between physical maltreatment and children’s antisocial behavior.

According to the authors, their findings support the hypothesis that physical maltreatment is an environmental risk variable that is causally linked to children’s antisocial behavior. They recommend that the prevention of physical maltreatment be a public health priority. In light of the fact that 879,000 children per year are maltreated in the United States (National Child Abuse and Neglect Data System, 2002), the researchers conclude, physical maltreatment and its effects on children merit close attention. (81 References)
SEXUAL ABUSE, ANTISOCIAL BEHAVIOUR AND SUBSTANCE USE: GENDER DIFFERENCES IN YOUNG COMMUNITY ADOLESCENTS

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AUST N Z J PSYCHIATRY, 38:34-41, January/February 2004

Adolescents with a history of child sexual abuse (CSA) face many problems with regard to their psychosocial development. For example, they are at greater risk for major depression, anxiety, posttraumatic stress disorder, conduct disorder, and substance use/dependence. In the cross-sectional study presented here, the authors investigated the gender-specific relationships between self-reported CSA, antisocial behavior, and substance use in a large community sample of adolescents drawn from 27 high schools in South Australia. Surveys were conducted on three separate occasions, when the adolescents were approximately 13 (N=2,596), 14 (N=2,475), and 15 (N=2,290) years of age. A comprehensive questionnaire elicited information on CSA, frequency and severity of substance use, depressive symptomatology (Center for Epidemiological Studies Depression Scale), antisocial behavior (22-item adapted Self-Report Delinquency Scale), and family functioning (McMaster Family Assessment Device-General Functioning Subscale). Logistic regression analyses were conducted through use of HLM V5.05, with a population-average model.

In the model considered, reported CSA was found to be significantly and independently associated with antisocial behavior and substance use. After confounding factors of depressive symptomatology and family dysfunction were taken into account, young sexually abused adolescents (age 13) were found to be at greatly increased risk for serious and extreme antisocial behavior, compared with nonabused adolescents. For older boys, the association between CSA and antisocial behavior remained consistently strong, with risks (adjusted) increased eightfold to tenfold at age 14 and fourfold at age 15. Age differences were not statistically significant. In sexually abused girls, the risk for antisocial behavior was increased twofold to threefold after adjustment for family dysfunction and depressive symptomatology. In boys, adjusted associations between CSA and serious substance abuse were not significant at age 13 but ranged from eightfold to threefold at ages 14 to 15. For extreme substance use, the risk increased more than fourfold at all ages. In sexually abused girls, the risk of serious and extreme substance use increased twofold to fourfold at age 13 but was not significant at age 14.

The authors conclude that CSA is a risk factor for the development of antisocial behavior and substance use in young adolescents and that clinicians should be aware of gender differences. (36 References)
CHILDHOOD PHYSICAL AND SEXUAL ABUSE AND SUBSEQUENT ALCOHOL AND DRUG USE DISORDERS IN TWO AMERICAN-INDIAN TRIBES

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Childhood physical and sexual abuse and substance use disorders are known to co-occur in many individuals, although the precise nature of this relationship has yet to be established empirically. The authors examined the relationship between childhood physical and sexual abuse and subsequent lifetime alcohol or drug use disorders among American Indians (AIs) by evaluating cross-sectional and retrospective data collected from a structured epidemiological interview. A sample of 3,084 AIs from two tribal populations (Southwest; N=1,446 and Northern Plains; N=1,638) participated in a large-scale, community-based study.

Childhood physical abuse prior to age 13 was experienced by approximately 7% of each tribal population, with females reporting higher rates than males. The prevalence of childhood sexual abuse was similar to United States general population estimates, with 4% to 5% of both tribal populations reporting such abuse. As was the case with childhood physical abuse, females reported higher rates of childhood sexual abuse than males. Bivariate multinomial logistic regression models indicated that the effect of childhood physical abuse was large and significant for all substance use disorders in the Northern Plains group and for substance dependence in the Southwest group. Childhood sexual abuse was significantly related to all substance use disorders (except alcohol abuse) in the Northern Plains population but only to drug dependence in the Southwest tribe. Correlations were found between lifetime substance use disorders and the following: psychiatric and medical comorbidities, parental alcohol problems, and adult experiences of physical attacks. Multivariate multinomial logistic regression models showed that when all other variables were held constant, childhood physical abuse significantly increased the odds of lifetime alcohol and drug dependence in the Northern Plains population. Childhood sexual abuse significantly increased the odds of drug abuse in the Northern Plains group but not in the Southwest tribe.

In each tribe, women were 50% to 92% less likely than men to experience alcohol and drug abuse or dependence. There was a significant relationship between age and substance use disorder, with the odds of a subsequent diagnosis of drug dependence or abuse being less likely with increasing age in both tribes and the odds more than doubling with increasing age for alcohol dependence in the Northern Plains group. (43 References)
BOOKS RECEIVED FOR REVIEW


*Stress, the Brain, and Depression*, by Herman M. van Praag, Ron de Kloet, and Jim van Os. Cambridge University Press, 2004. 283 pages, $110.00.
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BIOL PSYCHIATRY, 54:474-84, August 15, 2003

Some recent studies have suggested that pathological gambling may be related to dysregulated dopamine neurotransmission. In the current investigation, the authors examined prepulse inhibition as a putative measure of endogenous dopamine brain activity in pathological gamblers. Prepulse inhibition is the reduction in response amplitude to a stimulus (S2) when S2 is immediately preceded by a brief tone or prepulse (S1). Prepulse inhibition of the acoustic startle reflex is considered to be an operational measure of sensory motor gating, a mechanism thought to protect the processing of S1 by inhibiting disruptive responses to S2 (Graham, 1975).

The study sample was composed of 17 subjects who met DSM-IV criteria for a pathological gambling disorder (eight men, nine women; mean age, 36.9 years) and 21 healthy controls (10 men, 11 women; mean age, 32.9 years). Two probes of prepulse inhibition were recorded: prepulse inhibition of the acoustic eye-blink startle response as an index of sensory motor gating and prepulse inhibition of the auditory P300 event-related potential as an index of sensory gating. Both measures were recorded under passive listening and two-tone prepulse discrimination conditions. All the gamblers and controls participated in the acoustic startle reflex task. A subsample of 10 pathological gamblers (three men, seven women; mean age, 34.3 years) and 10 healthy controls (two men, eight women; mean age, 34.9 years) participated in the auditory P300 event-related potential task. Compared with the control subjects, the pathological gamblers exhibited disrupted sensory motor gating on all measures of prepulse inhibition. Sensory motor gating deficits of eye-blink responses were most profound at 120-millisecond prepulse lead intervals in the passive listening task and at 240-millisecond prepulse lead intervals in the two-tone prepulse discrimination task. Sensory gating of P300 was also impaired in the pathological gamblers; they exhibited prepulse-induced attenuation of the frontal P300, especially in the attend prepulse task with a 500-millisecond prepulse lead interval.

In line with earlier neurobiological findings, the current data suggest that there may be increased endogenous brain dopamine activity in pathological gamblers. However, the authors note, because multiple and diverse neurotransmitter systems are involved in startle response generation and prepulse inhibition, the results of the present study only provide indirect evidence for altered dopamine function. (61 References)
GAMBLING URGES IN PATHOLOGICAL GAMBLING
A Functional Magnetic Resonance Imaging Study

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ARCH GEN PSYCHIATRY, 60:828-36, August 2003

Pathological gambling (PG) is classified as an impulse control disorder. Gambling urges in PG often immediately precede engagement in self-destructive gambling behavior. Identifying neural correlates of gambling urges in PG could improve the understanding of the brain mechanisms underlying PG and could aid in the development of effective treatments for the disorder. In the present investigation, the authors used echoplanar functional magnetic resonance imaging to assess brain functioning in subjects while they were viewing videotaped scenarios with happy, sad, or gambling thematic content. In addition, subjects were asked to rate the quality and magnitude of their emotional and motivational responses to the various scenarios.

The study sample was composed of 10 pathological gamblers and 11 control subjects. All the participants were right-handed men who were between the ages of 18 and 65 years and who had no history of major neurological illness or injury. Subjective responses to viewing happy and sad videotaped scenarios were generally moderate and were similar in the controls and the PG subjects. However, subjective responses to the gambling scenarios were generally more robust in the PG subjects than in the controls. The greatest differences were observed in reports of gambling urges in response to the gambling videotapes. None of the PG subjects reported gambling urges during the viewing of the happy or the sad scenarios, while all 10 reported gambling urges when viewing the gambling scenarios. Only three of the 11 control subjects reported gambling urges while viewing gambling scenarios. The most pronounced between-group differences in neural activities were observed during the initial period of viewing of the gambling scenarios; compared with controls, PG subjects displayed relatively decreased activity in the frontal and orbitofrontal cortex, caudate/basal ganglia, and thalamus. Distinct patterns of regional brain activity were observed in specific temporal epochs of videotape viewing, e.g., differences localized to the ventral anterior cingulate during the final period of gambling videotape viewing and corresponding to the presentation of the most provocative gambling stimuli.

The authors conclude that in men who are pathological gamblers, the presentation of gambling cues elicits gambling urges and leads to a temporally dynamic pattern of brain activity changes in frontal, paralimbic, and limbic brain structures. (45 References)
RISK FACTORS FOR PATHOLOGICAL GAMBLING

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ADDICT BEHAV, 29:323-35, February 2004

To better understand pathological gambling, the authors assessed potential risk factors within three domains: gambling behaviors; substance abuse and other problem behaviors, such as criminal offending; and sociodemographic factors. From August 1999 through October 2000, they conducted a national random-digit-dial telephone survey with a representative sample of United States residents who were 18 years of age or older. A total of 2,631 interviews were conducted; analyses were based on information gathered from the 2,168 respondents who had gambled in the year prior to the interview.

Measures of gambling included the Diagnostic Interview Schedule (DIS)-IV for pathological gambling, the frequency of 15 different types of gambling, and the size of the win or loss on the last gambling occasion. Other measures included the quantity and frequency of alcohol consumption, the frequency of illicit drug use and criminal offending, and the DIS-IV for alcohol and drug abuse and dependence. The results showed that frequency of gambling was significantly related to gambling pathology. Every instance of weekly gambling (52 occasions of gambling in the past year) increased pathological symptoms by 26%. The average win or loss was also highly related to gambling pathology. Every 100-dollar increase in the average win/loss was associated with a 65% increase in the number of pathological gambling symptoms. Participation in a greater number of types of gambling was strongly predictive of gambling pathology, even after frequency of gambling and size of win or loss were taken into account. Casino gambling was found to be associated with a high risk of gambling pathology; lottery, cards, and bingo were associated with a moderately high risk. Alcohol abuse was strongly predictive of gambling pathology, even when gambling behaviors were held constant. Being African-American, Hispanic, or Asian and having a low socioeconomic status were significant risk factors for pathological gambling, even after gambling frequency, size of wins and losses, number of types of gambling, substance use, and criminal offending were all taken into account.

According to the authors, the current findings indicate that diagnoses of pathological and problem gambling may have complex causes that extend beyond gambling frequently or making large bets. The risk for pathological gambling appears to be related to gambling versatility, alcohol pathology, and membership in at-risk sociodemographic groups. (23 References)
A widespread increase in gambling opportunities has led to concern about the prevalence of pathological gambling. In the study presented here, the authors explored the precipitants of relapse (defined as gambling after two weeks of abstinence) in a naturalistic sample of 101 pathological gamblers (65 men, 36 women; age range, 19 to 77 years; mean age, 39 years) who had recently quit gambling. After an initial face-to-face interview, the subjects were randomly assigned to one of the following: (1) a retrospective condition in which participants were initially interviewed face-to-face and again at three, six, and 12 months; or (2) a prospective condition in which subjects participated in the aforementioned interviews but also provided weekly telephone reports of gambling, life events, and moods over the past few days. These weekly contacts continued until relapse or for a maximum of three months.

Of the 101 participants, 72 were followed at three months, 71 at six months, and 80 at 12 months. Relapse rates were very high; only 8% of those successfully followed were entirely free of gambling during the 12-month study period. Relapses ranged from minor ones that were of little consequence to major ones that led to a number of negative effects. Overall, about half of the relapses were associated with an extremely negative consequence in at least one life area, most often the financial one. While relapses were highly variable, they occurred most frequently in the early or late evening, when the individual was alone and thinking about finances. Self-rated moods prior to gambling also varied considerably, with positive moods being reported as often as negative ones. The types of relapse precipitants identified by the subjects in their open-ended descriptions ranged from cognitive factors to emotional factors to situational aspects. The most frequently reported precipitants were having optimistic thoughts about winning (23% of relapses) and feeling the need to make money (17%). Men were more likely than women to cite the need to make money as a relapse precipitant. Men were also more likely to attribute relapses to unstructured time or boredom. Women, on the other hand, were more likely to cite dealing with negative situations or emotions as a reason for relapse.

In pathological gambling, the process of relapse is a complex one and involves more than one precipitating factor. Basing a categorization on the factor that a gambler cites as the major precipitant appears to be insufficient in fully conceptualizing the experience of relapse. (55 References)
GAMBLING PARTICIPATION AND PROBLEMS AMONG SOUTH EAST ASIAN REFUGEES TO THE UNITED STATES

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PSYCHIATR SERV, 54:1142-8, August 2003

Pathological gambling is a disorder that involves preoccupation with, tolerance of, and loss of control relating to, gambling. Although being a member of an ethnic minority group appears to be associated with gambling disorders in countries throughout the world, little research has focused specifically on the prevalence of these disorders in Asian populations. In the present investigation, the authors assessed the rates of gambling participation and gambling problems among South East Asian refugees. In all, 96 subjects who had immigrated to the United States from Laos (N=30), Cambodia (N=30), or Vietnam (N=36) and who attended community service organizations for these ethnic groups in Connecticut were asked to complete the South Oaks Gambling Screen (SOGS), which had been translated into their respective native languages. Possible scores on the SOGS range from 0 to 20, with a score of 0 to 2 indicating nonproblem gambling, a score of 3 or 4 being indicative of problem gambling, and a score of 5 or more being indicative of pathological gambling. Demographic data and information on recent gambling activities were also obtained.

Extraordinarily high rates of gambling participation and problems were found in this sample of South East Asian refugees. All but three of the respondents reported gambling over the course of their lifetimes; 95% had gambled during the previous year, and 93% had gambled in the past two months. More than 60% of the respondents reported that they wagered more than $100 on a typical gambling day, and 42% reported wagering more than $500 in the two-month period prior to the interview. The SOGS classified 27 of the study participants as nonproblem gamblers (scores of 0 to 2), 11 as problem gamblers (scores of 3 or 4), and 58 as pathological gamblers (scores of 5 or higher). Thus, the lifetime prevalence of pathological gambling was found to be approximately 59%. Rates of gambling problems did not differ across the three ethnic groups. However, age (being younger), gender (being male), and marital status (being divorced or separated) were all found to be significant predictors of pathological gambling.

According to the authors, the current results point to the need for further research into the social, environmental, and cultural context of gambling among South East Asian refugees. They conclude that ethnically sensitive prevention and intervention strategies are needed to address the extraordinarily high rates of gambling problems in this population. (27 References)
GAMBLING PARTICIPATION AND PROBLEMS AMONG OLDER ADULTS

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J GERIATR PSYCHIATRY NEUROL, 16:172-7, September 2003

The proliferation of gambling opportunities throughout North America over the past 20 years has been accompanied by an increase in gambling participation and an associated rise in rates of pathological gambling. While there has been a dramatic rise in gambling participation among older adults over the past several decades, few studies have evaluated rates of gambling participation and problems in this population. In the present investigation, the authors examined the gambling behaviors of 492 older adults (65 years of age or older) recruited from bingo sites (N=132) and senior centers (N=360) throughout Connecticut. All completed the South Oaks Gambling Screen (SOGS). SOGS scores range from 0 to 20 and classify individuals as nonproblem gamblers (scores of 0-2), problem gamblers (scores of 3-4), or probable pathological gamblers (scores of 5 or above).

Overall, 91.7% of the sample reported gambling during the course of their lifetime; 100% of those recruited at bingo events, and 88.6% of those recruited at senior centers had lifetime experience with gambling. Compared with subjects recruited from senior centers, those recruited at bingo sites had higher SOGS scores, reported gambling more frequently over the past year, and reported spending greater amounts of money on a typical gambling day during the previous year. According to the SOGS, 89.4% of the total sample were classified as nonproblem gamblers, 5.9% as problem gamblers, and 4.7% as pathological gamblers. The lifetime rate of combined problem and pathological gambling was 12.9% in the bingo site sample, 9.7% in the senior center sample, and 10.6% in the total sample. Compared with nonproblem gamblers, those classified as problem or pathological gamblers were more likely to be male (52% versus 27%) and to be younger (73 years of age versus 76 years). Finally, when compared with the group of nonproblem gamblers, the group of problem/pathological gamblers reported a higher frequency of gambling and greater gambling expenditures both in the past two months and in the past year.

The current results indicate that active older adults recruited from community settings exhibit higher rates of problem and pathological gambling than older adults drawn from national samples. The researchers suggest that more attention be directed to the causes, correlates, prevention, and treatment of disordered gambling in older adults. (27 References)
PATHOLOGICAL GAMBLING AMONG ELDERLY VETERANS

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J GERIATR PSYCHIATRY NEUROL, 17:13-9, March 2004

While pathological gambling is found proportionately more often among the young, the number of problem and pathological gamblers found among the elderly is definitely increasing. This growth is likely to continue as the overall population ages and as legalized gambling opportunities continue to expand. The author's aim was to examine elderly patients (60 years of age or older) admitted to a residential gambling treatment program and compare them with a younger cohort on a variety of mental health factors and measures.

A retrospective chart review was performed for 37 elderly gamblers (36 men, one woman; age range, 60 to 84 years; mean age, 65.8 years) consecutively admitted to the Gambling Treatment Program of a Veterans Administration medical center between December 1999 and December 2002. These elderly subjects were compared with 98 younger gamblers (90 men, eight women; age range, 25 to 59 years; mean age, 46.7 years) consecutively admitted over a one-year period. All met DSM-IV criteria for pathological gambling. On intake, the gamblers completed the Addiction Severity Index (ASI) and a variety of mental health questionnaires. Although the elderly gamblers were more likely to be retired and the younger gamblers were more likely to be unemployed and disabled, the two cohorts demonstrated similar degrees of impairment on the ASI composite employment severity score. While a sizable proportion of the older cohort reported a lifetime history of trauma or abuse, elderly gamblers were significantly less likely than younger gamblers to report a history of emotional and physical abuse but equally as likely to report a history of sexual abuse. Compared with younger subjects, older subjects were significantly less likely to have a lifetime history of both alcohol and drug abuse/dependency. While elderly gamblers were less likely than younger gamblers to have made a past suicide attempt or to have made multiple suicide attempts, they were just as likely to have a lifetime history of serious suicidal ideation.

Three patterns of problem gambling were noted in the sample of elderly gamblers studied here. For example, many subjects had been gambling heavily for several years and were continuing a pattern of long-standing duration. Alternatively, some individuals had engaged in controlled gambling for a number of years, and it had become uncontrollable fairly recently. Finally, some of the elderly had begun gambling relatively recently and had developed a severe problem in a fairly short period of time. (33 References)
SUICIDE ATTEMPTS AMONG VETERANS SEEKING TREATMENT FOR PATHOLOGICAL GAMBLING

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J CLIN PSYCHIATRY, 64:1031-8, September 2003

Studies of problem gamblers have found that completed suicide, suicide attempts, and suicidal ideation are common outcomes related to gambling behavior. However, there is little information in the scientific literature regarding the suicide attempts of pathological gamblers. In the investigation presented here, the author conducted a retrospective chart review of 114 individuals (104 men, 10 women) consecutively admitted to the Gambling Treatment Program of the Louis Stokes VA Medical Center over a 12-month period (September 2000-September 2001). All subjects met DSM-IV criteria for pathological gambling. Relevant information was obtained from the admission history and physical examination, as well as from a variety of self-report questionnaires and structured instruments, including the South Oaks Gambling Screen, the Barratt Impulsivity Scale (BIS-10), and the Addiction Severity Index (ASI).

Forty-five patients (39.5%) reported that they had made at least one suicide attempt at some time in their lives, with the majority of these attempters (52.3%) stating that their most recent attempt had been by overdose. Forty-four percent of the attempters had made only one suicide attempt, while 56% had made two or more attempts. In all, 42% of gamblers with a history of alcohol dependence and 58.8% of those with a history of drug dependence reported at least one past suicide attempt. Sixty-four percent of the suicide attempters reported that their most recent attempt was related to gambling, and 63% of those who reported this relationship had a history of substance abuse/dependence. Of the total sample, 93% were found to have some combination of psychiatric and substance abuse diagnoses in addition to pathological gambling. Virtually all of the suicide attempters carried an Axis I psychiatric diagnosis on admission. When the ASI severity scores of suicide attempters and nonattempters were examined, the author found that a history of suicide attempts was significantly related to severity of psychiatric symptoms and to family problems on admission. Among gamblers with a history of drug and/or alcohol dependence, BIS-10 mean total impulsivity scores differentiated suicide attempters from nonattempters.

The author concludes that pathological gamblers have high rates of attempted suicide, are highly impulsive, and suffer from high rates of comorbid psychiatric disorders and social disruptions. A combination of these risk factors may contribute to their potential for suicidal behavior. (42 References)
PATTERNS AND CORRELATES OF GAMBLERS ANONYMOUS ATTENDANCE IN PATHOLOGICAL GAMBLERS SEEKING PROFESSIONAL TREATMENT

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ADDICT BEHAV, 28:1049-62, August 2003

Although Gamblers Anonymous (GA), a self-help fellowship based on the model of Alcoholics Anonymous, is a popular intervention among gamblers, many who attend GA later present for professional treatment. The author of the present study evaluated gambling and psychosocial problems in individuals seeking professional treatment for gambling problems and compared those with and without a history of GA attendance.

The subjects were drawn from a retrospective analysis of 342 individuals seeking professional treatment for pathological gambling in the state of Connecticut between August 1998 and July 2000. All were over 18 years of age, had a diagnosis of pathological gambling, and reported at least one gambling day in the month prior to admission. At treatment intake, subjects were asked to complete the Addiction Severity Index and the South Oaks Gambling Screen (SOGS). Of the 342 gamblers, 184 (54%) had attended GA one or more times prior to initiating professional treatment, while 158 (46%) had not attended GA at any time before seeking professional treatment. Compared with non-GA attendees, GA attendees tended to be older, had higher incomes, and were less likely to be single. Upon entering professional treatment, subjects with a history of GA attendance had more significant gambling problems than those who had never attended GA. The GA attendees had higher scores on the SOGS, more years of gambling problems, higher gambling debts, and a greater need for gambling treatment. While GA attendees had fewer current drug problems than nonattendees, they did report more severe family and social problems. In terms of treatment participation, about half of the subjects with a history of GA attendance became re-engaged in GA once they initiated professional treatment. Compared with subjects who had never attended GA, those with previous GA involvement were also more likely to become actively involved in professional therapy and to be abstinent from gambling two months after beginning professional treatment. Logistic regression analysis revealed that the number of professional sessions and GA meetings attended during treatment were independently associated with short-term abstinence.

According to the author, the current data suggest that among individuals who enter professional treatment for gambling problems, there are substantial differences between those who have a history of GA attendance and those who have never attended GA. These differences may have an impact on treatment recommendations and outcomes. (36 References)
RETROSPECTIVE REVIEW OF TREATMENT RETENTION
IN PATHOLOGICAL GAMBLING

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COMPR PSYCHIATRY, 45:83-7, March/April 2004

Pathological gambling is a significant public health problem that often results in a distinctive pattern of persistent and disabling psychological symptoms. Although research on pathological gambling is increasing, there are few studies that examine the correlates of treatment retention. In the investigation presented here, the authors conducted a chart review and telephone follow-up of 50 outpatients (25 men, 25 women; age range, 21 to 65 years; mean age, 47.7 years) who had a primary DSM-IV diagnosis of pathological gambling and who were treated in a clinical setting for up to four years. Standard scales were used to rate subjects at baseline and at two-month intervals. Assessment tools included the Clinical Global Impressions Scale for Pathological Gambling, the Yale-Brown Obsessive Compulsive Scale Modified for Pathological Gambling, and the Gambling Symptom Assessment Scale. Subjects who dropped out were contacted by telephone to determine their reasons for discontinuing treatment.

The mean duration of treatment for all subjects was 360.4 days (range, 60 to 1,470 days). Of the 50 subjects initially assessed, 26 (52%) remained in treatment, and 24 (48%) dropped out. The mean duration of treatment was 553.7 days for those who continued to receive therapy and 151 days for those who discontinued treatment. Current comorbidity was present in 15 (62.5%) of the 24 subjects who discontinued therapy and in 11 (42.3%) of those who remained in treatment. Of the 26 outpatients who remained in treatment, 25 (96.2%) were considered to be treatment responders (minimal or no gambling urges and/or behaviors) during at least one assessment period. Of the 24 subjects who dropped out, 14 (58.3%) had achieved response during at least one two-month assessment period. The difference in response rates between the two groups was statistically significant. Among the subjects who dropped out of treatment, the primary reasons for discontinuation were missing the thrill of gambling and hoping that gambling (winning) would eliminate financial concerns. The main predictor of remaining in treatment was the presence of a supportive social network in the patient’s life.

According to the authors, a large percentage of patients who are pathological gamblers discontinue treatment. The current study identifies certain variables that appear to be correlated with treatment continuation. These data may provide insight into the factors that might motivate pathological gamblers to remain in treatment. (22 References)
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AM J PSYCHIATRY, 161:59-66, January 2004

Social phobia is a common anxiety disorder that can greatly interfere with normal social and occupational functioning. It is characterized by a persistent fear of situations in which an individual might be exposed to the scrutiny of other people. Like several other anxiety disorders, social phobia aggregates in families and is genetically influenced. Genetic linkage analysis can provide the means to identify genomic locations that harbor susceptibility for genetically influenced disorders. In the study presented here, the authors attempted to identify loci for social phobia.

The researchers conducted a genome-wide linkage scan (i.e., tested enough genetic markers to query the entire genome) in 17 American pedigrees (163 subjects) ascertained through probands with panic disorder. Several anxiety disorders segregated in these families; diagnoses were based on structured interviews. Of the 163 individuals studied, 56 were diagnosed with definite social phobia and four, with probable social phobia. A total of 422 markers (18 X chromosome markers, 404 autosomal markers) with an average spacing of less than 10 centimorgans were genotyped. Multipoint lod score and nonparametric (Zlr score) linkage analyses for social phobia were completed with Allegro and Genehunter X software. Two regions provided statistical support for linkage at the “suggestive” level, with the results indicating that the strongest evidence for linkage to social phobia was on chromosome 16. A Zlr score of 3.41 was observed for chromosome 16 near marker D16S415, in the context of lod scores higher than 2 under several models (with the most notable parametric model results based on the assumption of recessive inheritance). The second region, on chromosome 9 at marker D9S157, showed a lod score of 1.94 (dominant/broad model) and a corresponding Zlr score of 1.58. Additional areas of interest were identified on chromosomes 14 and 18.

According to the authors, a confluence of strong “suggestive” results obtained under different analytic models, taken together with the presence in the genomic region of a favored candidate gene (SLC6A2 [“solute carrier family 6 member 2”], the norepinephrine transporter protein locus that encodes NET1), supports the possibility of a social phobia risk locus on chromosome 16. While a chromosome 16 locus may be important in determining risk for social phobia, it is less likely to be important in determining risk for simple phobia and does not appear to contribute to panic disorder or agoraphobia. (42 References)
LEFT HEMISPHERE DYSFUNCTION DURING VERBAL DICOTIC LISTENING TESTS IN PATIENTS WHO HAVE SOCIAL PHOBIA WITH OR WITHOUT COMORBID DEPRESSIVE DISORDER

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Behavioral, electrophysiological, and imaging studies have found evidence that anxiety disorders are associated with left hemisphere dysfunction or with higher than normal activation of right hemisphere regions. However, few studies have examined regional brain activation in individuals with social phobia, and the influence of comorbid depressive disorders remains unknown. In the present investigation, the authors used dichotic listening tests to assess lateralized cognitive processing in patients with social phobia, depression, or comorbid social phobia and depression.

The researchers used a two-by-two factorial design in which one factor was social phobia (present versus absent), and the second factor was depressive disorder (present versus absent). A total of 125 unmedicated patients (25 with social phobia alone, 82 with a depressive disorder alone, and 18 with comorbid social phobia and depression) and 44 healthy comparison subjects were assessed by means of dichotic fused-words, consonant-vowel syllable, and complex tone tests. Compared with the subjects without social phobia (patients with depression alone and healthy controls), the patients with social phobia (with or without a comorbid depressive disorder) had a smaller left hemisphere advantage for perceiving dichotic words and consonant-vowel syllables. However, there was no significant difference between groups in terms of the right hemisphere advantage for processing complex tones. The difference in perceptual asymmetry between subjects with and without social phobia was not modulated by the presence of a depressive disorder or by gender. Compared with nondepressed women, depressed women had a markedly larger left hemisphere advantage for processing words; however, this difference was not found to be evident among the men.

According to the authors, the results of the current study provide support for the hypothesis that social phobia is associated with dysfunction of the left hemisphere regions that mediate verbal processing. Given the importance of verbal processes in social interactions, the researchers note, this dysfunction may contribute to the stress and difficulty experienced by patients with social phobia when they are in social situations. (29 References)
QT DISPERSION IN PATIENTS WITH SOCIAL PHOBIA

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QT dispersion (QTd) is the maximal interlead difference in QT intervals on the surface 12-lead electrocardiogram (ECG). An increase in QTd is found in various cardiac diseases and reflects cardiac autonomic imbalance. It has recently been associated with increased anxiety levels, thereby predisposing affected individuals to fatal heart disease. In the study presented here, the authors assessed QTd in individuals with social phobia, analyzing it as a marker of anxiety-induced cardiac dysregulation.

The study sample was composed of 16 physically healthy, nondepressed outpatients with social phobia (nine men, seven women; mean age, 37.9 years) and 15 physically and mentally healthy controls (nine men, six women; mean age, 35.6 years). Among the group with social phobia, the mean age at onset of the disorder was 10.9 years, and the average duration of the illness was 28 years. All ECG recordings were performed in the same quiet room during spontaneous breathing, following 10 minutes of adjustment in the supine position. QTd and rate-corrected QTd were measured in all participants, and the Liebowitz Social Anxiety Scale (LSAS) was scored concomitantly. The intra- and inter-observer reproducibilities of QTd were highly correlated. The results indicated that the mean QTd was significantly higher in the patients with social phobia than in the normal controls (70 milliseconds [ms] versus 43 ms). The mean rate-corrected QTd also proved to be significantly higher in the patients than in the controls (75 ms versus 46 ms). Scores on the LSAS fear or anxiety subscale and the LSAS avoidance subscale were significantly higher in the group with social phobia than in the control group and also were significantly correlated with QTd and rate-corrected QTd values. Age at onset of social phobia correlated negatively with the two LSAS subscales and with duration of social phobia. No significant correlation was found between duration of social phobia and QTd values.

The authors conclude that long-term social phobia is associated with an increase in QTd. This association may result from prolonged anxiety and, in turn, a decrease in vagal modulation and/or an increase in sympathetic modulation. Further large-scale epidemiological studies are needed to determine whether increased QTd could serve as a trait or state marker and whether alterations in QTd have predictive value for cardiac morbidity and mortality in patients with social phobia and other anxiety disorders. (25 References) EAF
SOCIAL PHOBIA IN THE AUSTRALIAN NATIONAL SURVEY OF MENTAL HEALTH AND WELL-BEING (NSMHWB)

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PSYCHOL MED, 33:637-46, May 2003

Drawing on a large-scale epidemiological study (Australian National Survey of Mental Health and Well-Being [NSMHWB]), the authors present data on the prevalence, sociodemographic correlates, and comorbidity of social phobia. They also report on the prevalence and comorbidity of avoidant personality disorder, which is often conceptualized as a severe form of social phobia and which DSM-IV allows to be diagnosed concurrently with social phobia.

Data were obtained from a stratified sample of 10,641 individuals (18 years of age or older) who participated in the NSMHWB. A modified version of the Composite International Diagnostic Interview was used to determine the presence of social phobia, as well as other DSM-IV anxiety, affective, and substance use disorders. Participants were also screened for the presence of nine ICD-10 personality disorders, including anxious personality disorder, the ICD-10 disorder most similar to DSM-IV avoidant personality disorder (APD). The estimated 12-month prevalence of social phobia was found to be 2.3%; this figure was lower than rates reported in several recent nationally representative epidemiological surveys and closer to those reported in the Epidemiological Catchment Area study and in other DSM-III studies. Individuals with social phobia were more likely to classify themselves as separated/divorced/widowed or never married; they were also more likely to report themselves as unemployed or “not in the labor force.” Comorbidity was prominent among those with social phobia, with 78.1% meeting criteria for some other disorder, most commonly another anxiety disorder (53.4%). In the majority of cases, the onset of social phobia preceded the onset of major depression (65.5% of cases in which criteria for both were met in the preceding 12 months), alcohol abuse (62.1%), and generalized anxiety disorder (60.6%). In all, 35.8% of those who met criteria for social phobia also screened positively for APD. Compared with individuals with social phobia alone, those with social phobia and APD were more likely to meet criteria for another anxiety disorder, another personality disorder, major depression, or dysthymia; however, those with social phobia and APD appeared to be significantly less likely to meet criteria for alcohol abuse and dependence.

The authors conclude that social phobia is a highly prevalent, highly comorbid disorder in the Australian community. According to the researchers, the current findings provide support for the theory that proposes that APD is a severe variant of social phobia. (53 References)
Selective mutism is defined as refusing to speak or withholding speech in some situations while displaying normal speech in other settings. Children with selective mutism display many symptoms considered to be characteristic of social anxiety disorder (e.g., social avoidance, experiencing distress in social situations, fear of talking to strangers), and diagnostic studies of children with selective mutism have found that almost all of them meet DSM-IV criteria for social phobia. The authors of the present investigation attempted to determine whether children with selective mutism would be more socially anxious than children who had social anxiety disorder but who were not selectively mute.

The study sample was composed of 23 children (10 boys, 13 girls; mean age, 9.5 years) with social phobia alone and 23 children (10 boys, 13 girls; mean age, 9.4 years) with social phobia and a comorbid diagnosis of selective mutism. All the children and their parents participated in a comprehensive assessment of social anxiety and related aspects of psychopathology. Measures included the Child Behavior Checklist (CBCL), the Social Phobia and Anxiety Inventory for Children, the State-Trait Anxiety Inventory for Children Trait subscale, the Fear Survey Schedule for Children-Revised, and a behavioral assessment task. The findings were conflictual with regard to whether children with selective mutism experienced more severe social anxiety than children with social phobia alone. Using different measurement strategies, clinicians and observers rated children with selective mutism as significantly more socially anxious than those with social phobia alone. However, children’s self-report data revealed no between-group differences in levels of general social anxiety or specific anxiety experienced during a role-playing task. No significant between-group differences were found on the CBCL Internalizing and Externalizing scales, or on the CBCL Anxious/Depressed and Withdrawn subscales. While children with selective mutism scored higher on the CBCL Delinquency subscale than children with social phobia alone, the scores were not in the clinically significant range.

These results confirm that many children with selective mutism meet criteria for social phobia. However, assuming that the primary clinical distinction between children with selective mutism and those with social phobia alone is simply a difference in the severity of social anxiety does not fully characterize the differences between these two groups. (15 References)
THE LIEBOWITZ SOCIAL ANXIETY SCALE FOR CHILDREN AND ADOLESCENTS: AN INITIAL PSYCHOMETRIC INVESTIGATION

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 42:1076-84, September 2003

Fear of social or performance situations in which an individual is exposed to possible scrutiny or unfamiliar people is the hallmark of social phobia. Recognition of the importance of social phobia has led to increased interest in studying the etiology and treatment of this disorder in youth. While several psychometrically sound self-rating instruments have been developed for use with children and adolescents, there are no clinician-rating scales designed to assess the severity of social anxiety in children and adolescents. In the study presented here, the authors examined the psychometric properties of the Liebowitz Social Anxiety Scale for Children and Adolescents (LSAS-CA), a newly developed clinician rating scale that assesses anxiety and avoidance in 24 situations (Masia et al., 1999). The LSAS-CA is currently being used in many clinical settings and in national pharmacological trials of social phobia in children and adolescents.

In all, 154 children and adolescents (61 males, 93 females; age range, 7 to 18 years; mean age, 13.4 years) participated in an assessment that consisted of a diagnostic interview, the LSAS-CA, and other measures of psychopathology and impairment. Within seven days of the initial assessment, 61 of these subjects were administered a second LSAS-CA by a different rater who was blind to diagnosis. Of the 154 study participants, 97 had a primary diagnosis of social phobia, 23 were diagnosed with anxiety disorders other than social phobia, and 32 had no psychiatric diagnosis (nonpsychiatric controls). High internal consistency (α=.90-.97 for the full sample and .83-.95 for the social phobia group) and test-retest reliability (intraclass correlation coefficient=0.89-0.94) were obtained for LSAS-CA total and subscale scores. LSAS-CA scores were more strongly associated with measures of social anxiety and general impairment than with a measure of depression. The subjects with social anxiety disorder had significantly higher LSAS-CA scores than the subjects with other anxiety disorders and the nonpsychiatric controls. An LSAS-CA cutoff score of 22.5 represented the best balance of sensitivity and specificity when distinguishing between individuals with social phobia and normal controls, whereas a cutoff score of 29.5 was optimal for distinguishing subjects with social phobia from those with other anxiety disorders.

The authors conclude that the LSAS-CA appears to be a reliable and valid instrument for assessing social anxiety disorder. (43 References) EAF
PREDICTORS OF RESPONSE IN GENERALIZED SOCIAL PHOBIA:
EFFECT OF AGE OF ONSET

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J CLIN PSYCHOPHARMACOL, 24:42-8, February 2004

While selective serotonin reuptake inhibitors (SSRIs) have become the gold standard in the pharmacotherapy of social phobia, little is known about predictors of treatment response, and current evidence is inconsistent and inconclusive. The authors conducted a 20-week, double-blind study in which 204 outpatients (age range, 19 to 56 years; mean age, 36.2 years) with generalized social phobia (GSP) were randomly assigned to receive sertraline (flexible dose ranging from 50 to 200 mg/day) or placebo. Primary outcome measures were the Clinical Global Impression-Improvement scale (CGI-I) and the Brief Social Phobia Scale (BSPS). A number of dependent measures were assessed, including the Marks Fear Questionnaire-Social Phobia subscale, the Sheehan Disability Scale, the CGI-I, and the BSPS. Possible predictors of treatment response that were evaluated included age, age of onset of GSP, duration of illness, gender, and presence of comorbid major depressive disorder and/or avoidant personality disorder. Age of onset of GSP was subdivided into three categories: early (younger than 9 years of age), adolescent (9 to 18 years old), and adult (age 19 or older).

Compared with placebo, sertraline proved to be effective in the treatment of patients with GSP. Age, duration of illness, and comorbid avoidant personality disorder did not prove to be significant predictors of treatment outcome. Across dependent measures, gender was predictive of treatment outcome; women showed a response to sertraline that was roughly equivalent to that of men, but showed a response to placebo that was stronger than that of men. Age of onset was found to be predictive of outcome, as patients with later-onset (especially adult-onset) GSP tended to have a better response to treatment than those with earlier-onset GSP. This finding could not be accounted for by either severity or duration of illness. Later age of onset was associated with high end-state symptom response or remission as defined by a BSPS score of 15 or less or a CGI-I score of 1(very much improved).

The authors conclude that the superior treatment response of patients with late-onset GSP may have been mediated by the degree of social and family disability. The relationship between social phobia and social support is worthy of further investigation. (38 References)
EXPOSURE THERAPY AND SERTRALINE IN SOCIAL PHOBIA:
1-YEAR FOLLOW-UP OF A RANDOMISED CONTROLLED TRIAL

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BR J PSYCHIATRY, 182:312-8, April 2003

In this follow-up study of the treatment of social phobia, the authors attempted to determine whether the effects of exposure therapy and sertraline would be maintained 28 weeks after the cessation of active medical treatment. In all, 375 patients (147 men, 228 women; mean age, 39.9 years) with generalized social phobia were randomly assigned to receive sertraline or placebo (with or without the addition of exposure therapy) for a period of 24 weeks. Assessment instruments included the Mini International Neuropsychiatric Interview, the Clinical Global Impression-Social Phobia severity subscale, the Social Phobia Scale, the Fear of Negative Evaluation scale, the Marks Fear Questionnaire, and the mental health subscale of the 36-item Short Form Health Survey. Of the 375 patients evaluated at baseline, 346 were assessed at week 24 (end of treatment), and 328 were available for assessment at week 52 (follow-up). The same psychometric tests were used at all three assessment points.

Results of the psychometric assessments indicated that all four treatment groups (sertraline only, sertraline plus exposure therapy, exposure therapy plus placebo, and placebo) showed significant improvement over the course of the study (from baseline to week 52). Patients who had been given exposure therapy or placebo showed further improvement in social phobia symptoms during follow-up. Patients who had been treated with sertraline (either alone or in combination with exposure therapy) showed no further improvement during the follow-up period and even had a tendency to deteriorate. This deterioration was significant only on the 36-item Short Form Health Survey. At week 52 the patients who had received sertraline alone or sertraline plus exposure therapy showed significant deterioration when compared with those who had received exposure therapy alone or placebo.

According to the authors, exposure therapy, sertraline, and the combination of exposure therapy and sertraline all appear to be effective treatments for individuals with social phobia. However, while patients treated with exposure therapy alone seem to show further improvement after the end of active treatment, those treated with sertraline have a tendency to deteriorate after the cessation of medication. The researchers conclude that exposure therapy administered alone is more effective in the long-term than when it is given in combination with sertraline. (28 References)
COGNITIVE THERAPY VERSUS FLUOXETINE IN GENERALIZED SOCIAL PHOBIA: A RANDOMIZED PLACEBO-CONTROLLED TRIAL

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J CONSULT CLIN PSYCHOL, 71:1058-67, December 2003

Social phobia is a common and disabling disorder that is associated with marked vocational underachievement and an increased risk of depression, suicide, and alcohol abuse. While treatment-seeking rates for this condition are low in comparison with those for other anxiety disorders, in the last 15 years considerable progress has been made in developing effective pharmacological and psychological therapies for individuals with social phobia. In the study presented here, 60 patients who met DSM-IV criteria for generalized social phobia (mean age, 33.2 years; mean duration of social phobia, 13.3 years) were randomly assigned to one of three treatment conditions: cognitive therapy, fluoxetine plus self-exposure, or placebo plus self-exposure. Allocation to fluoxetine or placebo was double-blind. After 16 weeks, the medication blind was broken. Patients initially allocated to cognitive therapy or to fluoxetine plus self-exposure continued their respective treatments for an additional three months (booster period). Patients initially allocated to placebo were withdrawn from the trial at 16 weeks and offered their choice of cognitive therapy, fluoxetine plus self-exposure, or a combination of both treatments. Assessments were completed at pretreatment, midtreatment (eight weeks), posttreatment (16 weeks), end of booster period, and 12-month follow-up.

All three treatment conditions were associated with significant improvement (pretreatment to midtreatment and pretreatment to posttreatment) on most assessment measures. At both midtreatment and posttreatment, cognitive therapy proved to be superior to the other two treatment conditions on measures of social phobia, while fluoxetine plus self-exposure and placebo plus self-exposure did not differ from each other. At both midtreatment and posttreatment, the three treatment conditions were similar with regard to their effects on measures of general mood. Assessments conducted at the end of the booster period and at the 12-month-follow-up indicated that cognitive therapy remained superior to fluoxetine plus self-exposure.

According to the authors, the overall pattern of results obtained in the current investigation indicates that cognitive therapy is an effective treatment for individuals with generalized social phobia. Patients treated with cognitive therapy improved significantly more than those who received self-exposure instructions in combination with fluoxetine or placebo, and they maintained these gains at the one-year follow-up. (64 References)
POST-EVENT RUMINATION AND NEGATIVE SELF-APPRAISAL IN SOCIAL PHOBIA BEFORE AND AFTER TREATMENT

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J ABNORMAL PSYCHOL, 113:136-44, February 2004

The role of post-event rumination in the maintenance of social phobia has recently been the focus of theoretical and empirical attention. Post-event rumination refers to the tendency for socially phobic individuals to engage in negative rumination following a social or performance event, such as a speech or a social interaction. In the present study, the authors investigated the relationships between self-appraisals of performance, symptom severity, and post-event rumination in individuals with social phobia; they also evaluated the potential effect of treatment on these variables.

The study sample was composed of two groups: 43 individuals who met DSM-IV criteria for social phobia and 30 nonanxious controls. Following diagnostic assessment, the participants were asked to give a three-minute impromptu speech on a topic of their choice and were told that an independent judge would rate their performance by viewing a videotape of their speech. The participants were asked to evaluate their own performance immediately after the speech and then again, one week later. They also completed a questionnaire that was designed to measure the frequency with which participants engaged in both positive and negative rumination during the week following the speech. A subgroup (N=20) of individuals from the socially phobic group repeated the study after completing a 12-week cognitive-behavioral program for the treatment of social phobia. In general, the self-appraisals of speech performance completed by the socially phobic group were significantly more negative than those completed by the control group. Over the course of the week following the speech, the socially phobic individuals maintained these negative self-appraisals, whereas the nonclinical controls showed increased positivity about their performance. During the week following the speech task, the socially phobic group engaged in significantly more negative rumination than the control group. More severe social anxiety was associated with poorer appraisals of speech performance and the tendency to engage in more frequent negative rumination. Following successful cognitive-behavioral treatment, there was a reduction in both negative self-appraisals and negative rumination.

According to the authors, the results of the current study indicate that negative appraisals of performance appear to be remarkably stable in socially phobic individuals, while self-perceptions of performance seem to improve over time in nonanxious individuals. (40 References)
Abstracts and Reviews of Selected Literature in Psychiatry, Neurology, and their Allied Fields

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A Randomized Placebo-Controlled Trial of Risperidone for the Treatment of Aggression, Agitation, and Psychosis of Dementia
FAMILIAL PATTERNS OF RISK IN VERY LATE-ONSET ALZHEIMER DISEASE

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ARCH GEN PSYCHIATRY, 60:190-7, February 2003

Alzheimer disease (AD) is a highly age-dependent, late-onset disorder. The incidence of AD appears to peak after 85 years of age. While genetic factors are implicated in AD with substantially earlier age-of-onset, the familial characteristics of high-incidence very late-onset AD (VLOAD, defined herein as AD with age of onset at 85 years or older) remain undetermined. The authors examined the risk for AD in first-degree relatives of VLOAD probands, in relatives of probands with earlier-onset AD (onset before age 85), and in relatives of nondemented elderly probands.

The sample was composed of 809 parents and siblings of 144 VLOAD probands, 4,235 parents and siblings of 793 earlier-onset AD probands, and 7,646 parents and siblings of 1,493 nondemented elderly probands. Demographic information was obtained, and the Alzheimer's Disease Risk Questionnaire was used to screen for dementia, cognitive impairment, and memory loss. Cumulative risks and five-year interval-specific hazard rate ratios for AD were calculated in the relatives of the two AD proband groups and in the relatives of the nondemented elderly group. In the relatives of the earlier-onset AD proband group, the risk for AD first exceeded 2% at age 65 and 10% at age 77. By ages 85, 90, and 95, the cumulative risks for AD in this group were 22.1%, 26.5%, and 30.6%, respectively. In the relatives of the VLOAD probands, the cumulative risk first exceeded 2% at age 71 and 10% at age 87. At ages 85, 90, and 95, cumulative risks for AD were 8.8%, 16.7%, and 30.7%, respectively. In relatives of the nondemented elderly, the risk for AD first exceeded 2% at age 72 and 10% at age 88. At ages 85, 90, and 95, cumulative risks reached 8.2%, 11.7%, and 19%, respectively. Hazard rate ratios in relatives of the VLOAD group were not significantly different than those in the relatives of the nondemented elderly. However, relatives of the earlier-onset AD probands (with the exception of those aged 90 to 94) had significantly higher hazard rates than relatives of the nondemented group. The relatives of the earlier-onset AD proband group had hazard rate ratios ranging from 19.7 in those aged 50 to 54 years to 1.2 in those aged 90 to 94 years; ratios dropped with each successive five-year age interval.

The authors conclude that at least through the middle of the ninth decade of life, relatives of probands with VLOAD have a lower risk for AD than relatives of probands with earlier-onset AD. The relatively increased risk of AD in relatives of individuals with earlier-onset AD is highest at younger ages and diminishes as age increases. (47 References)
THE PREVALENCE OF FRONTAL VARIANT FRONTOTEMPORAL DEMENTIA AND THE FRONTAL LOBE SYNDROME IN A POPULATION BASED SAMPLE OF 85 YEAR OLDS

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J NEUROL NEUROSURG PSYCHIATRY, 74:867-71, July 2003

Frontotemporal dementia (FTD) is a primary degenerative dementia, with severe atrophy in the frontal and anterior frontal lobes. Its most common subtype is frontal variant FTD (fvFTD), which is characterized by progressive changes in personality and behavior (with emotional and motivational blunting) and impairments in personal and social conduct. A frontal lobe syndrome (FLS) often accompanies dementia disorders such as Alzheimer’s disease (AD) and vascular dementia (VAD). In the study presented here, the authors investigated the prevalence of FLS and fvFTD in a representative sample of 85-year-olds in Gothenburg, Sweden.

The sample comprised 451 individuals (131 men, 320 women). They were evaluated by means of a neuropsychiatric examination and an interview with a key informant. A subsample (N=238) underwent computed tomography (CT) of the head. On the basis of the Lund-Manchester research criteria, a symptom algorithm was constructed and used to identify individuals with FLS and fvFTD. Dementia was diagnosed according to DSM-III-R criteria. A diagnosis of dementia was not a requirement for a diagnosis of FLS or fvFTD. Diagnoses of FLS and fvFTD were made blindly to diagnoses of dementia. The prevalence of FLS was 19% (N=86), with no differences being found between men and women. Of those with FLS, 75 (87%) fulfilled DSM-III-R criteria for other types of dementia, mainly Alzheimer’s disease and vascular dementia. The prevalence of fvFTD was found to be 3.1% (N=14). Of those with fvFTD, 64% (N=9) did not meet DSM-III-R criteria for dementia, and five had previously been diagnosed with Alzheimer’s disease. Of the 238 individuals who underwent a CT scan, 53 had FLS, and six had fvFTD. Among those with FLS, 92.5% (N=49) had moderate-to-severe frontal atrophy, as compared with 48.6% (N=90) of those without FLS. All six individuals who had fvFTD and underwent a CT scan were found to have moderate-to-severe frontal atrophy. FLS was found in 35.3% of those with moderate-to-severe frontal atrophy, but in only 2.9% of those without moderate-to-severe frontal atrophy.

The authors found that FLS was common in 85-year-old individuals, especially among those with dementia disorders. The prevalence of fvFTD (3%) was considerably higher than what would be expected in this age group. In addition, a majority of those who were found to have fvFTD did not meet DSM-III-R criteria for dementia. (40 References)
A STUDY OF STEREOTYPIC BEHAVIOURS IN ALZHEIMER’S DISEASE AND FRONTAL AND TEMPORAL VARIANT FRONTOTEMPORAL DEMENTIA

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J NEUROL NEUROSURG PSYCHIATRY, 74:1398-1402, October 2003

Frontotemporal dementia (FTD) manifests itself in two principal forms: frontal variant FTD (fvFTD) and temporal variant FTD (semantic dementia). While fvFTD is characterized by marked changes in personality and behavior, semantic dementia presents with a progressive fluent aphasia secondary to a breakdown in semantic knowledge, with preservation of speech output skills, perceptual and visual-spatial functions, and episodic memory. Recent studies have suggested that the overall prevalence of stereotypic behaviors is higher in FTD than in Alzheimer’s disease. The authors’ aims were (1) to document the prevalence and pattern of stereotypic behaviors in patients with Alzheimer’s disease, fvFTD, and semantic dementia; and (2) to examine the relationship between stereotypic and other neuropsychiatric behaviors and markers of cognitive decline.

A total of 59 patients participated in the study: 28 with Alzheimer’s disease (14 men, 14 women; mean age, 61.6 years), 18 with fvFTD (15 men, 3 women; mean age, 61.1 years), and 13 with semantic dementia (7 men, 6 women; mean age, 66.5 years). All patients were assessed with the Neuropsychiatric Inventory (NPI), the Mini-Mental State Examination, Addenbrooke’s Cognitive Examination, and the Clinical Dementia Rating Scale. They were also rated on a newly devised Stereotypic and Ritualistic Behavior Subscale (SRB), which was designed as an addendum to the NPI. There were no significant differences across the three diagnostic groups in terms of age, sex, or severity of cognitive deficits. The results indicated that the overall NPI score was significantly higher in the group with fvFTD than in the other two groups; however, the patients with fvFTD and the patients with semantic dementia showed a similar, and significantly increased, prevalence of stereotypic behaviors on the SRB subscale. Within the FTD group as a whole, these behaviors were more likely to be complex (e.g., preoccupation with counting and/or clock watching, rigid adherence to routine), whereas in the Alzheimer’s disease group, such behaviors (when present) tended to be more simple stereotypies or stimulus-bound repetitive behaviors. Stereotypic behaviors were not correlated with either disease severity or extent of cognitive impairment in the fvFTD group, but were in the other two groups.

This study confirms previous reports that stereotypic behaviors occur significantly more often in patients with FTD than in those with Alzheimer’s disease. Complex stereotypic behaviors appear to be a core feature of the dementing syndrome in FTD and may reflect early and specific deficits in orbitofrontal circuitry and basal ganglia involvement. (26 References) EAF
THE INCIDENCE OF MENTAL AND BEHAVIORAL DISTURBANCES IN DEMENTIA: THE CACHE COUNTY STUDY

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J NEUROPSYCHIATRY CLIN NEUROSCI, 15:340-5, Summer 2003

Most dementias are irreversible and progressive, causing global cognitive and functional decline and leading, ultimately, to death. Mental and behavioral disturbances, such as delusions, hallucinations, depression, and agitation typically occur. According to estimates derived from clinical samples, as many as 70% to 90% of demented patients experience at least one mental or behavioral disturbance during the course of their illness. The authors of the present study assessed the incidence of mental and behavioral disturbances in a population-based sample of 355 individuals who were diagnosed with dementia and who were residents of Cache County, Utah.

The Neuropsychiatric Inventory (NPI) was used to assess the prevalence of 10 categories or domains of mental and behavioral disturbances that occur in dementia: delusions; hallucinations; agitation/aggression; depression; anxiety; elation; apathy; disinhibition; irritability; and aberrant motor behavior, such as wandering or pacing. Of the 355 residents with dementia, 119 had an NPI score of 0 (no symptoms in any domain) at baseline and consequently were at risk for the incidence of NPI-ascertained disturbances at follow-up examinations conducted approximately 18 months later. NPI follow-up data were obtained on 61 (51%) of these 119 participants. Of the 61 individuals with follow-up data, 42 (69%) exhibited at least one NPI-ascertained disturbance. In terms of individual symptom domains, delusions were found to be the most common (28%), followed by apathy (21%) and aberrant motor behavior (21%). When the obtained prevalence of 69% was combined with a previously estimated prevalence of 61%, the cumulative 18-month prevalence of mental and/or behavioral disturbances in dementia approached 90%.

The current data add to the growing body of evidence which illustrates that comorbid psychiatric symptoms occur with a high degree of frequency in patients with dementia; the results also demonstrate that even demented patients who are asymptomatic at a given time may still be at very high risk for developing psychiatric disturbances later. According to the authors, the present findings argue for a routine assessment of psychiatric disturbances in all patients with dementia, even in those who have never experienced symptoms of mental or behavioral disturbances. (33 References)
PSYCHIATRIC SYMPTOMS VARY WITH THE SEVERITY OF DEMENTIA IN PROBABLE ALZHEIMER’S DISEASE

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J NEUROPSYCHIATRY CLIN NEUROSCI, 15:346-53, Summer 2003

The neuropathological progression of Alzheimer’s disease (AD) follows a hierarchical order that begins in the mesial temporal lobe and continues to the frontal-temporal-parietal heteromodal association areas. Although behavioral symptoms occur more frequently as AD progresses, patients may manifest depression, disruptive behavior, and/or psychosis at any stage of the illness. The authors examined the relationships among major depression, agitation, aggression, and psychosis as they occur within the context of the constellation of psychiatric symptoms/syndromes that are commonly present in AD patients as a function of dementia severity.

The study sample was composed of 1,155 patients (349 men, 806 women) with a diagnosis of probable AD. On the basis of Mini-Mental State Examination scores, the severity of cognitive impairment was considered to be mild in 438 patients, moderate in 563, and severe in 154. Major depression was found to occur less frequently in patients with severe cognitive deficits than in those with mild or moderate cognitive deficits. However, agitation, aggression, and psychosis were found to occur more frequently in the moderate and severe stages of AD. Major depression was associated with anhedonia, sleep disorders, depressed mood, low self-esteem, anxiety, and hopelessness in mild, moderate, and severe stages of dementia. Agitation was associated with aggression and psychosis in mild and moderate stages of dementia. Psychosis was found to be associated with aggression in moderate and severe stages of AD. In addition, a constellation of psychiatric symptoms (e.g., anxiety, wandering, irritability, inappropriate behavior, uncooperativeness, emotional lability) found to be associated with agitation, aggression, and psychosis varied according to the severity of the dementia. Both education and race were found to be independently associated with psychosis. While education was associated with psychosis in mild and moderate stages of AD, race was associated with psychosis in moderate and severe stages of the disease.

The current data show that psychiatric symptoms and syndromes, with the exception of major depression, occur more frequently in the more severe stages of AD, and that similar behaviors can occur within the context of different behavioral syndromes. (47 References)
FREQUENCY AND CHARACTERISTICS OF ANXIETY AMONG PATIENTS WITH ALZHEIMER’S DISEASE AND RELATED DEMENTIAS

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J NEUROPSYCHIATRY CLIN NEUROSCI, 15:180-6, Spring 2003

In the cross-sectional analysis presented here, the authors used the anxiety subscale of the Neuropsychiatric Inventory (NPI) to assess the prevalence and characteristics of anxiety in patients with Alzheimer’s disease (AD), vascular dementia (VaD), and frontotemporal dementia (FTD), and in normal elderly control subjects. The also examined the relationships between anxiety and the following: other behavioral disturbances as measured by the NPI; cognitive decline as measured by the Mini-Mental State Examination (MMSE); and instrumental activities of daily living as measured by the Functional Activities Questionnaire (FAQ).

The study population comprised 191 subjects with dementia and 40 normal control subjects. The demented subjects were drawn from the UCLA Alzheimer’s Disease Center database and included 115 patients with probable AD, 43 patients with VaD, and 33 patients with FTD. Anxiety was reported less frequently in patients with AD than in those with VaD or FTD. Caregivers reported the presence of anxiety in 30 patients with probable AD (26.1%), 22 patients with VaD (51.2%), and 18 patients with FTD (54.5%). Comparisons between groups revealed a significant difference in the presence of anxiety between the AD and VaD groups and between the AD and FTD groups. The mean anxiety score of the AD group was significantly lower than that of the FTD group and that of the VaD group. All dementia groups had significantly higher scores than the control group. These comparisons remained significant when analyses were adjusted for the covariates of age, age at onset of the disorder, educational level, and MMSE score. In the AD group, there was an inverse correlation between anxiety score and total MMSE score, indicating that the level of anxiety increased as mental status deteriorated with advancing disease. Also, in the AD group, there was a correlation between anxiety and disability (as measured by the FAQ score), and anxiety tended to be more prevalent among AD patients with an earlier age at onset (before 65 years of age).

The current data suggest that anxiety occurs frequently in patients with diverse forms of dementia. Among patients with AD, the authors note, anxiety appears to be most common in those with more severe cognitive deterioration and an earlier age at onset. (27 References)
A COLLABORATIVE STUDY OF THE EMERGENCE AND CLINICAL FEATURES OF THE MAJOR DEPRESSIVE SYNDROME OF ALZHEIMER’S DISEASE

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The authors describe the initial results of a collaborative, clinicopathologic study of the major depressive syndrome of Alzheimer’s disease. In all, 243 cognitively impaired patients with probable Alzheimer’s disease (100 men, 143 women) and 151 nondemented elderly comparison subjects (70 men 81 women) were recruited and characterized by a consortium of four Alzheimer’s disease research centers and the Geriatric Psychiatry Branch of the National Institute of Mental Health. All sites administered the Clinical Assessment of Depression in Dementia, a structured, anchored diagnostic interview that was developed to reliably diagnose and characterize major depressive episodes in this population.

Despite the use of a common, reliable methodology for the assessment of major depressive episodes, the prevalence of major depression in Alzheimer’s disease varied widely across recruitment sites, ranging from 22.5% to 54.4%. This site-related variance was not explained by differences in ages of Alzheimer’s disease patients at the time of study; severity of dementia; prevalence of delusions/hallucinations; or presence of premorbid history of major depression. The prevalence of major depressive episodes among Alzheimer’s disease patients in the aggregate sample exceeded that among elderly comparison subjects and reached nearly 50% in the most severely demented patients. Alzheimer’s disease patients with a current major depressive episode had an earlier mean age at onset and a higher mean Hamilton Depression Rating Scale score and were more likely to be experiencing psychotic symptoms than those who had not developed a major depressive episode. Although the major depressive episodes of Alzheimer’s disease patients and nondemented elderly comparison subjects included similar numbers of depressive symptoms, patients with Alzheimer’s disease were more likely to report indecisiveness or a diminished ability to concentrate, and were less likely to experience sleep disturbances and feelings of worthlessness or excessive guilt during their depressive episodes.

The current findings suggest that the major depressive syndrome of Alzheimer’s disease may be one of the most frequently occurring mood disorders among older adults. (43 References)
Alzheimer’s disease is associated with hippocampal atrophy and loss of function of cortical neurons. In the randomized, double-blind, placebo-controlled study presented here, the authors examined the effect of the acetylcholinesterase inhibitor donepezil on magnetic resonance markers of neurodegeneration in patients with Alzheimer’s disease.

The sample was composed of 67 patients with mild to moderate Alzheimer’s disease. Over a period of 24 weeks, 34 were treated with donepezil (5 mg/day for the first 28 days and 10 mg/day thereafter), and 33 received placebo. The two groups were comparable in terms of age, race, gender, and severity of symptoms. The patients were reevaluated at six-week intervals to measure change from baseline in several outcome measures, including right, left, and total hippocampal volumes (measured with magnetic resonance imaging); brain concentrations of N-acetylaspartate (measured with proton magnetic resonance spectroscopy); and cognitive function (assessed with the Alzheimer’s Disease Assessment Scale cognitive subscale). In all, 51 (76%) of the 67 patients completed the study protocol (28 in the donepezil group and 23 in the placebo group). The results indicated that at some of the interim assessments, mean normalized measures of N-acetylaspartate concentration tended to be higher in the donepezil-treated patients than in the placebo-treated patients, but these differences were not significant at endpoint. At endpoint, as compared with the placebo-treated patients, the donepezil-treated patients had significantly smaller mean decreases in total and right hippocampal volumes and a smaller, nearly significant mean decrease in left hippocampal volume. Donepezil, relative to placebo, was associated with significantly greater improvements in cognitive function at every time point throughout the study (weeks 6, 12, 18, and 24).

According to the authors, the present findings raise the possibility that donepezil may have a beneficial effect on brain structure. While clearly needing confirmation, the current data suggest that in addition to providing cognitive benefits, donepezil may also slow the short-term progression of hippocampal atrophy in Alzheimer’s disease. (41 References)
MEMANTINE IN MODERATE-TO-SEVERE ALZHEIMER’S DISEASE

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N ENGL J MED, 348:1333-41, April 3, 2003

Glutamate, the principal excitatory neurotransmitter in the brain, stimulates a number of postsynaptic receptors, including the N-methyl-D-aspartate (NMDA) receptor. Overstimulation of the NMDA receptor by glutamate has been implicated in neurodegenerative disorders. The authors of the present study conducted a trial of the efficacy of memantine, an NMDA antagonist, in the treatment of outpatients with Alzheimer’s disease.

The sample consisted of 252 patients (82 men, 170 women; mean age, 76 years) who met criteria for moderate-to-severe Alzheimer’s disease and who were randomly assigned to receive placebo (N=126) or 20 mg of memantine daily (N=126) for a period of 28 weeks. The primary efficacy variables were the Clinician’s Interview-Based Impression of Change Plus Caregiver Input (CIBIC-Plus) and the Alzheimer’s Disease Cooperative Study Activities of Daily Living Inventory modified for severe dementia (ADCS-ADLsev). The secondary efficacy endpoints included the Severe Impairment Battery and other measures of cognition, function, and behavior. Treatment differences between baseline and endpoint were assessed. Missing observations were accounted for by using the most recent previous observation (the last observation carried forward). The data were also analyzed with only the observed values included, without replacing the missing values (observed-cases analysis). In all, 71 patients (42 assigned to placebo and 29 assigned to memantine) discontinued their assigned treatment before week 28; the remaining 181 (84 receiving placebo and 97 receiving memantine) completed the study and were evaluated at week 28. Patients receiving memantine had a better outcome than those receiving placebo, according to the results of the CIBIC-Plus (P=0.06 with the last observation carried forward, P=0.03 for observed cases); the ADCS-ADLsev (P=0.02 with the last observation carried forward, P=0.003 for observed cases); and the Severe Impairment Battery P<0.001 with the last observation carried forward, P=0.002 for observed cases). Memantine was not associated with a significant frequency of adverse events.

This study provides evidence that modulating NMDA receptors to reduce glutamate-induced excitotoxicity alleviates the symptoms of Alzheimer’s disease. This novel approach is distinct from the cholinomimetic mechanism of all currently approved treatments for Alzheimer’s disease. (27 References)
A RANDOMIZED PLACEBO-CONTROLLED TRIAL OF RISPERIDONE FOR THE TREATMENT OF AGGRESSION, AGITATION, AND PSYCHOSIS OF DEMENTIA

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J CLIN PSYCHIATRY, 64:134-43, February 2003

Agitation, aggression, and psychosis (delusions and hallucinations) complicate dementia in 60% to 90% of cases, with most symptoms appearing in the later stages of the disease. The prevalence of these symptoms is particularly high in nursing-home residents. In the randomized, double-blind, placebo-controlled trial presented here, the authors examined the efficacy and safety of risperidone, an atypical antipsychotic, for the treatment of aggression, agitation, and psychosis in elderly nursing-home patients with dementia.

A total of 345 elderly patients who had a DSM-IV diagnosis of dementia of the Alzheimer’s type, vascular dementia, or a combination of the two, and who exhibited significant aggressive behaviors were randomly assigned to receive a flexible dose of placebo (N=172) or risperidone (up to a maximum dose of 2 mg/day, N=173) for a period of 12 weeks. Outcome measures were the Cohen-Mansfield Agitation Inventory (CMAI), the Behavioral Pathology in Alzheimer’s Disease (BEHAVE-AD) rating scale, the Clinical Global Impression of Severity (CGI-S) scale, and the Clinical Global Impression of Change (CGI-C) scale. Of the 345 patients assigned to treatment, 337 received at least one dose of study drug (170 in the placebo group and 167 in the risperidone group). In all, 114 (67%) of the placebo-treated patients and 122 (73%) of the risperidone-treated patients completed the trial. All efficacy analyses were based on an intent-to-treat population. Efficacy was measured as the shift from baseline to endpoint in CMAI, BEHAVE-AD, and CGI scores. As assessed by the CMAI total aggression subscale, risperidone was significantly more effective than placebo in reducing aggression. This improvement was noted by week 4 and continued throughout treatment. Similar improvement was also seen in the risperidone group with regard to the CMAI total non-aggression subscale and the BEHAVE-AD total and psychotic symptoms subscales. At endpoint, CGI-S and CGI-C scores indicated significantly greater improvement in the risperidone group than in the placebo group. Overall, 94% of the risperidone group and 92% of the placebo group reported at least one adverse event.

The authors conclude that treatment with low-dose risperidone (mean dose=0.95 mg/day) resulted in significant improvement in the aggression, agitation, and psychosis associated with dementia. (28 References)
DIGEST of NEUROLOGY and PSYCHIATRY

Abstracts and Reviews of Selected Literature in Psychiatry, Neurology, and their Allied Fields

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A 21-YEAR LONGITUDINAL ANALYSIS OF THE EFFECTS OF PRENATAL ALCOHOL EXPOSURE ON YOUNG ADULT DRINKING

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ARCH GEN PSYCHIATRY, 60:377-85, April 2003

Contemporary accounts of the etiology of alcoholism typically acknowledge a range of determinants, including genetic, biological, psychological, and social factors. Recent evidence has begun to link fetal alcohol exposure with adolescent and adult substance use problems in humans. The authors of the present study used information gathered from interviews conducted with women in prenatal care during midpregnancy to predict alcohol-related outcomes assessed in their offspring at age 21 years.

From November 4, 1974, through October 2, 1975, assessments were made of maternal drinking during pregnancy, maternal smoking, use of caffeine and other drugs, and demographic factors. Family history of alcohol-related problems were evaluated by means of parental interviews when offspring were 14 years of age and updated when offspring were 21 years of age. Measures of parental use of alcohol and other drugs and several aspects of the family environment were assessed at seven different stages (prenatally through age 21). At age 21, 433 young adult offspring (227 men, 206 women) provided self-reports of drinking quantity and frequency and completed the Alcohol Dependence Scale (ADS) as a measure of alcohol-related problems and dependence. At the 21-year follow-up, 359 (82.9%) of the offspring considered themselves to be current drinkers, and 74 (17.1%) considered themselves to be current or lifelong alcohol abstainers. The subjects who considered themselves to be drinkers reported drinking an average of 5.77 times per month and imbibing an average of 3.79 drinks per drinking occasion. In all, 36.5% reported having five or more drinks on at least one occasion during the past month. Thirty-five (8.1%) of the 433 offspring scored 10 or higher on the ADS, which was indicative of at least a mild degree of alcohol dependence. Univariate, partial least squares, and regression analyses indicated that prenatal alcohol exposure was significantly associated with alcohol problems in offspring at 21 years of age. This relationship persisted independently of the effects of family history of alcohol problems, nicotine exposure, other prenatal exposures, and postnatal environmental factors, including parental use of other drugs. Prenatal nicotine exposure was not found to be associated with alcohol problems in offspring at age 21.

The current data provide evidence for a relationship between prenatal alcohol exposure and the degree of negative consequences that may result from heavy drinking in young adulthood. (48 References)
FAMILY TRANSMISSION OF MARIJUANA USE, ABUSE, AND DEPENDENCE

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 42:834-41, July 2003

Marijuana is the second most common substance used daily by adolescents in the United States. Marijuana use is associated with substantial clinical problems, including cognitive impairment, poor school performance, and a risk for developing abuse or dependence. In the present study, the authors examined the familial aggregation of marijuana-related behavior across three levels of severity (use, abuse, and dependence).

The study sample was composed of adolescents who were in residential or outpatient treatment for substance abuse and conduct problems, members of their families, and matched control families. A total of 2,546 individuals from 781 families were interviewed with structured research instruments. The treatment group consisted of 447 families with 447 adolescents in treatment, 186 fathers, 399 mothers, 171 brothers, and 144 sisters. The matched control group consisted of 334 matched adolescents, 248 fathers, 310 mothers, 165 brothers, and 142 sisters. Risk ratios were computed, and a family transmission analysis was utilized. Multiple-group (control and treatment) structural equation modeling was used to obtain maximum-likelihood estimates of (1) population prevalence rates for marijuana use, abuse, and dependence; and (2) family transmission parameters underlying spousal, parent-offspring, and sibling correlations for these behaviors. Compared with relatives of adolescents in the control group, relatives of adolescents in the treatment group had elevated rates of lifetime marijuana use, abuse, and dependence, with estimated risk ratios ranging from 1.5 to 3.3. There were significant spousal correlations across all three levels of severity (0.70 for use, 0.33 for abuse, and 0.40 for dependence). There were also significant parent-offspring and sibling correlations for all three measures of marijuana-related behavior, with parent-offspring correlations ranging from 0.17 to 0.30, and sibling correlations ranging from 0.34 to 0.44. Between 25% and 42% of the variance in the liability for adolescent marijuana-related behavior was attributable to factors transmitted from parents to children.

In the current investigation, the authors found familial aggregation of marijuana-related behavior across three measures of severity (use, abuse, and dependence). Their results suggest significant parent-offspring transmission of risk, sibling environmental influences, and assortative mating for all three levels of marijuana use. (43 References)
NEUROBEHAVIORAL DISINHIBITION IN CHILDHOOD PREDICTS EARLY AGE AT ONSET OF SUBSTANCE USE DISORDER

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AM J PSYCHIATRY, 160:1078-85, June 2003

Several studies have found an association between the liability for early age at onset of substance use disorder and a deficient capacity to control behavior and regulate emotion commensurate with situational demands. The authors of the present longitudinal investigation had three main objectives. First, they sought to examine the extent to which boys (age range, 10 to 12 years) at high average risk and low average risk for substance use disorder differed on a construct of neurobehavioral disinhibition, which was derived from measures of executive cognitive functioning, emotion regulation, and behavior control. Secondly, the researchers attempted to evaluate the extent to which neurobehavioral disinhibition predicted substance use frequency at mid-adolescence (age 16). Lastly, they sought to determine whether substance use disorder outcome at age 19 could be predicted by neurobehavioral inhibition.

Boys at high average risk for substance use disorder (N=47) were those whose biological fathers met DSM-III-R criteria for lifetime substance use disorder. Boys at low average risk (N=65) were those whose biological fathers had no history of lifetime substance use disorder or any other axis I or axis II disorder in adulthood. A baseline assessment was conducted when the boys were between the ages of 10 and 12, with follow-up evaluations being carried out when the boys were 16 years old and again when they were 19. The neurobehavioral disinhibition score significantly discriminated the boys at high average risk from those at low average risk when they were between the ages of 10 and 12 years. Neurobehavioral disinhibition at age 16, in conjunction with substance use frequency and risk status group, predicted substance use disorder at age 19 with 85% accuracy and accounted for 50% of the variance in Drug Use Screening Inventory overall problem density score. Neurobehavioral disinhibition was a stronger predictor of substance use disorder (odds ratio=6.83) than substance use frequency (odds ratio=3.19).

The current findings indicate that neurobehavioral disinhibition differentiates preadolescent boys who are at high and low average risk for a substance use disorder. The data also suggest that neurobehavioral disinhibition may not portend substance use but rather may be an indicator of liability to develop substance use disorder. (46 References)
PSYCHIATRIC MORBIDITY AND SUBSTANCE USE IN YOUNG PEOPLE AGED 13-15 YEARS: RESULTS FROM THE CHILD AND ADOLESCENT SURVEY OF MENTAL HEALTH

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BR J PSYCHIATRY, 182:509-17, June 2003

Psychoactive substance use has been found to be strongly associated with psychiatric morbidity in both adults and adolescents. In order to clarify which particular licit or illicit substances are most strongly linked with psychiatric disorders in early adolescence, the authors explored the relationship between psychiatric morbidity and smoking, drinking, and cannabis use in a sample of 2,624 adolescents (1,312 boys, 1,312 girls) who were between 13 and 15 years of age. Data were drawn from a national mental health survey of children living in England, Scotland, and Wales. The relationship between psychiatric morbidity and smoking, drinking, and cannabis use was examined by means of logistic regression analyses.

In all, 307 of the children were classified as having a psychiatric diagnosis; 66 were diagnosed with a depressive disorder, 104 were diagnosed with some other emotional disorder, and 137 were classified as having other (nonemotional) psychiatric disorders, such as disruptive behavior or pervasive developmental disorders. With regard to substance use, 286 adolescents were classified as regular drinkers (drank alcohol at least once a week), 222 considered themselves to be regular smokers, and 216 reported that they had used cannabis. Older age was a significant risk factor for use of all three substances (alcohol, tobacco, and cannabis). The 15-year-old adolescents were almost three times as likely to be regular smokers and regular drinkers as the 13-year-old children. Having a psychiatric disorder was associated with an increased risk of substance use. Smoking, drinking, and cannabis use were consistently interrelated, with more frequent use of any one substance carrying an increased risk for using the other two. Analyses of the interactions between smoking, drinking, and cannabis use indicated that the relationship between psychiatric morbidity and substance use could be primarily explained by regular smoking and that the risk for psychiatric disorder was additionally augmented by regular cannabis use.

In the current study, links between substance use and psychiatric disorders were primarily accounted for by smoking. The authors conclude that this strong relationship is likely to be due to a combination of underlying constitutional factors and drug-specific effects resulting from consumption over the period of adolescent growth and development. (31 References)
Persons living with a severe and persistent mental illness (SPMI) such as schizophrenia or bipolar disorder often abuse alcohol or other drugs. At least 20% of all individuals diagnosed with an SPMI have a current substance use disorder (SUD), and approximately 50% meet criteria for an SUD at some point during their lifetime (Regier et al., 1990). Persons with an SPMI routinely experience impairment in social and cognitive domains, while SUDs also engender cognitive, social, and psychiatric problems. It follows, therefore, that individuals dually diagnosed with an SPMI and an SUD would experience more cognitive, social, and psychiatric impairment than persons diagnosed with an SPMI alone. In the present investigation, the authors attempted to determine the extent to which variables representing cognitive function, social role function, and psychiatric status would be related to SUDs among outpatients diagnosed with an SPMI.

The study sample was composed of 56 outpatients (mean age, 38.2 years) who volunteered to complete diagnostic and social role function interviews, self-report inventories, and neuropsychological tests. The majority (64%) had a primary diagnosis of schizophrenia, with the remainder being assigned diagnoses of bipolar disorder (29%) or schizoaffective disorder (7%). All the participants had a history of psychiatric hospitalization, and nearly all (95%) were taking psychiatric medications. Fifteen patients (27%) met criteria for substance abuse or dependence within the past six months and were classified as current abusers; 26 (46%) had met full criteria for an SUD at one time but not within the last six months (former abusers), and 15 (27%) had never had an SUD (never abusers). Multinomial logistic regression analyses indicated that both current and former abusers reported more subjective feelings of distress than those who never abused substances. Contrary to expectations, however, both groups of substance abusers performed better on tests of nonverbal cognitive functioning than the group that had never had an SUD. Between-group differences were also found in the realm of social functioning, with former abusers demonstrating better instrumental role functioning than patients who never abused substances. No differences were found between current and former abusers.

According to the authors, the results of the present study challenge assumptions about the additive effects of comorbid disorders on cognitive and social functioning. (61 References)
THE ROLE OF DRINKING IN SUICIDAL IDEATION:
ANALYSES OF PROJECT MATCH DATA

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J STUD ALCOHOL, 64:402-8, May 2003

Although alcohol dependence is a potent risk factor for suicide (Harris & Barraclough, 1997), only about 7% of alcoholics actually commit suicide (Inskip et al., 1998). To examine the associations between suicidal ideation and both the intensity (drinks per drinking day) and frequency of alcohol consumption, the authors conducted a longitudinal study of 1,561 treated alcoholics (1,187 men, 374 women). Data were drawn from Project MATCH, a multi-site clinical trial of various psychosocial treatments for alcoholism. Measures of depression, general alcoholism severity, and antisocial personality disorder were included in multivariate analyses to ensure that any findings regarding drinking and suicidal ideation accounted for depression, and that drinking did not merely serve as a variable marker for more severe alcoholism. All analyses were stratified by gender. Assessments were conducted at study entry (baseline), and at three-, nine-, and 15-month follow-ups. Reports of suicidal ideation were based on the 30-day period prior to each assessment point.

Of the women in the study, 15.5% reported suicidal ideation at baseline; 6.4%, at the three-month follow-up; 3.6%, at the nine-month follow-up; and 5.4%, at the 15-month follow-up. Among the men, 9.9% reported suicidal ideation at study entry; 4.9%, at three months; 4.2%, at nine months; and 4.6%, at 15 months. Gender patterns were found in the associations between suicidal ideation and drinking. In female alcoholics, intense drinking (e.g., 12 drinks per drinking day) was associated with suicidal ideation regardless of the frequency of alcohol consumption, whereas light drinking (e.g., one drink per drinking day) was related to suicidal ideation only in the context of more frequent drinking (intensity-frequency interaction). Drinking intensity, but not drinking frequency, was a significant predictor of suicidal ideation in men. Antisocial personality in men, but not in women, was related to suicidal ideation. An association between depression and suicidal ideation was found in both men and women.

According to the authors, the fact that intensity of drinking, but not baseline alcoholism severity, was associated with suicidal ideation in both women and men suggests that drinking intensity is etiologically related to suicidal ideation and does not merely serve as a variable marker for a more severe subtype of alcoholism. (43 References)
Regular measurement of craving during substance abuse treatment may prove helpful in monitoring patients’ clinical status and potentially assessing their risk for using drugs in the near future. Effective treatment may reduce the correlation between craving and subsequent drug use by helping patients to abstain from drug use, despite the fact that they may be experiencing high levels of craving. The aim of the present study was to examine the associations among cocaine craving, psychosocial treatment, and subsequent cocaine use.

The current investigation was carried out in the context of the National Institute on Drug Abuse Collaborative Cocaine Treatment Study, which was designed to compare the effects of various psychosocial treatment regimens on cocaine-dependent outpatients. After screening and stabilization, patients were randomly assigned to one of four treatment conditions for 24 weeks: (1) individual drug counseling plus group drug counseling; (2) supportive-expressive psychodynamic therapy plus group drug counseling; (3) cognitive therapy plus group drug counseling; or (4) group drug counseling only. The sample was composed of 449 patients. Craving for cocaine was assessed weekly with a three-item version of the Cocaine Craving Scale, which yielded a composite score ranging from 0 to 27. A composite score of 1-5 indicated mild craving; 6-11, moderate craving; and 12-27, severe craving. Weekly cocaine use was assessed by means of self-reports and urine screenings. When the researchers controlled for the previous week’s cocaine use, they found that a higher composite score on the craving questionnaire was associated with a greater likelihood of cocaine use in the subsequent week; each 1-point increase on the composite score of the Cocaine Craving Scale increased the likelihood of cocaine use in the following week by 10%. However, among the patients who received individual drug counseling plus group drug counseling (the treatment condition with the best overall cocaine use outcome), increased craving scores were not associated with greater likelihood of cocaine use in the subsequent week.

In this study, a three-item questionnaire on cocaine craving predicted the relative likelihood of cocaine use during the subsequent week. The relationship between craving and subsequent cocaine use varied by treatment condition, suggesting that the most effective treatment in the study may have weakened the link between craving and subsequent use. (33 References)
BEHAVIORAL FAMILY COUNSELING AND NALTREXONE FOR MALE OPIOID-DEPENDENT PATIENTS

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Misuse of heroin and other opioids is on the rise in the United States, with recent data indicating that heroin has become the most common primary illicit substance used by individuals entering drug abuse treatment programs. Naltrexone is an opioid antagonist that has proven to be effective in blocking the subjective reinforcing effects of opioid-based drugs. In the present study, the authors compared the efficacy of behavioral family counseling (BFC) with that of individual-based treatment (IBT) in a sample of male opioid-dependent patients. The researchers predicted that BFC would produce better outcomes than IBT. More specifically, they hypothesized that BFC, in conjunction with a family-based naltrexone compliance contract, would produce better primary outcomes (greater abstinence from opioids), better intermediate outcomes (greater naltrexone compliance and longer retention in treatment), and better secondary outcomes (more abstinence from drugs other than opioids and more positive psychosocial functioning).

In all, 124 men who were seeking treatment for opioid dependence and who were living with a family member were randomly assigned to 24 weeks of BFC (N=62) or IBT (N=62). Patients in the BFC condition had both individual and family sessions and took naltrexone daily in the presence of a family member. Patients in the IBT condition were given naltrexone and were asked in counseling sessions about their compliance, but there was no family involvement. Outcome data were collected from patients and family members during and immediately after treatment and at quarterly follow-ups for 12 months posttreatment. The results indicated that compared with their IBT counterparts, BFC patients ingested more doses of naltrexone, attended more scheduled treatment sessions, stayed continuously abstinent longer, and had significantly more days abstinent from opioids and other illicit drugs during treatment and in the year after treatment. The BFC patients also had significantly fewer drug-related, legal, and family problems at the 12-month follow-up.

The current data provide support for the hypothesis that BFC produces better primary, intermediate, and secondary outcomes than IBT. According to the authors, a BFC daily “sobriety contract” or “recovery contract” may be a noncoercive way to encourage compliance with pharmacotherapy (e.g., naltrexone) and commitment to treatment and recovery. (40 References) EAF
THE ROLE OF PSYCHIATRIC DISORDERS IN PREDICTING
DRUG DEPENDENCE TREATMENT OUTCOMES

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AM J PSYCHIATRY, 160:890-5, May 2003

Previous research has shown that psychiatric disorders are common among people who abuse alcohol and drugs, but few studies have examined the relationship between psychiatric disorders and drug treatment outcome. In the present investigation, the authors studied comorbid psychiatric disorders in a group of drug-dependent subjects newly admitted to treatment (N=425) in order to evaluate the role of psychiatric disorders in predicting drug dependence treatment outcome. They successfully reinterviewed 401 of these individuals (94% of the baseline in-treatment sample) and determined their drug abuse status at 12-month follow-up. Outcome was measured in terms of the following: (1) number of illicit drugs used at follow-up; (2) number of DSM-III-R illicit drug dependence criteria met at follow-up; and (3) number of illicit drugs for which full DSM-III-R dependence diagnostic criteria were met at follow-up.

Any psychiatric disorder (defined as the presence of any comorbid condition other than alcohol dependence) was found in 74% of the sample. Alcohol dependence was the most common comorbid psychiatric disorder, with a prevalence of 63%. Other comorbid psychiatric diagnoses commonly found were antisocial personality disorder (44%), phobic disorder (41%), major depression (25%), dysthymia (12%), and generalized anxiety disorder (10%). Analyses indicated that several baseline psychiatric disorders predicted poorer outcomes at follow-up. For example, major depression predicted use of a larger number of illicit substances and the presence of more drug dependence diagnoses and symptoms. Alcohol dependence predicted more drug dependence diagnoses; antisocial personality disorder predicted use of a larger number of illicit substances, and generalized anxiety disorder predicted the presence of more drug dependence diagnoses. Among men, the presence of psychiatric disorders in general, the presence of major depression, and the presence of antisocial personality disorder were associated with poorer outcomes. Among women, the presence of phobias was predictive of a better treatment outcome.

These findings confirm the impact of different comorbid psychiatric disorders on substance abuse treatment outcomes. However, the manner in which outcomes were influenced depended on the specific comorbid psychiatric disorder and the patient’s gender. (22 References)
INDIVIDUAL AND SOCIAL/ENVIRONMENTAL PREDICTORS OF ALCOHOL AND DRUG USE 2 YEARS FOLLOWING SUBSTANCE ABUSE TREATMENT

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ADDICT BEHAV, 28:627-42, June 2003

Researchers and clinicians alike acknowledge the high rates of continued drug use following treatment for substance abuse. In the present investigation, the authors evaluated the interrelationships between client background characteristics and domains of risk for posttreatment substance use (interpersonal assets and social/environmental factors) measured early in treatment; they also examined ways in which these factors predicted alcohol and drug use two years following substance abuse treatment.

Participants were recruited from urban and suburban inpatient and outpatient substance abuse treatment centers. Subjects were asked to complete a series of self-report questionnaires within their first month of treatment and were requested to participate in a follow-up interview two years after the baseline assessment. Of 241 eligible participants, 180 completed the follow-up interview. Individual factors (coping, self-efficacy, resource needs, and expectations for sober fun), social/environmental factors (craving, exposure to substances, negative social influences, and involvement in substance-using leisure activities), and background characteristics measured during treatment were used to predict alcohol and drug use during follow-up by means of manifest variable regression analysis. The data showed that 76.1% of the sample used alcohol during follow-up. The average number of drinking days was 764.04. The average consumption on drinking days was 9.5 standard drinks, with 71.9% of the sample consuming five or more drinks per occasion. Approximately half of the participants (52.9%) used at least one other drug during follow-up: 34.1% used marijuana, and 31.1% used cocaine. The number of days of cocaine and marijuana use varied, with the average being 169 days for both substances. The results indicated that poorer self-efficacy, greater involvement in substance-using leisure activities, being single, and having a lower income directly predicted alcohol use. Greater resource needs, greater involvement in substance-using leisure activities, being a minority, and being single directly predicted drug use. Income, gender, problem severity, marital status, and race were also found to be indirect predictors of alcohol and drug use during follow-up.

The extent of posttreatment substance abuse found in the present study provides further evidence of the limited long-term effectiveness of substance abuse treatment and points to the need for additional strategies to prolong treatment effectiveness and deter relapse. (60 References)
BOOKS RECEIVED FOR REVIEW


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TREATMENT OF GENERALISED ANXIETY DISORDER WITH A SHORT COURSE OF PSYCHOLOGICAL THERAPY, COMBINED WITH BUSPIRONE OR PLACEBO

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J AFFECT DISORD, 72:267-71, December 2002

Generalized anxiety disorder (GAD) is one of the most commonly occurring anxiety disorders. Although pharmacotherapy has proven to be effective in the short-term treatment of GAD, the long-term nature of the disorder and the potential for relapse indicate that GAD patients would benefit from exposure to learning-based therapy. However, very few studies have examined the efficacy of combining drug therapy and psychological treatment for patients with GAD. In the present investigation, 60 patients (age range, 18 to 65 years) who met DSM-III-R criteria for GAD were randomly assigned to receive buspirone or placebo, combined with anxiety management training (AMT) or non-directive therapy (NDT), for a period of eight weeks.

Four treatment groups were designated as follows: buspirone and AMT, buspirone and NDT, placebo and AMT, and placebo and NDT. Buspirone (5 mg) and placebo were administered in a flexible manner, beginning with three capsules per day during the first week of treatment and then allowing for an increase of up to six capsules per day for the remainder of the trial. Patients were assessed at baseline (week 0), at mid-treatment (week 4), and at end of treatment (week 8). Rating instruments included the Hamilton Rating Scale for Anxiety, the Hospital Anxiety and Depression Scale, the Zung Self Rating Anxiety Scale, the General Health Questionnaire, and the Mood Rating Scale. Of the 60 patients who initially entered the trial, three dropped out before the first session of psychological treatment, five dropped out before the mid-treatment assessment, and eight left before the end of treatment. There were no baseline differences between patients who completed the trial and those who did not, although patients in the buspirone groups were more likely to drop out. Of the 44 patients (17 men, 27 women) who completed the trial, 11 received buspirone and AMT; seven, buspirone and NDT; 12, placebo and AMT; and 14, placebo and NDT. Composite anxiety scores at weeks 0, 4, and 8 revealed no significant differences between the treatment groups. A significant linear trend was found, indicating that all four treatment groups improved significantly between baseline and the end of the trial (week 8).

According to the authors, the current results suggest that a short course of psychological therapy, whether accompanied by active medication or not, is an effective treatment for patients with GAD. (24 References)
PREGABALIN IN GENERALIZED ANXIETY DISORDER: A PLACEBO-CONTROLLED TRIAL

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AM J PSYCHIATRY, 160:533-40, March 2003

Until recently, the pharmacotherapy of generalized anxiety disorder mainly has involved benzodiazepines, monoamine reuptake inhibitor antidepressants, and buspirone. In the double-blind, placebo-controlled study presented here, the authors evaluated the efficacy and safety of the novel agent pregabalin in the treatment of patients with this disorder.

Patients who met DSM-IV criteria for generalized anxiety disorder were randomly assigned to one of four treatment groups. In all, 276 (112 men, 164 women) received at least one dose of their assigned medication and were included in the intent-to-treat population. The four treatment conditions were as follows: pregabalin, 150 mg/day (N=69); pregabalin, 600 mg/day (N=70); lorazepam, 6 mg/day (N=68); and placebo (N=69). A one-week placebo lead-in was followed by a four-week, double-blind treatment phase, and then by a one-week dose taper. The primary efficacy measure was change in Hamilton Anxiety Rating Scale total score between baseline and endpoint (week 4 or last observation from the double-blind phase carried forward). Fewer patients given lorazepam (59%) completed the trial than did those given 150 mg/day of pregabalin (90%), 600 mg/day of pregabalin (71%), or placebo (73%). Hamilton Anxiety Rating Scale total scores decreased in all treatment groups over the course of the study. The mean baseline-to-endpoint decreases were significantly greater in the patients who received pregabalin, 150 mg/day, pregabalin, 600 mg/day, and lorazepam than in those who received placebo. An analysis of observed cases by week showed that relative to placebo, pregabalin, 600 mg/day, and lorazepam rapidly reduced mean Hamilton anxiety scale total scores, even as early as the week 1 observation. The adverse events reported most frequently by pregabalin-treated patients were somnolence and dizziness. No pregabalin-treated patients experienced a serious adverse event, and the discontinuation of pregabalin did not cause any significant withdrawal effects.

According to the authors, the results of the present investigation indicate that pregabalin is an effective, rapidly acting, and safe medication for the treatment of patients with generalized anxiety disorder. In short-term therapy, cessation of pregabalin does not appear to generate the withdrawal symptoms often associated with benzodiazepine discontinuation. (29 References)
PAROXETINE TREATMENT OF GENERALIZED ANXIETY DISORDER:
A DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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AM J PSYCHIATRY, 160:749-56, April 2003

Generalized anxiety disorder is characterized by excessive worry and anxiety centered around routine events and activities, such as work or academic performance. In the multi-site, double-blind, placebo-controlled study presented here, the authors assessed the efficacy of two fixed doses of paroxetine, a selective serotonin reuptake inhibitor, in the treatment of this illness.

Outpatients with generalized anxiety disorder and no other axis I disorder were eligible for the study if they had a score of at least 20 on the Hamilton Rating Scale for Anxiety (including a score of 2 or higher on the anxious mood and tension items). Following a one-week placebo run-in phase, the patients were randomly assigned to eight weeks of treatment with paroxetine (20 mg/day or 40 mg/day) or placebo. The primary outcome measure was change from baseline in total score on the Hamilton anxiety scale. Response was defined as a rating of “very much improved” or “much improved” on the Clinical Global Impression global improvement measure, while remission was denoted by a Hamilton anxiety scale score of 7 or less. Change in functional impairment was assessed by means of the Sheehan Disability Scale. Of 566 patients who were randomly assigned to a medication condition (intent-to-treat population), 426 (75.3%) completed the eight-week trial. Completion rates were not substantially different in the group given placebo (77.8%), the group given 20 mg/day of paroxetine (76.1%), or the group given 40 mg/day of paroxetine (72.6%). At eight weeks, reductions in total score on the Hamilton anxiety scale were significantly greater in both paroxetine-treated groups than in the placebo group. Response was achieved by 68% of the patients who received 40 mg/day of paroxetine, by 62% of those who received paroxetine, and by 46% of those who received placebo. Remission was attained by 36% of the 40 mg/day-paroxetine group, by 30% of the 20 mg/day-paroxetine group, and by 20% of the placebo group. On all three domains of the Sheehan Disability Scale (work, social life, and family life), significantly greater improvement was seen with paroxetine than with placebo. Both doses of paroxetine were well tolerated. Most adverse events were mild to moderate in severity, were apt to occur at the beginning of treatment, and were likely to diminish over time.

According to the authors, the current findings demonstrate that paroxetine appears to be an efficacious and well-tolerated treatment for patients with generalized anxiety disorder. (30 References)
Efficacy and Tolerability of Paroxetine for the Long-Term Treatment of Generalized Anxiety Disorder

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Several clinical studies have demonstrated the efficacy and tolerability of paroxetine in the short-term treatment of generalized anxiety disorder (GAD). The authors of the present investigation attempted to evaluate the long-term efficacy and safety profile of paroxetine by assessing the potential for relapse after discontinuation of medication.

In the single-blind treatment phase of the 32-week study, 652 adults who met DSM-IV criteria for GAD and who scored 4 or higher (moderately to extremely ill) on the Clinical Global Impressions-Severity of Illness (CGI-S) scale received paroxetine for eight weeks. Following this single-blind phase, patients whose CGI-S score had decreased by at least two points to a score of 3 or less (no illness or mild illness) entered the 24-week double-blind treatment phase and were randomly assigned to receive paroxetine (N=278) or placebo (N=288). The primary efficacy parameter was the proportion of patients who relapsed during the double-blind treatment phase. Relapse was defined as an increase of at least two points on the CGI-S (relative to the patient’s score at the end of the single-blind phase) to a score of 4 or higher, or withdrawal due to lack of efficacy. The results indicated that paroxetine-treated patients were significantly less likely than placebo-treated patients to relapse during the 24-week double-blind phase; only 10.9% of the paroxetine group relapsed, as compared with 39.9% of the placebo group. Placebo-treated patients were almost five times more likely to relapse than paroxetine-treated patients. Statistical significance in favor of paroxetine was demonstrated for all secondary efficacy parameters, including functional status. At the end of the double-blind phase, twice as many paroxetine-treated patients (73%) as placebo-treated patients (34.4%) were considered to be in remission from GAD. Paroxetine was well tolerated, with no unexpected adverse events being reported.

According to the authors, the results of their investigation clearly demonstrate the continued efficacy of paroxetine in the long-term treatment of patients with GAD. The researchers conclude that paroxetine is a logical choice for the long-term medical management of this common and disabling psychiatric disorder. (35 References)
FLUOXETINE FOR THE TREATMENT OF
CHILDHOOD ANXIETY DISORDERS

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 42:415-23, April 2003

Anxiety disorders affect up to 20% of children and adolescents. Although
childhood anxiety disorders are common and often accompanied by significant
morbidity, there are very little data to support the efficacy of pharmacotherapy
for youths with anxiety disorders. The purpose of the present study was to
assess the efficacy and tolerability of fluoxetine for the acute treatment of
children and adolescents with generalized anxiety disorder (GAD), separation
anxiety disorder (SAD), and/or social phobia (SP).

In all, 74 anxious youths (34 boys, 40 girls; age range, 7 to 17 years; mean
age, 11.8 years) with significant functional impairment were randomly assigned
to receive fluoxetine 20 mg/day (N=37) or placebo (N=37) for a period of 12
weeks. Most of the subjects had more than one anxiety disorder; 63% had GAD,
54% had SP, 47% had SAD, 24% had simple phobia, 5% had selective mutism,
and 1% had a prior panic disorder. Approximately 60% of the subjects had a
family history (parents and/or siblings) of anxiety and/or mood disorders.
Assessment instruments included the Clinical Global Impression scale, the
Pediatric Anxiety Rating Scale, and the Screen for Child Anxiety Related
Emotional Disorders. Fifty-nine subjects (80%) completed the 12-week protocol.
All measures indicated that fluoxetine was effective in reducing anxiety
symptoms and improving functioning. Using intent-to-treat analysis, the authors
found that 61% of fluoxetine-treated patients and 35% of placebo-treated
patients showed much to very much improvement. Despite this improvement,
however, a substantial group of patients remained symptomatic. Examination of
SP, GAD, and SAD as distinct disorders revealed that youths with SP and GAD
responded better to fluoxetine than to placebo, but only SP was a moderator of
clinical and functional response. Severity of the subject’s illness at intake and a
family history positive for anxiety disorders predicted a poorer functional
response at the end of the study. Fluoxetine was well tolerated; a few patients
experienced mild, transient headaches and gastrointestinal side effects.

According to the authors, these findings indicate that fluoxetine is an
efficacious and well tolerated drug for the acute treatment of children and
adolescents with anxiety disorders. They recommend that future research focus
on determining the optimal level and length of treatment needed to achieve full
remission and prevent recurrence. (38 References)
COGNITIVE-BEHAVIORAL TREATMENT OF GENERALIZED ANXIETY
DISORDER AMONG ADOLESCENTS: A CASE SERIES

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 42:327-30, March 2003

Studies exploring the age at onset of generalized anxiety disorder (GAD) have found that adult patients often spontaneously report having been worriers all their lives. In most individuals, GAD develops gradually during adolescence and reaches clinical significance during young adulthood. Despite the fact that GAD, together with specific phobias, is the anxiety disorder that occurs most frequently before the age of 18, few researchers have attempted to examine the characteristics of GAD in children and adolescents. In the present investigation, the authors evaluated the efficacy of a cognitive-behavioral treatment for a small group of adolescents with GAD.

Seven adolescents (three boys, four girls) participated in the study; three were 18 years old, three were 17, and one was 16. The Anxiety Disorders Interview Schedule for DSM-IV (ADIS-IV) was used to diagnose participants and evaluate treatment outcome. Other assessment instruments included the Penn State Worry Questionnaire, the Worry and Anxiety Questionnaire, the Worry Domains Questionnaire-Adolescent form, the Beck Anxiety Inventory, and the Children’s Depression Inventory. Daily self-monitoring of time spent worrying each day was done during baseline, treatment, and follow-up assessments. One-hour therapy sessions were conducted weekly, with treatment consisting of awareness training, worry interventions, and relapse prevention. The worry interventions specifically targeted intolerance of uncertainty, beliefs about worry, problem solving, and cognitive avoidance. According to the ADIS-IV evaluation of GAD diagnostic criteria, scores on self-report questionnaires, and reports of time spent worrying every day, three adolescents experienced a clinically significant decrease in GAD symptoms at post-test (after receiving cognitive-behavioral treatment), and this improvement was maintained at the six- and 12-month follow-up assessments. Two participants showed a moderate decrease in GAD symptoms, with this improvement being partly maintained at both follow-up assessments. Another remained basically unchanged at post-test and failed to complete the follow-up assessments. One of the seven adolescents did not complete treatment, dropping out after the fifth therapy session. For the six completers, the average length of treatment was 13.2 sessions.

Despite some limitations (e.g., small sample size, study design), the authors note, the present case series report appears to indicate that it is possible to treat adolescent GAD with interventions derived from a specific conceptualization of excessive worry. (21 References)
COGNITIVE-BEHAVIORAL TREATMENT OF LATE-LIFE GENERALIZED ANXIETY DISORDER

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J CONSULT CLIN PSYCHOL, 71:309-19, April 2003

Given its time-limited, symptom-focused, and collaborative nature, cognitive-behavioral therapy (CBT) may be a useful approach for treating anxiety disorders in older adults. The primary goals of the present study were: (1) to assess the efficacy of CBT, relative to a minimal contact control condition (MCC), in older adults (age 60 years and over) with generalized anxiety disorder (GAD); (2) to evaluate the effects of treatment on primary outcome variables (worry and anxiety), coexistent symptoms (depressive symptoms and specific fears), and quality of life through the use of both self-report inventories and independent clinician ratings of symptom severity; and (3) to examine the durability of treatment over a follow-up interval of one year.

The initial sample was composed of 85 older adults (21 men, 64 women; mean age, 66.2 years) who met DSM-IV diagnostic criteria for GAD. After the pretreatment assessment, but before randomization, five participants dropped out. The remaining 80 were randomly assigned (in small groups of four to six members) to CBT (N=39) or MCC (N=41). CBT sessions were conducted weekly for a period of 15 weeks. Specific components included education and awareness training (Session 1), progressive deep muscle relaxation (Sessions 2-5), cognitive therapy (Sessions 6-10), and graduated exposure (Sessions 10-15). Of the 80 subjects randomly assigned to CBT or MCC, 14 dropped out of the study before the posttreatment assessment; there were no differences in dropout rates between the two treatment conditions. An additional two participants dropped out of the study over the course of the one-year follow-up period. Results of both intent-to-treat analyses and completer analyses revealed that the CBT group, relative to the MCC group, exhibited significant improvement in worry, anxiety, depression, and quality of life. At posttreatment, 45% of those who received CBT, but only 8% of those who received MCC, were classified as treatment responders. At posttreatment, 55% of the CBT group continued to meet criteria for GAD, as compared with 81% of the MCC group. While most gains made by subjects in the CBT group were maintained or enhanced over the course of the one-year follow-up, posttreatment scores for those who participated in CBT failed to indicate a return to normative functioning.

According to the authors, the current data provide support for the potential use of CBT in treating late-life GAD. (67 References)
A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF CLASSICAL HOMEOPATHY IN GENERALIZED ANXIETY DISORDER

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J CLIN PSYCHIATRY, 64:282-7, March 2003

The use of alternative medicine is increasing rapidly in the United States. Homeopathy, a form of alternative medicine, is commonly used to treat medical and psychological conditions. However, its prevalent use has not been supported by robust, methodologically sound research. In the study presented here, the authors evaluated the efficacy of homeopathy in the treatment of generalized anxiety disorder (GAD), a mental disorder characterized by an enduring pattern of excessive apprehension and distress and by mental and bodily complaints.

Forty-four patients (18 men, 26 women; mean age, 46.1 years) who met DSM-IV criteria for GAD entered a 10-week, randomized, double-blind, placebo-controlled trial of individually tailored homeopathic remedy. Homeopathic therapy was administered by an expert who followed the traditional routines of homeopathic diagnosis and prescription. The main outcome measure was the Hamilton Rating Scale for Anxiety (HAM-A). Additional assessment tools included the Brief Symptom Inventory, the Psychological General Well-Being Index, the Hamilton Rating Scale for Depression, the Beck Depression Inventory, Spielberger's State-Trait Anxiety Inventory, and a visual analogue scale of subjective distress. Psychiatric assessments were carried out at pretreatment, at mid-study (five weeks), and at posttreatment (10 weeks). Of the 44 participants initially randomized to homeopathic medication (N=22) or placebo (N=22), three (one from the active drug group and two from the placebo group) were not available for the five-week evaluation, and an additional two dropped out before the end of the study. In all, 39 subjects completed the study (20 from the homeopathic drug group and 19 from the placebo group) and were available for the final psychiatric assessment. A consistent pattern of response was observed for the HAM-A and most of the other rating scales: (1) a nonsignificant group main effect, (2) a significant time main effect, and (3) a nonsignificant group-by-time interaction. The main improvement in most psychometric scores occurred between the initial and mid-study assessments, with less change being observed thereafter. Eight subjects in each group met criteria for clinical response, with no significant between-group differences. Two subjects in each group met standard criteria for remission at both the five- and 10-week evaluations.

According to the authors, the results of the current study show no clinical or statistical advantage for homeopathic therapy over placebo in the treatment of GAD and associated symptoms. (39 References)
CAPSULOTOMY FOR REFRACTORY ANXIETY DISORDERS: LONG-TERM FOLLOW-UP OF 26 PATIENTS

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AM J PSYCHIATRY, 160:513-21, March 2003

In some instances, patients with severe anxiety disorders may benefit from neurosurgery. The objective of the present study was to evaluate the long-term efficacy and safety of capsulotomy in patients with nonobsessional anxiety disorders. Capsulotomy is a procedure whereby bilateral lesions are produced in the anterior limb of the internal capsule.

Twenty-six patients (11 men, 15 women) who had undergone stereotactic, bilateral thermocapsulotomy were followed up one year after the procedure (short-term) and again after a mean of 13 years (long-term). The primary diagnoses of the patients were generalized anxiety disorder (N=13), panic disorder (N=8), and social phobia (N=5). Patients were assessed by a number of psychiatric status rating scales and a battery of neuropsychological tests. Ratings were done by two investigators who were not involved in patient selection or postoperative treatment. A quantitative magnetic resonance imaging (MRI) evaluation was conducted to search for common anatomic denominators. Eighteen of the 26 patients were available for the long-term follow-up; 17 were interviewed in person, and one, by telephone. Relatives of these 18 patients were also interviewed. For the study sample as a whole (26 patients), the mean preoperative Brief Scale for Anxiety score was 22. At the one-year follow-up (25 patients), the mean score was 4.6, and at the long-term follow-up (18 patients), it was 9.9. The reduction in anxiety ratings was significant at both short- and long-term follow-up. At the one-year follow-up, 92% of the patients (23/25) were considered to be responders; at the long-term follow-up, 67% (12/18) were classified as responders. At long-term follow-up, seven patients were rated as impaired with regard to clinical frontal lobe functioning. The most prominent adverse symptoms were apathy and executive dysfunction. Neuropsychological performance was significantly poorer in the patients with adverse symptoms. Analysis of the MRI scans failed to reveal any common anatomic denominators in the responders.

According to the authors, thermocapsulotomy appears to be an effective treatment for selected cases of nonobsessional anxiety. However, they note, this procedure may carry a significant risk for adverse symptoms indicative of impaired functioning of the frontal lobe. (33 References)
A FOLLOW-UP STUDY OF DSM-III-R GENERALIZED ANXIETY DISORDER WITH SYNDROMAL AND SUBSYNDROMAL MAJOR DEPRESSION

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J AFFECT DISORD, 73:229-36, February 2003

Comorbidity may be studied at the level of either individual symptoms/traits (dimensional analyses) or formal diagnostic categories (syndromal analyses). Generalized anxiety disorder (GAD) and major depression (MD) frequently occur together at both syndromal and subsyndromal levels. Using both categorical and dimensional analyses, the authors of the present report prospectively examined the course of syndromal and subsyndromal depressive symptoms in patients with a primary DSM-III-R diagnosis of GAD.

Thirty-nine outpatients (12 men, 27 women) with GAD and concomitant depressive symptoms, both with (N=23) and without (N=16) syndromal MD, participated in an 11-week clinical trial of adinazolam. Approximately 18 months after the initial baseline screening, they were re-evaluated by means of a structured diagnostic interview and a battery of rating scales. While the sample appeared to be relatively homogeneous at baseline, by the 18-month follow-up, three distinct groups were discernible. Twenty-three patients (59%) continued to meet criteria for syndromal GAD, 10 patients (26%) were in partial remission with subsyndromal symptoms of GAD, and six patients (15%) were in complete remission. Of the 23 patients who had syndromal MD at the baseline evaluation, 13 (56%) continued to meet criteria for syndromal MD at follow-up. Chi-square analysis indicated a significant relationship between comorbid MD and GAD at follow-up. All of the patients who met criteria for syndromal MD at follow-up continued to meet criteria for syndromal GAD as well. Further chi-square analyses showed that gender, marital status, presence of comorbid MD, simple or social phobia, and previous episodes of GAD were not significant factors in terms of differentiating patients who remained syndromal for GAD or MD from those who were subsyndromal or in remission at follow-up.

According to the authors, their findings lend support to the validity of the diagnosis of GAD made at the time of the baseline interview. The fact that 85% of the patients in this study still had syndromal or subsyndromal symptoms of GAD at long-term follow-up serves to demonstrate the chronic nature of this disorder and fits well with the conceptualization of GAD as a “hard-wired,” stable pattern of lifelong emotional reactivity that has been labeled by Akiskal (1998) the “anxious temperament type.” Patients with subsyndromal anxiety and depressive symptoms may be at special risk for syndromal disorders over time, the authors conclude. (36 References)
DIGEST of NEUROLOGY and PSYCHIATRY

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**BOOKS RECEIVED FOR REVIEW**
VENTRICULAR AND PERIVENTRICULAR STRUCTURAL VOLUMES IN FIRST- VERSUS MULTIPLE-EPISODE BIPOLAR DISORDER

Stephen M. Strakowski, MD (Bipolar and Psychotic Disorders Research Program, Dept. of Psychiatry, Univ. of Cincinnati College of Medicine, Cincinnati, OH 45267-0559; e-mail: strakosm@e-mail.uc.edu); Melissa P. DelBello, MD; Molly E. Zimmerman, MA; Glen E. Getz, MA; Neil P. Mills, BS; Jennifer Ret, BA; Paula Shear PhD; and Caleb M. Adler, MD

AM J PSYCHIATRY, 159:1841-7, November 2002

Ventriculomegaly has been found in patients with bipolar disorder, although it is not known whether such ventricular enlargement occurs at illness onset or progresses over the course of the disorder. It has also not been determined whether ventriculomegaly in bipolar disorder reflects acquired volume loss or underdevelopment of periventricular structures. The authors hypothesized that bipolar patients who had experienced multiple episodes would have larger ventricles than bipolar patients who were experiencing their first episode and that ventricular volumes would be associated with course of illness.

The study sample was composed of 32 healthy subjects (16 males, 16 females; mean age, 24 years) and 35 inpatients who met DSM-IV criteria for bipolar disorder, type I, with a manic or mixed current episode. Of the bipolar patients, 18 (11 males, seven females; mean age, 22 years) met criteria for the “first-episode group,” and 17 (six males, 11 females; mean age, 25 years) met criteria for the “multiple-episode group.” All patients and healthy subjects underwent magnetic resonance imaging (MRI) scanning. MRI was used to measure lateral and third ventricular volumes as well as periventricular structures. The periventricular structures measured included the thalamus, which is adjacent to the lateral and third ventricles; the hippocampus, which abuts the temporal horn of the lateral ventricle; and the striatum (i.e., caudate and putamen), which bounds the main body of the lateral ventricles. The multi-episode patients had significantly larger lateral ventricles than the first-episode patients and the healthy subjects, even after periventricular and total cerebral volumes were taken into account. Having larger lateral ventricles was found to be associated with having a higher number of prior manic episodes. The total cerebral volume of the multiple-episode patients was smaller than that of the healthy subjects but not smaller than that of the first-episode patients. The putamen was significantly larger in the first-episode patients (and nearly so in the multiple-episode patients) than in the healthy subjects, although there was no difference between the patient groups.

The authors conclude that while lateral ventriculomegaly was found to be greater in multiple-episode bipolar patients, it did not appear to be secondary to small critical periventricular structures. The current data emphasize the importance of prospectively studying neuroanatomic changes in patients with bipolar disorder. (24 References)
Suicidality is commonly encountered in patients with bipolar disorder. Among bipolar patients who survive a first suicide attempt, however, little is known about likelihood of subsequent attempts or clinical features that could be relevant predictors of future attempts. The authors compared bipolar patients who had made one suicide attempt with those who had made more than one attempt on a wide range of demographic and clinical characteristics.

The study sample consisted of 52 adults (age range, 21 to 74 years; mean age, 43.37 years) who met DSM-IV criteria for bipolar I (N=43) or bipolar II disorder (N=9) and who had a documented history of at least one suicide attempt. Circumstances surrounding each lifetime suicide attempt were ascertained by means of direct interviews, questionnaires, and chart reviews. Information was also obtained with regard to family psychiatric histories, substance abuse histories, current psychopathology, and features of impulsivity and aggression. Of the 52 subjects, 19 had made only one suicide attempt over the course of their lifetime, and 33 had made multiple suicide attempts (two or more). The single and multiple attempters did not differ significantly in terms of major demographic variables, mean number of years ill, mean number of years since first suicide attempt, mean number of hospitalizations, proportion with a bipolar II diagnosis, percent with a history of rapid cycling, family history of bipolar disorder, or history of alcohol abuse. However, bipolar patients who made and survived a single suicide attempt were more likely than those who made multiple attempts to demonstrate high seriousness of suicidal intent at their first attempt. Each incremental increase in seriousness of intent was associated with a 65% diminished likelihood of making a subsequent suicide attempt. Single attempters were more likely than multiple attempters to be in a mixed affective state at the time of the attempt. Among multiple attempters, seriousness of suicidal intent at first attempt was significantly correlated with seriousness of intent at second attempt; this association also held true across the second and third attempts.

The authors conclude that multiple suicide attempts are common among bipolar patients. Bipolar patients who survive an initial suicide attempt involving a high degree of seriousness of intent appear less likely than those with a lower degree of seriousness of intent to make later attempts. Thus, single attempters may more closely resemble suicide completers, rather than those who make subsequent attempts. In bipolar patients, multiple suicide attempts are not necessarily associated with a higher risk of lethality among those who have survived a first suicide attempt. (22 References)
The authors studied the longitudinal symptom structure of bipolar I disorder (BP-I). Analyses were based on an ongoing follow-up of 146 patients with BP-I (65 males, 81 females; mean age, 39.2 years). Weekly affective symptom status ratings were analyzed by polarity and severity, with levels ranging from asymptomatic to subthreshold to full-blown major depressive and/or manic. Throughout follow-up, percentages of follow-up weeks at each level and number of shifts in symptom status and polarity were examined. In addition, two new measures of chronicity were evaluated in relation to previously identified predictors of chronicity in BP-I: (1) total percentage of follow-up weeks that patients experienced the full syndromal level of major depressive or manic symptoms, (2) and total percentage of follow-up weeks they experienced any affective symptoms at any level of severity.

Throughout follow-up (mean, 12.8 years), patients were symptomatically ill nearly half of the time (47.3% of total follow-up weeks). Patients experienced three times more depressive symptoms (31.9% of total follow-up weeks) than manic symptoms (9.3% of follow-up weeks), and depressive symptoms were found to occur five times more frequently than cycling/mixed symptoms (5.9% of follow-up weeks). Subsyndromal and minor depressive/dysthymic symptoms (22.9% of weeks) were much more prevalent than syndromal-level major depressive symptoms (8.9% of weeks). Subsyndromal manic and hypomanic symptoms (7% of weeks) were three times more common than symptoms at the threshold for mania (2.3% of weeks). Overall, most symptomatic weeks involved subsyndromal, minor depressive, and hypomanic symptoms (74%). Patients experienced changes in symptom status an average of six times per year and shifts in symptom polarity an average of more than three times per year. Greater chronicity during follow-up was found to be significantly associated with four predictors: poor social functioning in the five years prior to intake; longer duration of intake episode; depressive-only or cycling/mixed (versus manic-only) polarity of the intake episode; and comorbid drug-use disorder.

The authors conclude that the longitudinal weekly symptomatic course of BP-I is chronic. Overall, the symptomatic structure is primarily depressive rather than manic, and subsyndromal and minor affective symptoms predominate. Symptom severity levels fluctuate, often within the same patient, over time. BP-I is expressed as a dimensional illness that features the full spectrum of affective symptom severity and polarity. (29 References)
The aim of the present investigation was to determine whether “switching” (i.e., the direct transition from one mood polarity the other) has significant prognostic implications in patients with bipolar disorder. The study sample was composed of 97 bipolar patients (44 men, 53 women; mean age at time of recruitment, 43.6 years) whose first prospectively observed episode included at least one mood polarity switch (“switchers”) and 97 bipolar patients (46 men, 51 women; mean age at time of recruitment, 42.8 years) whose index episode was monophasic (“nonswitchers”). The two groups were compared in terms of the following variables: demographic and historical variables, symptomatic features of the index episode, time to recovery from the index episode, time spent in an affective episode during a prospective observation period, and psychopathological and psychosocial outcome at a 10-year follow-up interview.

Of the 97 switchers, 74 (76.3%) had an index episode characterized by one mood polarity switch, and 23 (23.7%) had an index episode characterized by at least two mood polarity switches (polyphasic episode). Among the 74 patients with only one mood polarity switch, the first period of abnormal mood was depressive in 33 (44.6%) and manic/hypomanic in 41 (55.4%). Among the 23 patients with at least two mood polarity switches, the first period of abnormal mood was depressive in 17 (73.9%) and manic/hypomanic in six (26.1%). Patients whose index episode included at least two mood polarity switches spent significantly more time in an affective episode during the observation period and had a significantly poorer psychopathological and psychosocial outcome 10 years after recruitment than those patients whose index episode included only one polarity switch or those patients whose index episode was monophasic (nonswitchers). Patients whose polyphasic index episode started with depression spent a significantly greater proportion of time in an affective episode and had a significantly poorer 10-year outcome than patients whose index episode started with mania or hypomania. Retention of the switching pattern throughout the observation period was seen in 65.2% of the patients whose index episode started with depression and in 42.4% of those whose index episode started with mania or hypomania.

In bipolar patients, the researchers conclude, an index episode that includes at least two mood polarity switches, especially if it starts with depression, appears to be associated with a poor long-term outcome. This pattern, the authors note, represents a significant target for new pharmacological and psychosocial treatment strategies. (27 References)
OBESITY AS A CORRELATE OF OUTCOME IN PATIENTS WITH BIPOLAR I DISORDER

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AM J PSYCHIATRY, 160:112-7, January 2003

In the investigation presented here, the authors examined the relationships between obesity and several indicators of severity of illness (including the likelihood of a recurrence) in 175 patients who had a diagnosis of bipolar I disorder and who had been treated for an acute affective episode and then followed throughout a period of maintenance treatment. The study sample was composed of 76 men and 99 women who had entered the Maintenance Therapies for Bipolar Disorder protocol between 1991 and 2000. Analyses focused on differences between obese and nonobese patients with regard to baseline demographic and clinical characteristics and treatment outcomes.

Of the 175 patients with bipolar I disorder, 62 (35.4%) met criteria for obesity, and 113 (64.6%) were not considered to be obese. Compared with the nonobese group, the obese group had significantly fewer years of education, more previous depressive episodes, more previous manic episodes, and higher baseline scores on the 17-item Hamilton Depression Rating Scale. The obese patients also required more time in the acute phase of treatment to achieve stable remission. Among the 125 patients who completed the acute phase of treatment and entered the maintenance phase, the percentage experiencing a recurrence was higher in the obese group (54.3%) than in the nonobese group (35.4%). A Kaplan-Meier survival analysis confirmed that the time to recurrence for patients who were obese at baseline was significantly shorter than the time to recurrence for those who were not obese at baseline. Significantly more obese (32.6%) than nonobese (13.9%) patients experienced depressive recurrences. A Kaplan-Meier survival analysis confirmed that time to depressive recurrence was significantly shorter in the obese group.

According to the authors, obesity is correlated with several indicators of poor prognosis and outcome in patients with bipolar I disorder. Preventing and treating obesity in bipolar patients could decrease the morbidity and mortality related to physical illness, enhance psychological well-being, and potentially improve the course of bipolar illness. The researchers support the development and testing of weight-control interventions specifically designed for patients with bipolar disorder and the implementation of these interventions in the routine care of bipolar patients. (27 References)

EAF
In light of the observed association between panic disorder and bipolar disorder and the possible negative influence of panic symptoms on the course of bipolar illness, the authors of the present investigation evaluated the effects of what they defined as “panic spectrum” conditions on the clinical course and treatment outcome in patients with bipolar I (BPI) disorder. They hypothesized that lifetime panic spectrum features would be associated with higher levels of suicidal ideation and a poorer response to acute treatment of the index affective episode in this patient population.

The study sample consisted of 66 patients (29 males, 37 females; age range, 18 to 61 years; mean age, 35.1 years) who met criteria for BPI disorder and who completed a self-report measure of lifetime panic-agoraphobic spectrum symptoms. The term “panic-agoraphobic spectrum” was used to refer to a broad array of features associated with DSM-IV panic disorder, including typical and atypical manifestations of core panic symptoms (such as panic-like somatic symptoms, anxious expectation, and agoraphobia), as well as a range of related temperamental or behavioral features (categorized as separation anxiety, stress sensitivity, medication sensitivity, illness-related phobias, and reassurance seeking). Patients whose self-report scores fell above and below a predefined clinical threshold for panic spectrum were compared in terms of clinical characteristics, presence of suicidal ideation during acute treatment, and acute treatment response. Of the 66 patients, 33 (50%) reported panic spectrum features above the predefined clinical threshold. These lifetime features were associated with more prior depressive episodes, higher levels of depressive symptoms, and greater suicidal ideation during the acute-treatment phase. In addition, the patients who reported high lifetime panic-agoraphobic spectrum symptom scores took 27 weeks longer than those who reported low scores to remit with acute treatment (44 weeks versus 17 weeks, respectively).

According to the authors, the current findings emphasize the crucial importance of assessing a broader range of panic features than those represented by the DSM-IV criteria for panic disorder. The data also highlight the importance of monitoring suicidal symptoms in bipolar patients who present with depressed or mixed symptom profiles that are complicated by panic spectrum features. (38 References)
A COMPARISON OF THE EFFICACY, SAFETY, AND TOLERABILITY OF DIVALPROEX SODIUM AND OLANZAPINE IN THE TREATMENT OF BIPOLAR DISORDER

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J CLIN PSYCHIATRY, 63:1148-55, December 2002

In this randomized, 12-week, double-blind, parallel-group, multicenter study, the authors evaluated the efficacy, safety, and tolerability of divalproex and olanzapine in the treatment of acute mania associated with bipolar disorder. The sample comprised 120 subjects who met DSM-IV criteria for bipolar disorder type I and who were hospitalized for treatment of an acute manic episode; 63 (35 males, 28 females; mean age, 38.9 years) were randomly assigned to receive divalproex, and 57 (30 males, 27 females; mean age, 38.1 years) were assigned to olanzapine. After an inpatient period of up to 21 days, the subjects were followed as outpatients for up to 84 days. Efficacy measures included the Mania Rating Scale (MRS), the Brief Psychiatric Rating Scale (BPRS), the Hamilton Rating Scale for Depression (HAM-D), and the Clinical Global Impressions-Part I, Severity of Illness scale (CGI-S). Safety and tolerability variables included changes in body weight from baseline to final evaluation and spontaneous reports of adverse events.

No significant differences were found between the two groups with regard to mean changes in MRS scores from baseline to day 21 of the study (−14.8 for the divalproex group, −17.2 for the olanzapine group). Mean changes in BPRS, HAM-D, and CGI-S scores from baseline to day 21 were similar in both treatment groups. No significant treatment differences were found for any efficacy variable in terms of changes from baseline to day 84, and the improvements in efficacy observed at day 21 persisted throughout the study. Mean changes in body weight from baseline to final evaluation were significantly greater in the olanzapine group (+8.8 lb [+4.0 kg]) than in the divalproex group (+5.5 lb [+2.5 kg]). Somnolence, weight gain, rhinitis, edema, and speech disorder (i.e., slurred speech) were each reported as an adverse event in a significantly greater proportion of olanzapine-treated than divalproex-treated subjects. No adverse events occurred significantly more often in the divalproex group. One olanzapine-treated subject died during the study; death was attributed to diabetic ketoacidosis.

The authors conclude that no significant differences in efficacy were found between divalproex and olanzapine. However, they note, divalproex was associated with a more favorable adverse-event profile and with significantly less weight gain. (33 References)
FEATURES ASSOCIATED WITH THE DELAYED INITIATION OF MOOD STABILIZERS AT ILLNESS ONSET IN BIPOLAR DISORDER

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While bipolar disorder remains highly prevalent in the general population, some studies have found delays of eight years or longer in the time between initial onset of symptoms and formal diagnosis of an affective disorder. Relatively little is known about the extent to which delays in the initiation of appropriate treatment influence the course, morbidity, and mortality of bipolar illness. The authors attempted to determine whether delays in the initiation of appropriate pharmacotherapy would negatively affect course of illness, functional outcome, and lifetime suicide risk among individuals with bipolar disorder.

The study sample was composed of 56 adult patients (mean age, 40.8 years) who met DSM-IV criteria for bipolar I disorder (N=46), bipolar II disorder (N=7), or bipolar disorder not otherwise specified (N=3). Lifetime affective episodes, traced to the initial onset of manic or depressive symptoms, were documented by means of the retrospective Life Chart Method (Leverich and Post, 1996). Information on pharmacotherapies and other treatment interventions was obtained through semistructured interviews. Efforts were made to obtain corroboration from prior medical or pharmacy records, family members, and/or patients’ treating psychiatrists. Lag times to the initiation of treatment with a mood stabilizer (after initial symptom onset and/or first lifetime affective episode) were assessed relative to functional outcome and history of lifetime suicide attempts. Of the 56 subjects, 38 (67.9) received some form of psychiatric treatment for their first lifetime affective episode; 30 (53.6%) received pharmacotherapy during their first affective episode. The mean lag time from initial symptom onset to any form of psychiatric treatment (typically psychotherapy alone) was 2.1 years, while the lag time until first mood stabilizer treatment was 9.8 years. A longer lag time (in years) between initial symptom onset and mood stabilizer initiation was significantly associated with poorer social adjustment in the past year, a greater number of annual hospitalizations, and a substantially increased risk for making a lifetime suicide attempt. Delayed initiation of mood stabilizers adversely affected outcome in these domains, regardless of whether the polarity of the index episode was manic or depressive. Prolonged delays to bipolar diagnoses and mood stabilizer initiation were associated with earlier age at affective symptom onset and milder severity of initial symptoms.

According to the authors, the current data indicate that the first few symptomatic years of bipolar illness may have a substantial impact on the future course of the disorder. Efforts to minimize delays in initiating appropriate pharmacotherapy during this time could prove to be essential in attempting to diminish adverse outcomes. (37 References)
A RANDOMIZED TRIAL COMPARING PAROXETINE AND VENLAFAXINE IN THE TREATMENT OF BIPOLAR DEPRESSED PATIENTS TAKING MOOD STABILIZERS

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J CLIN PSYCHIATRY, 63:508-12, June 2002

The treatment of depression in patients with bipolar disorder represents an understudied area in psychiatric research. While clinical trials assessing the efficacy of antidepressants generally have utilized a monotherapy design, monotherapy is more the exception than the rule, and most guidelines recommend using a combination of mood stabilizers and antidepressants, particularly when treating “breakthrough” episodes that occur during therapy with mood stabilizers. The aim of the present study was to assess the efficacy and safety of paroxetine and venlafaxine in the treatment of bipolar depressed patients who were already receiving mood stabilizers and to evaluate the potential for each of these drugs to induce mania or hypomania.

The subjects were 60 patients who met DSM-IV criteria for bipolar disorder and who presented with a major depressive episode while receiving mood stabilizers. Each scored over 17 on the 17-item Hamilton Rating Scale for Depression (HAM-D), and the blood levels of their mood stabilizers fell within therapeutic ranges. The patients were randomly assigned to receive either paroxetine (N=30) or venlafaxine (N=30) for six weeks in a single-blind manner. At the baseline visit, they were assessed with the HAM-D, the Young Mania Rating Scale (YMRS), and the Clinical Global Impressions (CGI) scale. HAM-D, YMRS, and CGI ratings were also obtained at week 1, week 2, week 4, and week 6 (endpoint). Spontaneous reports of adverse events were collected at each visit. Significant improvements in HAM-D scores between baseline and endpoint were seen in paroxetine-treated and venlafaxine-treated patients. There were no significant differences between the two drugs with regard to either safety or efficacy measures. According to intention-to-treat analysis, 43% (N=13) of paroxetine-treated patients and 48% (N=14) of venlafaxine-treated patients were considered to be responders. Adverse events were reported by 43% (N=13) of the paroxetine group and 50% (N=15) of the venlafaxine group. Only one (3%) paroxetine-treated patient switched to hypomania during the trial, whereas four (13%) venlafaxine-treated patients switched (two switched to hypomania and two switched to full mania).

The authors conclude that both paroxetine and venlafaxine are effective and safe in the treatment of acute depressive breakthrough episodes in patients with bipolar disorder. (21 References)
DIFFERENTIAL PRESCRIPTION OF MAINTENANCE ANTIPSYCHOTICS TO AFRICAN AMERICAN AND WHITE PATIENTS WITH NEW-ONSET BIPOLAR DISORDER

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J CLIN PSYCHIATRY, 63:658-64, August 2002

Antipsychotic medications are commonly prescribed as maintenance pharmacotherapy for patients with bipolar disorder. However, double-blind, placebo-controlled studies have yet to demonstrate a significant prophylactic effect of maintenance antipsychotic use in bipolar illness, and long-term use of antipsychotic medication may place patients at risk for neuroleptic-induced tardive dyskinesia. African American patients may be particularly at risk, because excess prescription of antipsychotics appears to be common in this population, although to date there have been no prospective studies designed to examine antipsychotic use over time in affectively ill African American patients. In the present investigation, the authors prospectively and longitudinally examined the prescribing patterns of antipsychotic medications for African American and white patients with bipolar disorder.

The study sample was composed of 58 patients who met DSM-IV criteria for bipolar I disorder, manic or mixed episode; they were recruited at the time of their first psychiatric hospitalization and subsequently followed for a period of up to two years. African American (N=24) and white (N=34) patients were compared on a number of outcome measures, including the following: (1) percentage of follow-up (weeks) during which an antipsychotic medication was prescribed; (2) percentage of follow-up (weeks) during which an antipsychotic was prescribed in the absence of psychotic symptoms; and (3) percentage of follow-up during which there was full medication compliance. The African American and white patients were found to be demographically similar. However, after controlling for differences in clinical course, the researchers found that (compared with white patients), African American patients received antipsychotic medications over a significantly greater percentage of follow-up time; were more likely to receive antipsychotics during periods in which psychotic symptoms were not in evidence; and were significantly more likely to be treated with conventional antipsychotics. African American patients exhibited poorer medication compliance than white patients, although this finding did not explain the differences in antipsychotic prescription patterns.

The current data indicate that even when African American and white patients with bipolar disorder are demographically similar, the former may be more likely to receive maintenance antipsychotic treatment. Future studies are needed to evaluate the factors that clinicians consider when deciding to prescribe antipsychotics to bipolar patients. (30 References)
**BOOKS RECEIVED FOR REVIEW**


DIGEST of NEUROLOGY and PSYCHIATRY

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STEPPS: A COGNITIVE-BEHAVIORAL SYSTEMS-BASED GROUP TREATMENT FOR OUTPATIENTS WITH BORDERLINE PERSONALITY DISORDER--A PRELIMINARY REPORT

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COMPR PSYCHIATRY, 43:301-10, July/August 2002

Borderline personality disorder (BPD) is a significant health problem that has received relatively little attention. Like other severe personality disorders, BPD tends to be resistant to traditional psychotherapeutic approaches. In the present study, the authors describe a new program for the treatment of BPD that involves systems-based cognitive-behavioral therapy (CBT) and skills training in a group therapy setting. Called STEPPS, an acronym for Systems Training for Emotional Predictability and Problem Solving, the program is designed to complement and enhance the efficacy of other treatments that a patient may be receiving, including medication and individual therapy. In addition to emphasizing CBT and skills training, the STEPPS program contains a systems component whereby not only BPD patients but also persons within their systems (e.g., family members, significant others, health care professionals) are included in the training process. STEPPS is manual-based, consists of 20 two-hour weekly group meetings with two facilitators, and sets specific goals to be accomplished each week.

Pilot data are presented from 52 subjects (49 women, three men) who participated in STEPPS groups between July 1997 and November 1998. All met DSM-IV criteria for BPD, and their mean age at program entry was 33 years (range, 18 to 51 years). The efficacy of STEPPS was assessed with the Positive and Negative Affectivity Scale (PANAS); the Beck Depression Inventory (BDI); and the Borderline Evaluation of Severity Over Time (BEST), a new self-report scale designed to measure impairment and change in persons with BPD. In terms of available data, 52 subjects had at least one weekly visit, 41 had at least four visits, and 28 had at least 10 visits. Results of a repeated-measures analysis with all available data showed that participants in the STEPPS program experienced a significant decrease in BPD-associated symptoms as measured by the BEST total score. Analysis of BEST scores by subscale indicated that over time, negative thoughts and feelings scores decreased marginally, positive behavior scores increased marginally, and negative behavior scores decreased significantly. There was a highly significant decrease in PANAS negative affect scores and a significant reduction in BDI scores.

Responses to two brief surveys (one mailed to patients and the other sent to therapists) indicated moderate to high levels of satisfaction with the treatment among both groups. STEPPS was viewed as being relatively easy to learn and as being complementary to whatever other treatments a patient may have been receiving. (36 References)
SELF-HARM BEHAVIORS ACROSS THE LIFE CYCLE:
A PILOT STUDY OF INPATIENTS WITH
BORDERLINE PERSONALITY DISORDER

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COMPR PSYCHIATRY, 43:215-8, May/June 2002

While there appears to be a strong association between borderline personality
disorder (BPD) and self-harm behavior, many clinicians believe that individuals
with personality disorders (including BPD) behaviorally “burn out” as they grow
older. The authors of the present investigation used a retrospective, self-report
approach to examine the prevalence of self-harm behaviors throughout the life
cycle (during eight consecutive age periods) among hospitalized patients with
and without BPD.

The study sample was composed of 83 psychiatric inpatients who had been
admitted to an urban community hospital: 43 (34 women, 9 men; mean age,
32.42 years) were diagnosed with BPD, and 40 (20 women, 20 men; mean age,
33.63 years) did not have BPD. While the BPD group contained significantly
more women than men, there were no differences between the BPD and non-
BPD groups in terms of age, race, marital status, or education. Self-harm
behaviors were assessed by means of a modified version of the Self-Harm
Inventory, a 22-item self-report measure of intentional self-harm. Consecutive
age periods were designated as follows: grades 1-6, grades 7-9, grades 10-12,
18-24 years of age, 25-29 years, 30-39 years, 40-49 years, and 50-59 years. The
results indicated that in the BPD group, the mean number of self-harm
behaviors (including behaviors with a high degree of lethality, such as
attempting suicide, cutting oneself, and overdosing) increased steadily until the
18-to-24-year-old period (during which time there was a dramatic increase), and
then remained relatively constant throughout the remaining age periods. The
non-BPD group exhibited a similar pattern. However, when the researchers
conducted separate independent-sample t tests and compared the means for the
two groups at each age period, they found that the means for the BPD group
were significantly higher than those of the non-BPD group at all life stages, with
the exception of the means reported for two age periods (grades 1-6 and 50-59
years of age).

According to the authors, the findings of the current investigation indicate
that not all patients with BPD experience behavioral “burnout.” This appears to
be particularly true for those patients who continue to undergo psychiatric
hospitalizations throughout the course of the life cycle. Therefore, the
researchers note, while individuals who receive outpatient treatment may be
expected to progress reasonably well and improve over time, those who continue
to undergo hospitalizations may remain at life-long risk with regard to self-harm
behaviors. (18 References)
Several reports have described the long-term outcome of patients with borderline personality disorder (BPD). In all of these studies, BPD patients improved symptomatically over time, and by 15-year follow-up, most were functioning at levels approaching normality. The authors of the present investigation attempted to identify possible predictors of long-term outcome in BPD by following a cohort of patients with BPD for a mean of 27 years.

At the time of the 27-year follow-up, 64 subjects (12 men, 52 women; mean age, 50.9 years) were available for interview. Assessment instruments included the Diagnostic Interview for Borderlines-Revised (DIB-R), the Social Adjustment Scale (SAS-SR), the Global Assessment of Functioning (GAF), and the Symptom Check List-90, which measures the overall level of psychiatric symptoms and contains a global severity index (GSI). Two self-report instruments were used to evaluate childhood experiences: the Parental Bonding Index (PBI), which measures recollections of parental affection and control over the first 16 years of life; and the Developmental Experiences Questionnaire (DEQ), which measures memories of childhood physical and sexual trauma. The following potential predictors of long-term outcome were examined: DIB scores at baseline; socioeconomic status at 15-year follow-up; DIB-R scores at 15-year follow-up; Health-Sickness Rating Scale (HSRS) scores (considered to be equivalent to GAF scores) obtained at 15-year follow-up; PBI scores; and DEQ scores. Outcome measures at 27-year follow-up included two interviewer measures (DIB-R scores and GAF scores) and two self-report measures (GSI scores and SAS-SR scores). No significant relationship was found between any of the four outcome measures and either DIB baseline scores or socioeconomic status at 15-year follow-up. Neither parental neglect nor overprotection (as measured by the PBI) was found to be related to any of the outcome measures. No relationship was found between the presence of childhood physical and/or sexual abuse (as measured by the DEQ) and any of the outcome variables. However, DIB-R scores obtained at 15-year follow-up and HSRS scores obtained at 15-year follow-up both proved to be significant predictors of outcome at 27-year follow-up. In both cases (DIB-R and HSRS), this relationship held true for all four outcome measures.

According to the authors, the findings of the current study suggest that levels of functioning at one point during adulthood are more useful predictors of later adult functioning in BPD than either childhood experiences or demographic factors. (37 References)
ATTACHMENT, PARENTAL BONDING AND BORDERLINE PERSONALITY DISORDER FEATURES IN YOUNG ADULTS

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Previous research has sought to examine the roles that childhood experiences, parental bonding, and attachment styles play in the development of borderline personality disorder (BPD), with these three types of constructs forming the basis for several developmental models of BPD. In the present investigation, the authors attempted to determine whether parental bonding patterns and attachment styles are significantly related to BPD features above and beyond what can be accounted for by negative childhood events (e.g., abuse, loss), Axis I disorders, and non-BPD Axis II symptoms.

The study sample was composed of 393 18-year-old college freshmen; 54.3% of the participants were female, 84.9% were Caucasian, and 6.9% were African American. Some 1.5% reported previous hospitalization for psychiatric reasons, and 25.8% reported prior outpatient mental health treatment. Each participant completed a number of semistructured interviews and self-report measures, including the following: the Structured Interview for DSM-IV Personality, the Diagnostic Interview for Borderlines-Revised, the Structured Clinical Interview for DSM-IV Axis I Disorders/Nonpatient Version 2.0, Hazen and Shaver's Revised Three-Category Measure of Attachment, and the Parental Bonding Instrument. Childhood physical and sexual abuse and childhood loss were assessed by means of the Familial Experiences Interview. Of the 393 participants, 10.2% reported childhood sexual abuse, 20.7% reported childhood physical abuse, 65.8% reported experiencing a loss in childhood, and 59.7% received a lifetime Axis I diagnosis. Hierarchical regression analyses revealed that parental bonding and attachment scores accounted for a significant amount of the variance in borderline factor scores above and beyond what was accounted for by gender, childhood adversity variables, Axis I disorder, and non-BPD personality disorder symptoms. In addition to gender, loss, Axis I disorder, and non-BPD Axis II symptoms, several individual parental bonding and attachment scores served as significant predictors of respective borderline scores. After all variables were entered, the following emerged as significant predictors of borderline factor scores: participant’s perception of care from his/her mother (negatively related), overprotection by the mother, autonomy encouraged by the mother, secure interpersonal attachment pattern (negatively related), and anxious or ambivalent attachment.

According to the authors, the results of the current study indicate that parental bonding patterns and attachment styles have a unique relationship with borderline features and should be considered in comprehensive etiological models of BPD. (31 References)
THE ROLE OF GENDER IN THE CLINICAL PRESENTATION OF PATIENTS WITH BORDERLINE PERSONALITY DISORDER

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J PERSONAL DISORD, 16:277-82, June 2002

In the last decade, the literature on the relationship between gender and borderline personality disorder (BPD) has generated a great deal of controversy but very little clarity. In the present investigation, the authors examined gender differences in patterns of comorbidity within an outpatient sample unselected for personality disorders; they also attempted to determine whether there were differences between male and female borderline patients in level of impairment.

Of 1,395 outpatients who participated in the study, 105 women and 44 men were diagnosed with BPD. Of these 149 patients, 131 (87.9%) were Caucasian, and their mean age was 31.4 years. The majority (N=132, 88.6%) had completed high school and/or had some college education. Fifty-one (34.2%) were married or cohabiting. There were significantly more women with BPD (105/869, 12.1%) than men with BPD (44/526, 8.4%). Female patients with BPD were significantly more likely to be younger than male patients with BPD (mean age, 29.9 years vs. 34.8 years, respectively). When the researchers examined gender differences in the comorbidity profiles of the BPD patients, they found that men were significantly more likely than women to meet criteria for a lifetime substance abuse disorder, intermittent explosive disorder (had it not been eliminated due to co-occurrence with BPD), and antisocial personality disorder, whereas women were significantly more likely than men to meet criteria for a lifetime eating disorder. To determine whether the pattern of comorbidity found in male and female BPD patients was specific to only those individuals with BPD, the authors examined the comorbidity profiles of the full study sample (excluding those who met criteria for BPD). Within this larger group (N=1,246), men were significantly more likely than women to meet criteria for a lifetime substance abuse disorder, intermittent explosive disorder, and antisocial personality disorder, whereas women were significantly more likely than men to meet criteria for a lifetime eating disorder, posttraumatic stress disorder, major depressive disorder, and panic disorder. A multivariate analysis of covariance revealed no significant differences between male and female BPD patients with regard to degree of overall impairment.

According to the authors, the results of the current investigation suggest that men and women with BPD, although equally distressed, present with different lifetime patterns of impulse-related disorders. (19 References)
Comorbidity among personality disorder (PD) diagnoses is a well-known phenomenon that has important implications for nosology, treatment, and models of psychopathology (Grilo et al., 2000). In the present study, the authors examined the comorbidity of DSM-IV borderline personality disorder (BPD) with other PDs in a group of adult monolingual (Spanish-speaking only) Hispanic psychiatric outpatients with clinically-derived diagnoses of current or lifetime substance use disorders.

The sample was composed of 100 patients (69 men, 31 women) with a mean age of 39.2 years; 77% had not completed high school, 65% were unemployed, and 62% were married. The majority (74%) were from Puerto Rico; 53% of the sample had resided in the United States for more than 11 years, 20% had lived in the United States for six to 10 years, and 27%, for fewer than six years. All the patients were administered the Spanish version of the Diagnostic Interview for DSM-IV Personality Disorders. To determine significant patterns of diagnostic co-occurrence, the writers compared the group of patients diagnosed with BPD (N=34) with the group of patients without BPD (N=66). BPD was found to be the most frequently diagnosed PD; the next most frequently occurring diagnoses were avoidant PD and obsessive-compulsive PD, each of which occurred in 31% of the patients. With the exception of schizoid PD, which occurred in only 2% of the patients, all PDs occurred at higher rates in the group with BPD than in the group without BPD. Bonferroni-corrected chi-square analyses revealed significant rates of co-occurrence between BPD and antisocial, avoidant, and depressive PDs. When the researchers performed separate chi-square analyses for men and women, they found that in women, no significant patterns of comorbidity emerged between BPD and any other PD. Among men, however, those with BPD had significantly higher rates of co-occurrence than those without BPD for the following three types of PD: antisocial PD (45.8% vs. 8.9%, respectively), avoidant PD (54.1% vs. 22.2%, respectively), and depressive PD (54.2% vs. 11.1%, respectively).

According to the authors, the results of the present study suggest that among monolingual Hispanic psychiatric outpatients with substance use disorders, gender may play a role in the nature of BPD comorbidity. The BPD diagnosis may represent a broader range of psychopathology in Hispanic men than in Hispanic women. (44 References)
DIMENSIONAL PERSONALITY PROFILES OF BORDERLINE PERSONALITY DISORDER IN COMPARISON WITH OTHER PERSONALITY DISORDERS AND HEALTHY CONTROLS

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J PERSONAL DISORD, 16:135-47, April 2002

Empirical evidence suggests that dimensional models provide a more adequate representation of personality disorders (PDs) than categorical models. However, findings regarding the relationship between borderline personality disorder (BPD) and broad dimensional measures of personality remain controversial. The present author examined the sensitivity and clinical specificity of dimensional personality profiles associated with BPD.

The study sample was composed of the following three groups: (1) 31 patients (27 women, four men; age range, 19 to 48 years; mean age, 28.7 years) who met DSM-IV criteria for BPD; (2) 31 patients (23 women, eight men; age range, 18 to 45 years; mean age, 31.8 years) who fulfilled diagnostic criteria for at least one nonborderline PD; and (3) 31 healthy control subjects (26 women, five men; age range, 22 to 36 years; mean age, 28.1 years). All three groups were matched for age and gender, and there were no significant differences between the two patient groups with regard to level of education, depressive symptomatology, or number of hospitalizations. All subjects were administered the Six-Factor Test, which measures the five-factor model of personality (FFM); the Temperament and Character Inventory (TCI); and the Dimensional Assessment of Personality Pathology (DAPP). Group differences on FFM, TCI, and DAPP dimensions were analyzed by means of nonparametric statistics. Neuroticism (FFM), Self-Directedness (TCI), and Emotional Dysregulation (DAPP) were identified as general markers of personality pathology and were significantly interrelated in all three groups. Emotional Dysregulation (DAPP) was found to be related to Harm Avoidance (TCI) in the control subjects and in the patients with PDs other than borderline. Extraversion (FFM) and Inhibitedness (DAPP) were inversely related in each of the three groups. Novelty Seeking (TCI) was consistently related to Dissocial Behavior (DAPP) in all three groups. In addition, consistent relationships between Conscientiousness (FFM), Persistence (TCI), and Compulsivity (DAPP) were found in each of the three groups. Compared with patients with other types of PD, those with BPD scored lower on Agreeableness (FFM), higher on Novelty Seeking (TCI) and Self-Transcendence (TCI), and higher on the DAPP higher-order dimensions of Emotional Dysregulation, Dissocial Behavior, and Inhibitedness.

According to the author, the results of the current investigation provide support for the assumption that borderline personality can be accurately described in terms of dimensional trait profiles. (34 References)
SEVERITY OF REPORTED CHILDHOOD SEXUAL ABUSE AND ITS RELATIONSHIP TO SEVERITY OF BORDERLINE PSYCHOPATHOLOGY AND PSYCHOSOCIAL IMPAIRMENT AMONG BORDERLINE INPATIENTS

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J NERV MENT DIS, 190:381-7, June 2002

Numerous studies have found that sexual abuse is common among patients with borderline personality disorder (BPD). The aims of the present investigation were: (1) to describe the severity of sexual abuse reported by a well-defined sample of borderline inpatients; and (2) to determine the relationship between the severity of reported childhood sexual abuse, other forms of childhood abuse, and childhood neglect and the severity of borderline symptoms and psychosocial impairment.

Two semistructured interviews of demonstrated reliability were used to assess the severity of adverse childhood experiences reported by 290 inpatients with BPD (mean age, 26.9 years; 80.3% female). Of the 290 patients, 181 (62.4%) reported a childhood history of sexual abuse, 250 (86.2%) reported other forms of childhood abuse, and 267 (92.1%) reported childhood neglect. Among the patients who experienced sexual abuse, more than 50% reported being abused both in childhood and in adolescence, on at least a weekly basis, for a minimum of one year, by a parent or other person well known to the patient, and by two or more perpetrators; more than 50% also reported that their abuse involved at least one form of penetration and the use of force or violence. When the authors used multiple regression modeling and controlled for age, gender, and race, they found that the severity of reported childhood sexual abuse was significantly related to the following: the severity of symptoms in all four core sectors of borderline psychopathology (affect, cognition, impulsivity, and disturbed interpersonal relationships), the overall severity of BPD, and the overall severity of psychosocial impairment. The severity of childhood neglect was significantly related to the severity of the affective, cognitive, dissociative, and interpersonal symptoms of BPD, as well as to the overall severity of BPD. The severity of other forms of childhood abuse (other than sexual abuse) was significantly associated with two of 10 factors studied, including the severity of psychosocial impairment.

Taken together, the authors conclude, the results of the present study indicate that the majority of sexually abused borderline inpatients may have been severely abused. The current data also suggest that the severity of childhood sexual abuse, other forms of childhood abuse, and childhood neglect may all play a role in the symptomatic severity and psychosocial impairment characteristic of BPD. (40 References)
TRAUMATIC EXPOSURE AND POSTTRAUMATIC STRESS DISORDER IN BORDERLINE, SCHIZOTYPAL, AVOIDANT, AND OBSESSIVE-COMPULSIVE PERSONALITY DISORDERS: FINDINGS FROM THE COLLABORATIVE LONGITUDINAL PERSONALITY DISORDERS STUDY

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J NERV MENT DIS, 190:510-8, August 2002

Although several studies have examined the associations between traumatic exposure, posttraumatic stress disorder (PTSD), and axis I disorders, relatively little attention has been paid to the complex interactions between trauma, PTSD, and personality disorders (PDs). As part of a naturalistic, multisite study, the authors assessed various types and aspects of traumatic exposure and rates of PTSD in the following groups: 86 subjects (39 women, 47 men) with schizotypal PD (STPD); 167 individuals (123 women, 44 men) with borderline PD (BPD); 153 participants (100 women, 53 men) with avoidant PD (AVPD); 153 subjects (91 women, 62 men) with obsessive-compulsive PD (OCPD); and 94 persons (56 women, 38 men) with major depressive disorder (MDD) and without PDs (comparison group). The mean age of the sample as a whole was 32.8 years.

Of the 653 study participants, 532 (81.5%) reported exposure to a DSM-IV criterion A traumatic event, and 378 (58%) reported experiencing a trauma in more than one category. High rates of trauma exposure were found in all groups. However, the proportion of subjects reporting a history of trauma was significantly higher in the BPD group (91.6%) than in the MDD (78.7%), AVPD (75.8%), and OCPD (75.8%) groups, although it was not significantly different from that in the STPD group (84.9%). Compared with each of the other groups, the BPD group reported a significantly higher rate of exposure to sexual traumas, including physical force/unwanted sexual contact (55.1%) and rape (36.5%). BPD participants also reported the highest rate of childhood sexual abuse (37.7%), the highest rate of lifetime PTSD (51%), and the earliest exposure to first traumatic event (mean age, 11.3 years). When compared with subjects in the other groups, those with more severe PDs (STPD and BPD) reported more types of traumatic exposure and higher rates of being physically attacked (both in childhood and adulthood).

The present results suggest a specific relationship between BPD and sexual trauma (childhood and adult) that does not exist between sexual trauma and other PDs. These data also support an association between severity of PD and severity of traumatic exposure. (34 References)
BORDERLINE PERSONALITY DISORDER AND AGE OF ONSET IN MAJOR DEPRESSION

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J PERSONAL DISORD, 16:189-99, April 2002

Among depressed patients with comorbid personality disorders (PDs), borderline PD (BPD) has been found to be one of the most common PDs in those with early-onset major depressive disorder (MDD). In the present report, drawn from the Rhode Island Methods to Improve Diagnostic Assessments and Services project, the authors examined: (1) the interrelationship between BPD and age of onset of depression; (2) the relationship of each of these variables to a series of demographic and clinical factors; and (3) the possibility that BPD accounts for observed differences between early- and late-onset MDD.

A total of 440 depressed outpatients were evaluated with semistructured interviews and subdivided according to age of onset of MDD and the presence or absence of comorbid BPD. BPD was found to be present in 56 patients and absent in 384 patients. Early-onset depression (before age 18) was diagnosed in 127 patients, while 313 patients presented with late-onset depression. Patients with BPD had an earlier onset of depression, and patients with early-onset depression were more likely to have BPD. Compared with patients without comorbid BPD, those with BPD were significantly younger; more severely depressed; more suicidal; more likely to have been hospitalized; more likely to have missed time from work; more likely to have high levels of social impairment; and more likely to have a lifetime history of specific phobia, posttraumatic stress disorder (PTSD), obsessive-compulsive disorder (OCD), alcohol use disorder, drug use disorder, eating disorder, somatoform disorder, and conduct disorder. Compared with patients with late-onset depression, those with early-onset depression were significantly younger, were less likely to be married, and had significantly longer episodes, more previous episodes, more serious suicide attempts, and greater levels of social impairment; they were also more likely to have comorbid diagnoses of social phobia, PTSD, and OCD. A multivariable, logistic regression analysis revealed that a diagnosis of comorbid BPD was significantly associated with an earlier age of MDD onset, a higher Hamilton Depression Rating Scale score, a lower Global Assessment of Functioning Score, specific phobia, alcohol disorder, and eating disorder. A second multivariable analysis showed that early-onset MDD was significantly associated with younger age at time of presentation, history of previous depressive episode, current episode of longer duration, history of serious suicide attempt, and presence of comorbid social phobia.

According to the authors, the current results indicate that BPD does not significantly account for the differences between early- and late-onset MDD. While BPD is common in early-onset MDD patients, comorbid BPD is not a universal feature of early-onset MDD. (25 References)
BOOKS RECEIVED FOR REVIEW


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Abstracts and Reviews of Selected Literature in Psychiatry, Neurology, and their Allied Fields

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CHARACTERISTICS OF SUICIDE ATTEMPTS IN A LARGE URBAN JAIL SYSTEM WITH AN ESTABLISHED SUICIDE PREVENTION PROGRAM

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PSYCHIATR SERV, 53:574-9, May 2002

Suicide is the leading cause of death in jails throughout the United States. In 1991, the King County Department of Adult and Juvenile Detention in Washington State adopted a suicide surveillance and prevention program. A review committee was formed to prospectively study the patterns of suicide attempts that occurred after the program’s implementation and to make recommendations for improvements. All first suicide attempts per jail booking that occurred over a 33-month period (October 1, 1996, to June, 30, 1999) were reviewed. For each attempt, characteristics of the attempt itself and of the individual who made it were abstracted and analyzed by trained staff members.

Over the course of the study period, a total of 132 first suicide attempts were made during 132 separate incarcerations by 124 individual inmates. Inmates who attempted suicide were much more likely to have a chronic psychiatric problem than inmates in the general jail population (77% versus 15%, respectively). In all, 75% of the 132 suicide attempts were made by inmates who had received a mental health evaluation from jail personnel prior to the attempt. Fifty-five (42%) of the 132 suicide attempts were made by inmates who were under formal suicide observation at the time of the attempt, while the remaining 77 attempts (58%) were made by inmates who were housed in a general area of the jail. Of the 55 attempts made by those under suicide observation, seven (13%) were made by inmates living in group housing, and 48 (87%) were made by inmates housed in isolation units. In all, 40% of the attempts made by inmates housed in a suicide observation unit occurred within the first three days of incarceration. With regard to those inmates who received a mental health evaluation before their suicide attempt but who were not under suicide observation, only 18% of their attempts occurred within the first three days of incarceration. With regard to those inmates who had not received a mental health evaluation prior to their suicide attempt, 61% of their attempts occurred within the first three days of incarceration. Attempts that were made in suicide observation units were associated with a significantly lower rate of transportation to an emergency department than attempts made in a general housing area of the jail.

On the basis of these findings, the jail system implemented a number of interventions, which included intensified suicide screening and treatment of inmates with active substance abuse problems and increased use of group-housing units for suicidal inmates. (15 References)
SUICIDALITY AFTER TRAUMATIC BRAIN INJURY: DEMOGRAPHIC, INJURY AND CLINICAL CORRELATES

Grahame Simpson (Brain Injury Rehabilitation Unit, Liverpool Hospital, Locked Bag 7103, Liverpool BC, New South Wales 1871, Australia); and Robyn Tate PSYCHOL MED, 32:687-97, May 2002

In spite of the high frequency of emotional distress seen in patients who have suffered a traumatic brain injury (TBI), few studies have examined suicidality in relation to TBI. In the present investigation, the authors attempted to: (1) determine the prevalence of hopelessness, suicide ideation, and suicide attempts after TBI; (2) identify clinical aspects of suicide ideation associated with heightened levels of distress; (3) ascertain the prevalence and role of key suicide risk factors both premorbidly and post-injury; and (4) examine predictors of suicide ideation and suicide attempts.

The sample was composed of 172 outpatients who had suffered a TBI and who attended a brain injury rehabilitation unit over a 24-month period. Assessment measures included the Beck Hopelessness Scale and the Beck Scale for Suicide Ideation. A substantial proportion of the sample scored within the clinical range on these measures, with 34.9% exhibiting moderate to severe levels of hopelessness and 22.7% reporting clinically significant levels of suicide ideation within the previous seven days. The post-injury suicide attempt rate was 17.4% over a mean period of five years. The lifetime suicide attempt rate prior to injury was 10.4%, but when post-injury attempts were included, the lifetime rate rose to 26.2%. There was a high degree of comorbidity between suicide attempts and emotional/psychiatric disturbance. Regression analyses showed that a high level of hopelessness was the strongest predictor of suicide ideation and that a high level of suicide ideation, in association with post-injury emotional/psychiatric disturbance, was the strongest predictor of post-injury suicide attempts. Neither the severity of the injury nor the presence of premorbid suicide risk factors contributed to elevated levels of post-injury suicidality.

Several clinical implications arise from the current investigation with regard to the assessment, management, and prevention of post-TBI suicidality. These include: (1) the recognition that suicidality is a common psychological reaction to TBI and requires proactive assessment; (2) an understanding that TBI patients may be at risk for suicidality, no matter how severe their injury is or at what age it occurs; (3) acknowledgment of the fact that any suicide risk assessment of individuals with TBI should include the interrelated triad of hopelessness, suicide ideation, and post-injury suicide attempts; (4) the recognition that particular monitoring and social support should be provided for those TBI patients who exhibit a broad spectrum of emotional/psychiatric disturbance; and (5) an understanding that patient services should explore ways of countering the widespread hopelessness commonly found in those individuals who have suffered a TBI. (34 References)
A TWIN STUDY OF GENETIC AND ENVIRONMENTAL INFLUENCES ON SUICIDALITY IN MEN

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PSYCHOL MED, 32:11-24, January 2002

Few studies of suicidal behavior have taken into account both genetic and environmental risk factors. In the present investigation, the authors examined the etiology of suicidality (suicidal ideation and/or suicide attempts) by assessing genetic and environmental risk factors in a nonclinical cohort of male-male twin pairs drawn from the Vietnam Era Twin Registry.

The study sample was composed of 3,372 twin pairs who had served in the military during the Vietnam era and who were surveyed in 1987 and 1992. The following variables were assessed: lifetime history of suicidal ideation and/or suicide attempts; level of combat exposure; sociodemographic factors (ethnicity; educational attainment; and age, marital status, and employment status at the 1992 interview); and lifetime history of DSM-III-R psychiatric disorders (major depression, bipolar disorder, childhood conduct disorder, adult antisocial personality disorder, panic disorder, posttraumatic stress disorder, alcohol dependence, and drug dependence). Genetic risk factors for suicidality were examined by means of a multinomial logistic regression model. Additive genetic, shared environmental, and non-shared environmental effects on suicidality were estimated by using structural equation modeling, while controlling for other risk factors. The lifetime prevalence rates for suicidal ideation and suicide attempts were 16.1% and 2.4%, respectively. Of the 163 twins who reported a history of lifetime suicide attempts, 149 (91.4%) also reported a history of lifetime suicidal ideation. A multinomial regression model indicated that the following were significant predictors of suicidal ideation: having a co-twin with a history of suicidality, being white, being unemployed, being other than married (never married or divorced/separated/widowed), having a history of a medium level of combat exposure, and having a history of psychiatric disorders. Co-twin's suicidality, unemployment, marital disruption, low educational attainment, and psychiatric disorders (with the exception of childhood conduct disorders) were found to be significant predictors of suicide attempts. Model-fitting suggested that suicidal ideation was influenced by additive genetic (36%) and non-shared environmental (64%) effects, while suicide attempts were influenced by additive genetic (17%), shared environmental (19%), and non-shared environmental (64%) effects.

The authors conclude that men may have a genetic susceptibility that is specific to both suicidal ideation and suicide attempts and that is not explained by the inheritance of common psychiatric disorders. (77 References)
PSYCHIATRIC SYMPTOMS AND THEIR RELATIONSHIP TO SUICIDAL IDEATION IN A HIGH-RISK ADOLESCENT COMMUNITY SAMPLE

Christianne L. Esposito, PhD (Brown University School of Medicine, Box G-BH, Providence, RI 02912); and George A. Clum, PhD

J AM ACAD CHILD ADOLESC PSYCHIATRY, 41:44-51, January 2002

It has been estimated that as many as one in 10 adolescent girls and one in 25 adolescent boys will make a suicide attempt at some point during their adolescence (Lewinsohn et al., 1996). Research has shown that between 80% and 90% of adolescents who make a suicide attempt have a diagnosable psychiatric disorder. In the current investigation, the authors examined the importance of diagnostic factors in the prediction of adolescent suicidal ideation in a high-risk community sample. The study sample was composed of 73 high-school students (37 males, 36 females; age range, 14 to 18 years; mean age, 16 years) who had been identified by school personnel (school psychologists, guidance counselors, and special education teachers) as exhibiting some type of emotional disturbance while in the school setting. The Schedule for Affective Disorders and Schizophrenia for School-Age Children-Epidemiologic Version 5 (K-SADS-E) was used for the assessment of psychiatric disorders, and the Modified Scale for Suicidal Ideation was used for the measurement of suicidal ideation.

The data revealed that 74% of the adolescents met criteria for a psychiatric disorder as assessed by the K-SADS-E. The most prevalent diagnosis was major depressive disorder, with approximately 40% of the sample meeting diagnostic criteria for this disorder. Approximately 56% of the adolescents reported current suicidal ideation. For most psychiatric disorders, symptomatology measured continuously was more highly correlated with suicidal ideation than symptomatology analyzed dichotomously. The severity of symptoms associated with mood disorders provided the strongest prediction of suicidal ideation. When examined in totality, the results suggested that the severity of symptoms associated with major depressive disorder, dysthymia, oppositional defiant disorder, alcohol dependence, drug dependence, and generalized anxiety disorder was related to the severity of suicidal ideation. However, only the severity of symptoms associated with major depressive disorder and dysthymia independently predicted suicidal ideation. No other diagnostic variables predicted suicidal ideation over and above mood disorder symptoms.

The current study lends support to previous investigations that have found a strong relationship between psychiatric disorders and suicidal ideation in adolescent populations. The authors suggest that an assessment of mood, disruptive behavior, substance use, and anxiety symptoms be conducted routinely in any child or adolescent presenting for treatment. Most importantly, they note, adolescents presenting with severe mood disorder symptoms should be closely assessed and monitored for suicidality. (25 References)
CHILDHOOD ADVERSITIES, INTERPERSONAL DIFFICULTIES, AND RISK FOR SUICIDE ATTEMPTS DURING LATE ADOLESCENCE AND EARLY ADULTHOOD

Jeffrey G. Johnson, PhD (New York State Psychiatric Institute, 1051 Riverside Dr., Unit 60, New York, NY 10032; e-mail: jjohnson@pi.cpmc.columbia.edu); Patricia Cohen, PhD; Madelyn S. Gould, PhD; Stephanie Kasen, PhD; Jocelyn Brown, MD; and Judith S. Brook, PhD
ARCH GEN PSYCHIATRY, 59:741-9, August 2002

Considerable effort has been devoted to the investigation of factors that increase the risk for suicide, a leading cause of death among adolescents and young adults. The authors used data from a community-based, prospective, longitudinal study (Children in the Community Study; Cohen and Cohen, 1996) to investigate the association between adversities encountered during childhood, interpersonal difficulties experienced during adolescence, and suicide attempts made during late adolescence or early adulthood. The sample consisted of 659 families who were from upstate New York and who were interviewed in 1975, in 1983, between 1985 and 1986, and between 1991 and 1993. The mean age of the offspring at the various interview points was five years (1975), 14 years (1983), 16 years (1985-1986), and 22 years (1991-1993).

Twenty-three individuals for whom there was no evidence of previous suicide attempts reported that they had attempted suicide when they were interviewed at a mean age of 22 years. Overall, 37 individuals reported that they had attempted suicide during adolescence or early adulthood; 16 stated that they had attempted suicide more than once during adolescence or early adulthood. After age, sex, psychiatric symptoms present during childhood and early adolescence, and parental psychiatric symptoms were controlled statistically, the researchers found that maladaptive parenting and childhood maltreatment were associated with an elevated risk for interpersonal difficulties during middle adolescence (mean age, 16 years) and for suicide attempts during late adolescence or early adulthood. A wide range of interpersonal difficulties experienced during middle adolescence was associated with risk for suicidal behavior after the covariates were controlled. Profound interpersonal difficulties during middle adolescence mediated the association between maladaptive parenting or childhood maltreatment and suicide attempts during late adolescence or early adulthood.

The current findings suggest that children who experience high levels of maladaptive parenting or child abuse may have difficulty in developing the social skills that are essential for the maintenance of healthy relationships with peers and adults. Without these skills, youths may become interpersonally isolated or may relate to others in an antagonistic manner. Such maladaptive patterns of interpersonal functioning may contribute to the onset of despair, hopelessness, and suicidal behavior. (52 References)
MENTAL DISORDERS IN ELDERLY SUICIDES:
A CASE-CONTROL STUDY

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AM J PSYCHIATRY, 159:450-5, March 2002

The aim of the current investigation was to examine the relationship between various psychiatric disorders and suicide in individuals who were 65 years of age or older. The authors used the psychological autopsy method to study 85 cases of suicide (46 men, 39 women; age range, 65 to 97 years; median age, 73 years). For comparison purposes, 153 living subjects (84 men, 69 women; age range, 67 to 100 years; median age, 77 years) were randomly selected from the tax register and interviewed face-to-face. Retrospective axis I diagnoses were made according to DSM-IV criteria on the basis of interview data and medical records.

While 97% (N=82) of the suicide group fulfilled criteria for at least one DSM-IV diagnosis, only 18% (N=28) of the comparison group did so. Recurrent major depressive disorder was found to be a very strong risk factor for suicide, as was substance use disorder. An elevated risk for suicide was also associated with minor depressive disorder, dysthymic disorder, psychotic disorder, single-episode major depressive disorder, and anxiety disorder. Thirty-one of the 82 nondemented individuals in the suicide group fulfilled criteria for more than one DSM-IV axis I diagnosis, but only one of the 139 nondemented individuals in the comparison group did so. Comorbid axis I disorders were present in 15 (38%) of the 39 elderly subjects with major depressive disorder who had committed suicide. Within the suicide group, 25% had seen a psychiatrist during their final month of life, and 60% had had contact with a psychiatrist at some point in time. None of the subjects in the comparison group had seen a psychiatrist during the month prior to interview, and only 9% reported a history of psychiatric contact. In all, 65% of the suicide group and 16% of the comparison group had received treatment for a depressive disorder at some point in time. While 49% of those in the suicide group had been treated for a depressive disorder during the past year, only 5% of those in the comparison group had received treatment for a depressive disorder.

According to the authors, the current data suggest that elderly individuals who commit suicide represent a heterogeneous group with regard to mental disorders; this finding, they note, indicates a need for differentiated prevention strategies. Detecting late-onset depressive disorder at the primary care level is one important approach to the prevention of suicide in late life. Interventions that target the needs of elderly individuals with other psychiatric diagnoses also require further development. (30 References)
AGE, GENDER, AND ETHNICITY DIFFERENCES IN PATTERNS OF COCAINE AND ETHANOL USE PRECEDING SUICIDE

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AM J PSYCHIATRY, 159:615-9, April 2002

Substance abuse and substance dependence have been widely recognized as risk factors for suicide. The goal of the present study was to examine the role of cocaine and ethanol in suicides completed in Fulton County, Georgia, during the second half of the 1990s. Extensive demographic and toxicology data on completed suicides (from 1994 through 1998) were obtained from the Fulton County Medical Examiner’s Office. Specific characteristics of the victims who had used cocaine, ethanol, or both substances before committing suicide were compared across demographic groups.

The records showed that there were 416 suicides in Fulton County between 1994 and 1998; 374 (89.9%) of these were considered to be fully informative with regard to cocaine and ethanol toxicology. Victims who died 48 hours or more after the self-inflicted injury were considered to be noninformative because of metabolic clearance of intoxicants; victims who were discovered in an advanced state of decomposition were also included in the noninformative group. There were no significant differences between the informative and noninformative suicide groups in terms of mean age, age distribution, demographic composition, method of suicide, or violence of method. At autopsy, cocaine was detected in 37 (9.9%) of the 374 informative suicides, and alcohol was detected in 108 (28.9%). Significant differences in sex, race, and age were found among the victims who had used cocaine and/or ethanol before committing suicide. Of all cocaine-positive victims, 54.1% were African American, and 45.9% were white. Almost all (94.6%) of the cocaine-positive suicide victims were male (51.4%, African American; 43.2%, white). While cocaine was detected in 11.4% of the male suicide victims, it was found in only 2.9% of the female victims. Ethanol was detected in significantly more white (33.1%) than African American (19.7%) suicide victims. There were no gender-based differences in ethanol use. Across all age groups, more white than African American victims used ethanol before committing suicide. Among teenagers, substance use before suicide differed dramatically between ethnic groups. While the vast majority (86.7%) of African American teenage victims did not use either cocaine or ethanol before committing suicide, 50% of the white teenage victims had used one or both of these substances.

Logistic regression analysis indicated that cocaine use before suicide was four times more likely in male victims than in female victims and almost twice as likely in African American victims than in white victims. It also showed that white victims were more than twice as likely as African American victims to have used ethanol before committing suicide. (11 References)
CHARACTERISTICS OF OPIATE DEPENDENT PATIENTS WHO ATTEMPT SUICIDE


Suicidal behavior frequently involves an interaction between distal risk factors that affect the threshold for attempting suicide and proximal (trigger) risk factors that precipitate the attempt. The author hypothesized that opiate-dependent suicide attempters (compared with opiate-dependent nonattempters) would report significantly more distal risk factors involving childhood trauma, family history of suicide, and/or personality traits, as well as significantly more proximal risk factors involving comorbidity with cocaine and/or alcohol dependence, major depressive disorder, and/or current physical disorder.

The study sample was composed of 246 patients who met DSM-IV criteria for opiate dependence. Information was obtained about sociodemographic variables, opiate dependence history, lifetime history of alcohol and/or cocaine dependence meeting DSM-IV criteria, lifetime history of suicide attempts, existence of a currently treated medical disorder, and history of suicidal behavior in first- and second-degree relatives. Assessment instruments included the Eysenck Personality Questionnaire (EPQ), the Hostility and Direction of Hostility Questionnaire (HDHQ), and the Childhood Trauma Questionnaire. Of the 246 opiate-dependent patients, 105 (82 men, 23 women; mean age, 43.8 years) had attempted suicide at some time in their lives, and 141 (133 men, 8 women; mean age, 44.6 years) had never attempted suicide. Compared with the nonattempters, significantly more of the suicide attempters were female and unemployed. The opiate-dependent patients who had attempted suicide also had significantly higher childhood trauma scores with regard to emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect. Significantly more of the suicide attempters had a lifetime history of alcohol and/or cocaine dependence; reported a history of major depressive disorder; and/or were currently being treated for a physical disorder. Of the 105 suicide attempters, 31 had a family history of suicidal behavior; in 12 cases, a first- or second-degree relative had committed suicide, and in 19, a first- or second-degree relative had attempted suicide. Of the 141 patients who had never attempted suicide, only 11 had a family history of suicidal behavior; in six cases, a first- or second-degree relative had committed suicide, and in five, a relative had attempted suicide. In terms of the EPQ, the suicide attempters had significantly lower extraversion scores and significantly higher neuroticism and psychoticism scores. The patients who had attempted suicide also had significantly higher hostility scores on the HDHQ.

The author concludes that suicidal behavior in opiate-dependent patients may involve risk factors from the family, childhood, personality, psychiatric, and physical domains. (35 References)
A history of childhood abuse in highly prevalent in adult patients with borderline personality disorder (BPD) and is associated with self-destructive behavior in both clinical and nonclinical samples. Viewing BPD as a “high risk” disorder, the authors attempted to determine whether a history of childhood sexual or physical abuse increased the likelihood of suicidal behavior in adult patients with BPD and whether childhood abuse was related to other known risk factors for suicidal behavior in persons with BPD.

The study sample was composed of 61 patients who met full diagnostic criteria for BPD (11 men, 50 women; age range, 18 to 50 years; mean age, 28.2 years). By means of structured interviews and self-reports, information was obtained on severity of BPD, axis I disorders, suicide history, hopelessness, impulsivity, impulsive-aggression, and antisocial traits. A 19-item, semi-structured Abuse History was used to ascertain childhood experiences of sexual and physical abuse. Of the 61 patients, 28 (four men, 24 women) reported definite histories of childhood sexual abuse, and 30 (four men, 26 women) reported definite histories of childhood physical abuse. Ten patients reported sexual abuse only, 12 reported physical abuse only, 18 reported combined abuse, and 21 reported no abuse. In all, 51 (83.6%) had a history of suicide attempts. Of the 28 patients with a history of childhood sexual abuse, 27 were suicide attempters. Patients with histories of childhood sexual abuse made more suicide attempts than patients who reported no childhood sexual abuse (mean number of lifetime attempts, 4.1 vs. 1.9, respectively). The occurrence and severity of childhood sexual abuse predicted adult suicidal behavior independently of other known risk factors. The odds for a sexually abused patient to attempt suicide in adulthood was over 10 times greater than the odds for a patient who had not been sexually abused in childhood. Given a history of childhood sexual abuse, the risk of adult suicidal behavior was increased by antisocial traits, severity of BPD, hopelessness, and the occurrence of a comorbid major depressive episode. No relationship was found between childhood physical abuse and adult suicidal behavior.

According to the authors, when a patient with BPD presents with a history of childhood sexual abuse, he or she should be carefully assessed for the presence of comorbid major depressive disorder. In addition, the researchers note, the severity of the BPD and the presence of hopelessness and antisocial traits should be viewed as possible contributors to an increased risk of suicidal behavior in such a patient. (54 References)
SUICIDE ATTEMPTS IN PATIENTS WITH BIPOLAR I DISORDER DURING ACUTE AND MAINTENANCE PHASES OF INTENSIVE TREATMENT WITH PHARMACOTHERAPY AND ADJUNCTIVE PSYCHOTHERAPY

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AM J PSYCHIATRY, 159:1160-4, July 2002

No patient population is at greater risk of suicide-related morbidity and mortality than individuals suffering from bipolar disorder (Goodwin and Jamison, 1990). In the study presented here, the authors computed the lifetime rates of suicide attempts in 175 patients with bipolar I disorder (77 men, 98 women; mean age, 35.1 years) and compared them with the rates obtained during a two-year period of intensive treatment with pharmacotherapy and with one or the other of two adjunctive psychosocial interventions. Data on prior suicide attempts were obtained retrospectively by means of interviews with the NIMH-Life-Chart method. Data on suicide attempts made during the clinical trial were collected systematically throughout the protocol.

The subjects entered the study during an acute mood episode and were treated primarily with lithium (or with divalproex or carbamazepine if lithium was not appropriate) and with either psychotherapy specific to bipolar disorder (which included help in regularizing daily routines) or nonspecific, intensive clinical management (which involved regular visits with empathic clinicians). The acute phase of treatment lasted until stabilization (defined as a period of four weeks during which a patient had a mean score of \( \leq 7 \) on the 17-item Hamilton Depression Rating Scale and \( \leq 7 \) on the Bech-Rafaelsen Mania Scale). Patients were then randomly reassigned to preventive maintenance treatment with one of the two psychosocial interventions. The pharmacotherapy regimen that had led to stabilization remained unchanged throughout the maintenance phase. A base rate of 1.05 suicide attempts per 100 patient-months was computed for the period before study entry. Patients experienced a threefold reduction in the rate of attempts during the acute treatment phase (0.31 attempts per 100 patient-months) and a 17.5-fold reduction during maintenance treatment (0.06 attempts per 100 patient-months). When the authors used Poisson log linear regression to model the relationship between number of suicide attempts and protocol stage (pretreatment, acute, maintenance), they found that the reductions in rates were significant in the acute and the maintenance phases, compared with the pretreatment phase.

According to the authors, a treatment program in a maximally supportive clinical environment can significantly reduce suicidal behavior in high-risk patients with bipolar I disorder. (19 References)
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Abstracts and Reviews of Selected Literature in Psychiatry, Neurology, and their Allied Fields

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BOOKS RECEIVED FOR REVIEW
ATTACHMENT IN ANOREXIA NERVOSA: 
A TRANSGENERATIONAL PERSPECTIVE

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BR J MED PSYCHOL, 74:497-505, December 2001

Both clinical and empirical investigations suggest that insecure attachment is common in eating-disordered populations. While clinical studies have addressed mother-daughter interactions, there has been little empirical research regarding the mother’s own attachment patterns and the possible intergenerational transmission of these patterns. The present authors examined the attachment status of patients with severe anorexia nervosa and that of their mothers. They hypothesized (1) that the patients would display a high level of insecurity; (2) that the mothers would show a higher rate of insecurity than that predicted by population norms; and (3) that attachment style associations might be found within mother-daughter pairs.

In all, 20 female inpatients with a DSM-IV diagnosis of anorexia nervosa (14 with a binge/purge pattern, six with a restricting pattern) and 12 of their mothers were administered the Adult Attachment Interview (AAI). The AAI is a semi-structured interview designed to elicit information about childhood and current experiences with attachment figures and about past trauma in the form of loss or abuse. The mothers also completed the Clinical Interview Schedule (Revised) as well as a demographic and clinical history questionnaire. The median age of the patients was 22 years (range, 15 to 46 years), and that of the mothers, 49 years (range, 40 to 81 years). Twelve patients had previously received inpatient treatment for an eating disorder. None of the mothers had a history of eating disorder. According to the AAI, 19 daughters (95%) and 10 mothers (83%) were rated as insecure with regard to attachment status. Of these, 15 daughters (79%) and seven mothers (70%) were rated as having a dismissive attachment style, a stance representative of a defensive turning away from potentially painful emotional material. Only one patient and two mothers were rated as having secure attachment patterns. The distribution of attachment patterns in both groups was significantly different from that of published norms. No significant association was found between the attachment styles of mother-daughter pairs.

In both mothers and daughters, idealization scores were found to be high and reflective functioning scores were found to be low. A high rate (67%) of unresolved loss was found among the mothers. According to the authors, a difficulty in emotional processing, exemplified by unresolved loss, may be transmitted to daughters and act as a risk factor for the development of anorexia nervosa. (18 References)
Numerous biological, psychological, familial, social, and cultural factors combine in various ways in the pathogenesis and clinical presentation of anorexia nervosa (AN). Modern psychobiological research conceptualizes personality as a complex adaptive system involving a bidirectional interaction between heritable neurobiological dispositions (temperament) and social learning (character). In the present study, the authors evaluated the temperament and character traits of anorectic outpatients and their parents and analyzed the correlation of temperament and character traits among members of anorectic families. The researchers also tested the ability of the Temperament and Character Inventory (TCI) to discriminate between normal controls and AN patients, their parents, and their families. The TCI is a 240-item (true/false) self-report instrument that measures four temperament dimensions (novelty seeking [NS], harm avoidance [HA], reward dependence [RD], and persistence [P]) and three character dimensions (self-directedness [SD], cooperativeness, and self-transcendence).

The TCI was completed by 50 female patients who met DSM-IV criteria for the restrictor type of AN and their parents (23 fathers and 25 mothers) as well as by 60 female control subjects and their parents (20 fathers and 20 mothers). The results of the TCI indicated that compared with the controls, the anorectic subjects scored lower in terms of NS and higher with respect to HA and P. The women with AN scored significantly lower than the control women with regard to SD. The mothers of the AN patients were lower in SD than the mothers of the control subjects. Compared with the fathers of the control subjects, the fathers of the anorectic individuals had significantly higher HA and RD scores and lower P and SD scores.

According to the authors, the current study demonstrates the importance of both temperament and character factors in AN patients and their families. The temperament triad found in the present group of anorectic subjects (high HA, low NS, and high P) corresponds to the traditional description of obsessive (or methodical) temperament types. The fact that low SD was found in all members of the anorectic family indicates that the psychopathology of AN extends beyond mere obsessiveness and combines obsessiveness with immaturity and poor character development. It appears that the individual psychopathologies of each family member in a unique familial setting interact to produce AN symptoms in susceptible members. (42 References)
CHILDHOOD ADVERSITIES ASSOCIATED WITH RISK FOR EATING DISORDERS OR WEIGHT PROBLEMS DURING ADOLESCENCE OR EARLY ADULTHOOD

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AM J PSYCHIATRY, 159:394-400, March 2002

The authors used data drawn from a prospective longitudinal study to investigate the association between childhood adversities and problems with eating or weight during adolescence and early adulthood. A community-based sample of 782 mothers and their offspring (397 males, 385 females) were interviewed during the childhood, adolescence, and early adulthood of the offspring. Childhood maltreatment, eating problems, environmental risk factors, temperament, maladaptive parental behavior, and parental psychopathology were assessed during childhood and adolescence. Eating disorders and problems with eating or weight in the offspring were assessed during adolescence and early adulthood.

Fifty-two offspring (43 females, nine males) received a diagnosis of eating disorder during adolescence or early adulthood. Those individuals who experienced physical neglect or sexual abuse during childhood were at elevated risk for eating disorders and for several types of eating or weight problems during adolescence or early adulthood. Low paternal affection toward the child, low paternal communication with the child, low paternal time spent with the child, low parental education, and poverty were each associated with one or more types of eating or weight problems in the offspring during adolescence or early adulthood. These associations remained significant after the effects of age, difficult temperament, childhood eating problems, and parental psychiatric disorders were controlled statistically. Numerous unique associations were found between specific childhood adversities and specific types of problems with eating or weight, and different patterns of association were seen in the male and female subjects. Offspring who experienced three or more kinds of maladaptive paternal behavior were approximately three times as likely as those who experienced no maladaptive paternal behaviors to have eating disorders during adolescence or early adulthood. The association between maladaptive paternal behaviors and risk of eating disorders in offspring remained significant after the effects of co-occurring childhood adversities were controlled statistically.

The present results are consistent with previous findings suggesting that childhood maltreatment and maladaptive paternal behavior may contribute to the development of eating disorders and that many types of childhood adversities may be associated with the risk of experiencing problems with eating or weight. (44 References)
TEASING HISTORY AND EATING DISORDER FEATURES:
AN AGE- AND BODY MASS INDEX-MATCHED COMPARISON
OF BULIMIA NERVOSA AND BINGE-EATING DISORDER

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COMPR PSYCHIATRY, 43:108-13, March/April 2002

Previous studies have found that early experiences of being teased about one's physical appearance may be associated with eating disturbances and body dissatisfaction. In the present investigation, the authors attempted to determine whether a history of being teased about physical appearance would be associated with distinct patterns of current symptomatology in two different eating-disordered groups: individuals with bulimia nervosa (BN) and persons with binge-eating disorder (BED). A group of 32 adult female outpatients with BN were compared with an age- and body mass index (BMI)-matched group of 32 adult female outpatients with BED. The mean age of the BN group was 32.13 years (range, 19 to 43 years), and that of the BED group was 36.31 years (range, 21 to 48 years). The mean BMI was 23.93 for the BN patients and 25.11 for the BED patients. A battery of standardized instruments was used to assess the following: physical appearance-related teasing history, current eating disorder features, body dissatisfaction, and psychological functioning (depression and self-esteem).

Compared with the age- and BMI-matched BED patients, the BN patients reported a significantly higher frequency of having been teased about their weight and size (WST) but a similar frequency of having been teased about their general appearance (GAT). While BN patients reported significantly greater dietary restraint than BED patients, the two groups did not differ significantly on other current eating disorder features (binge frequency, weight concern, shape concern, and eating concern), body dissatisfaction, or psychological functioning. Correlational analyses conducted separately within the BN and BED groups revealed few significant associations between teasing history and eating disorder features in either group. In the BN group, neither WST nor GAT was found to be significantly associated with eating disorder features or body dissatisfaction, but both were found to be significantly associated with lower self-esteem. In the BED group, WST was not associated with eating disorder features, body dissatisfaction, or psychological functioning, but GAT was associated with higher levels of dietary restraint and depression.

In the present investigation, physical appearance-related teasing history was not found to be associated with most eating disorder features in patients with BN or in patients with BED. However, the authors conclude, it appears that the association between different forms of teasing and psychological functioning may vary according to the type of eating disorder symptomatology presented. (30 References)
SELF-INJURIOUS BEHAVIOR IN WOMEN WITH EATING DISORDERS

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AM J PSYCHIATRY, 159:408-11, March 2002

Although there is a lack of comprehensive epidemiological data, clinical
reports indicate that from 4% to 10% of psychiatric patients injure themselves
deliberately. The objectives of the present study were twofold. First, the authors
assessed the lifetime and current occurrence of self-injurious behavior and its
phenomenology in patients with eating disorders. To identify high-risk patients,
they also investigated the possible impact of traumatic experiences, dissociation,
impulsivity, and obsessive-compulsive behavior on several aspects of self-
injurious behavior. Self-injurious behavior was defined as a self-inflicted direct
injury to the body without conscious suicidal intent.

The study sample was composed of 376 female inpatients (mean age, 24.3
years) who were being treated for an eating disorder. Of these, 119 patients met
DSM-IV criteria for anorexia nervosa, 137 fulfilled criteria for bulimia nervosa,
and 120 were diagnosed as having an eating disorder not otherwise specified. In
all, 130 patients (34.6%) reported injuring themselves at some point during their
lifetime, and 80 (21.3%) reported injuring themselves within the previous six
months. The highest rates of lifetime self-injurious behavior were found in the
patients with an eating disorder not otherwise specified (35.8%, N=43) and in the
patients with bulimia (34.3%, N=47). Among the self-injuring patients, 74.6%
(N=97) reported injuring themselves within the past 12 months, and 38.5%
(N=50) reported doing so within the past 30 days. In 64 patients (49.2%), the
onset of self-injurious behavior occurred after the onset of the eating disorder.
The onset of self-injurious behavior occurred before the onset of the eating
disorder in 33 patients (25.4%). In the remaining patients, the onset of the
eating disorder coincided with the onset of self-injurious behavior. When
multivariate analyses of behavior were computed across measures for two
factors (self-injurious behavior and diagnosis), the authors found that (compared
with noninjuring patients) self-injuring patients experienced a significantly
higher number of traumatic events, showed significantly higher dissociation
scores, and exhibited significantly more obsessive-compulsive thoughts and
behaviors. In addition, bulimic patients exhibited significantly higher impulsivity
scores.

According to the authors, the results of the present study strongly confirm
the relevance of self-injurious behavior as a comorbid feature of eating disorders
and point to the necessity of a routine screening for self-injurious behavior in
patients with eating disorders as well as the need for the development of a
standardized questionnaire. (51 References)
PREDICTORS OF TREATMENT UTILIZATION AMONG WOMEN WITH ANOREXIA AND BULIMIA NERVOSA

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AM J PSYCHIATRY, 159:140-2, January 2002

Several studies have examined the efficacy of treatment interventions for anorexia and bulimia nervosa. In the present investigation, the authors attempted to identify predictors of treatment utilization in women with eating disorders. In all, 246 women who met DSM-IV criteria for anorexia (N=136) or bulimia nervosa (N=110) completed prospective evaluations of eating disorder status, comorbid psychiatric disorders, global assessment of functioning, and treatment utilization (inpatient treatment, individual outpatient psychotherapy, inpatient or outpatient clinician-led group psychotherapy, and administration of medication [antidepressants or anxiolytics]). After intake interviews, follow-up interviews were conducted at six-month intervals, with the median follow-up period being 108 months.

Only 11 women (4%) reported receiving none of the forms of treatment assessed during follow-up. The number of women receiving treatment each year decreased as the duration of follow-up increased. Analyses revealed that significantly more women received treatment during the first year of the study than in the second year, but no significant differences in numbers were found between the second and third years, the third and fourth years, or the fourth and fifth years. Thus, women were most likely to receive some form of treatment during the first year of follow-up. Treatment utilization during a previous year significantly predicted treatment utilization during the subsequent year. Anorexic women spent significantly more time in inpatient and group treatment than bulimic women. However, the association between diagnostic status and group treatment was no longer significant when the authors controlled for inpatient treatment, and utilization of other forms of treatment did not differ significantly between the anorexic and bulimic women. Severity of eating disorder symptoms during each year significantly predicted treatment utilization during the subsequent year. Presence of a personality disorder at intake was associated with greater subsequent treatment utilization for all forms of intervention. Similarly, Global Assessment of Functioning Scale scores at intake significantly predicted subsequent treatment utilization across all interventions. Finally, a lifetime history of mood disorders predicted greater utilization of individual psychotherapy and antidepressant medication over the course of the follow-up period.

The authors conclude that women with more severe pathology have higher treatment utilization rates. (7 References)
THE EFFECT OF COGNITIVE-BEHAVIORAL THERAPY FOR BULIMIA NERVOSA ON TEMPERAMENT AND CHARACTER AS MEASURED BY THE TEMPERAMENT AND CHARACTER INVENTORY

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COMPR PSYCHIATRY, 43:182-8, May/June 2002

Cognitive-behavioral therapy (CBT) has proven to be a successful treatment method for reducing the symptomatology associated with bulimia nervosa (BN). In order to examine the impact of CBT on measures of temperament and character across treatment, the authors explored changes on the Temperament and Character Inventory (TCI) from pretreatment to one-year follow-up in a sample of women with BN. In all, 91 women who met DSM-III-R criteria for BN, who completed pretreatment measures, and who participated in a randomized controlled trial with a core treatment of BN were available for follow-up at one year. At pretreatment, the participants were administered the TCI as part of a larger assessment battery. They then received eight sessions of CBT and eight sessions of exposure with response prevention or relaxation training. The TCI was readministered at the one-year follow-up point.

Differences in TCI scale and subscale scores from pretreatment to one-year follow-up were preliminarily examined via a repeated measures analysis of variance for all scales. A formal assessment was then performed to compare change across treatment and one-year follow-up while controlling for the effects of covariates. More specifically, a repeated measures analysis of covariance was performed on each of the scales showing significant differences across time, with measures of clinical change (binge and purge frequency) and change in depression scores entered as covariates. The results revealed that between pretreatment and one-year follow-up, there were significant decreases in the TCI temperament scale of harm avoidance and increases in the TCI character scale of self-directedness. The observed differences in these scales were found to be independent of change in depression scores and other measures of therapeutic change (i.e., binge and purge frequency).

According to the authors, the present findings have implications both for the efficacy of CBT in the treatment of women with BN and for the value of personality measures as indicators of treatment efficacy. The current data suggest not only that self-directedness scores may be predictive of a successful outcome in the use of CBT, but also that CBT may have the ability to affect positive change in the very elements that constitute self-directedness. As such, change in self-directedness scores may constitute a measure of therapeutic change in the cognitive-behavioral treatment of BN. (29 References)
COGNITIVE-BEHAVIORAL THERAPY FOR BULIMIA NERVOSA: TIME COURSE AND MECHANISMS OF CHANGE

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J CONSULT CLIN PSYCHOL, 70:267-74, April 2002

While cognitive-behavioral therapy (CBT) has proven to be an effective treatment for bulimia nervosa (BN), its mechanisms of action have not been well established. The present authors conducted a randomized controlled trial of the treatment of BN that was designed to address the mechanisms of action of CBT. In this trial, 220 BN patients were randomly assigned to receive 19 individual sessions of either CBT or interpersonal psychotherapy (IPT) over a 20-week period and were followed for one year posttreatment. CBT focused primarily on treating the eating disorder and associated cognitive disturbances, while IPT concentrated primarily on achieving interpersonal change.

The results indicated that CBT had a rapid onset of action over the course of the 20 weeks of treatment. By Week 6, 62% of the final posttreatment improvement associated with CBT was already evident. At the end of treatment, vomiting was reduced by 80% in the CBT group and by 52% in the IPT group, while binge eating was reduced by 80% in the CBT group and by 44% in the IPT group. Both CBT and IPT produced significant within-group improvement in terms of concerns about body shape and weight. Mediator analyses revealed that mediators of binge eating frequency at posttreatment were change in dietary restraint at Weeks 4 and 6 and change in eating behavior self-efficacy. Mediators of purge frequency at posttreatment were change in dietary restraint at Weeks 4 and 6 and change in affective self-efficacy and eating behavior self-efficacy. At follow-up, dietary restraint at Week 4 was found to be the only significant mediator variable with regard to the outcome variable of binge eating frequency. For this outcome measure, there was no significant main effect of treatment, a finding that suggested that the treatment effect was totally mediated by the change in dietary restraint at Week 4. In all other cases, both the treatment effect and the mediator effect were significant, indicating partial mediation. There was no evidence to indicate that the therapeutic relationship was a mediator of change in either CBT or IPT.

According to the authors, the core finding of the present investigation is the fact that rapid change in dietary restraint emerged as the most clear-cut mediator of treatment outcome. This result provides empirical support for the theory that dietary restraint is a proximal antecedent of binge eating (Polivy and Herman, 1993) and bolsters the cognitive-behavioral model of the factors that maintain BN (Fairburn, 1997). (43 References)
A PLACEBO-CONTROLLED STUDY OF FLUOXETINE IN CONTINUED TREATMENT OF BULIMIA NERVOSA AFTER SUCCESSFUL ACUTE FLUOXETINE TREATMENT

Steven J. Romano, MD; Katherine A. Halmi, MD; Neena P. Sarkar, PhD; Stephanie C. Koke, MS (Lilly Research Laboratories, Lilly Corporate Center 2200, Indianapolis, IN 46285; e-mail: skoke@lilly.com); and Julia S. Lee, MS AM J PSYCHIATRY, 159:96-102, January 2002

While the efficacy of fluoxetine in the acute management of bulimia nervosa is well established, only a few controlled studies have addressed the issue of whether continuation of pharmacotherapy provides protection from relapse. The authors compared the efficacy and safety of fluoxetine with that of placebo in preventing relapse of bulimia nervosa during a 52-week period that followed an acute phase of successful fluoxetine therapy.

Male and female outpatients who met DSM-IV criteria for bulimia nervosa, purging type, were assigned to single-blind treatment with 60 mg/day of fluoxetine. After eight weeks of treatment, patients were considered to be responders if they experienced a decrease of at least 50% from baseline in the frequency of vomiting episodes during one of the two preceding weeks. Responders were randomly assigned to receive 60 mg/day of fluoxetine or placebo and were monitored for relapse for up to 52 weeks. Patients met relapse criteria if they experienced a return to the baseline frequency of vomiting that persisted for two consecutive weeks. Of 232 patients who received single-blind acute therapy, 150 (64.7%) met response criteria and were randomly assigned to receive either fluoxetine (N=76) or placebo (N=74). Fluoxetine-treated patients exhibited a significantly longer time to relapse than placebo-treated patients. Most of the relapses among the placebo-treated patients occurred during the first three months after randomization. Compared with the placebo group, the fluoxetine group had a lower number of relapses during the first three months and a more gradually decreasing probability of remaining relapse free. Analyses of mean change from randomization to endpoint for each primary and secondary efficacy measure provided further evidence of the beneficial effect of fluoxetine. Although both the fluoxetine-treated group and the placebo-treated group worsened over time on each measure, statistically significant differences favoring fluoxetine over placebo were observed for frequency of vomiting episodes, frequency of binge-eating episodes, Clinical Global Impression scale severity and improvement scores, patient's global impression score, and Yale-Brown-Cornell Eating Disorder Scale total score. There were no clinically relevant differences in safety between the fluoxetine and placebo groups.

The current study demonstrated that continued treatment with fluoxetine in bulimic patients who responded to acute fluoxetine therapy improved outcome and decreased the likelihood of relapse. (32 References)
AN OPEN-LABEL TRIAL OF SIBUTRAMINE IN OBESE PATIENTS WITH BINGE-EATING DISORDER

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J CLIN PSYCHIATRY, 63:28-30, January 2002

Selective serotonin reuptake inhibitors have been shown to significantly reduce binge-eating frequency in placebo-controlled studies of obese patients with binge-eating disorder. Sibutramine, a serotonin and norepinephrine reuptake inhibitor, has been approved by the United States Food and Drug Administration for the treatment of obesity (Ryan et al., 1995). Despite the clinical impression that sibutramine affects eating behavior, its use has not been studied in patients with binge-eating disorder. The authors conducted an open-label study in which they evaluated the efficacy and tolerability of sibutramine in obese patients with binge-eating disorder.

The study sample was composed of 10 female outpatients (mean age, 35.4 years) who were seeking treatment for obesity, who met DSM-IV criteria for binge-eating disorder, and who had no medical comorbidity. Comorbid DSM-IV Axis I disorders included current major depressive disorder (N=3), past major depressive disorder (N=1), generalized anxiety disorder (N=2), dysthymia (N=2), and social phobia (N=1). Sibutramine, 15 mg/day, was administered for a period of three months. Clinical evaluations were performed at two-week intervals during the first month of treatment and at the end of the second and third months. The Binge Eating Scale (BES) was used to assess the severity of binge-eating behavior, and the Beck Depression Inventory (BDI) was used to evaluate associated depressive symptoms. Information was also obtained from the patients with regard to number of days per week with binge-eating episodes, total number of binge-eating episodes per week, body weight, and adverse drug effects. Three of the 10 patients did not complete the study. The seven patients who did complete the trial experienced a complete resolution of binge-eating disorder (no binge-eating episodes at the end of treatment). The mean number of days per week with binge-eating episodes decreased significantly between baseline and endpoint (from 5.2 to 0.8), as did the total mean number of binge-eating episodes per week (from 8.2 to 1.4). From baseline to endpoint, the mean BES score fell from 31.2 to 15.2, the BDI score fell from 25.7 to 14.9, and there was a mean reduction in body weight. Most of the adverse reactions reported were benign and transitory in nature.

According to the authors, the present results suggest that sibutramine may be an effective and safe treatment for obese patients with binge-eating disorder. However, controlled studies with longer treatment periods are needed to confirm these preliminary observations. (15 References)
BOOKS RECEIVED FOR REVIEW


Abstracts and Reviews of Selected Literature in Psychiatry, Neurology, and their Allied Fields

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VALIDITY OF DSM-IV ADHD SUBTYPES IN A NATIONALLY REPRESENTATIVE SAMPLE OF AUSTRALIAN CHILDREN AND ADOLESCENTS

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 40:1410-7, December 2001

While attention deficit hyperactivity disorder (ADHD) was viewed as a single diagnostic category in DSM-III-R (American Psychiatric Association, 1987), in DSM-IV (American Psychiatric Association, 1994), ADHD was reconceptualized as a two-dimensional disorder consisting of clustered symptoms of inattention and hyperactivity/impulsivity from which three subtypes could be derived (predominantly inattentive, predominantly hyperactive-impulsive, and combined). In the present study, the authors examined the discriminant validity of DSM-IV ADHD subtypes in a nationally representative sample of Australian youths (N=3,597; age range, six to 17 years). The Diagnostic Interview Schedule for Children Version IV (including symptom-specific impairment questions) was administered to the children’s parents (response rate, 70%) and was used to identify DSM-IV ADHD subtypes. Children who did not meet criteria for ADHD were designated as controls. The parents also completed questionnaires designed to assess the children’s emotional and behavioral problems as well as their quality of life.

The results of the survey indicated that the current overall prevalence of DSM-IV ADHD was 7.5% (6.8% with impairment). With regard to subtypes, the inattentive type (3.7%) was found to be more common than the hyperactive-impulsive (1.9%) and combined (1.9%) types. ADHD was found to be more prevalent among males and to be linked to social adversity, particularly in those with the combined type of ADHD. Compared with non-ADHD controls, subjects in all three ADHD subtypes were rated as having more emotional and behavioral problems and a lower psychosocial quality of life; those with the combined type of ADHD were consistently rated as the most impaired. Children with the combined type of ADHD received higher ratings than those with the hyperactive-impulsive and inattentive types on externalizing behavior problems, interference with family activities, and symptom-specific impairments with schoolwork and peer-related activities. Compared with children with the hyperactive-impulsive type of ADHD, those with the inattentive type were rated as having lower self-esteem and more social and school-related problems, but fewer externalizing problems.

According to the authors, the present findings provide support for the view that DSM-IV ADHD subtypes are distinct clinical entities with impairments in multiple domains. (26 References)
FAMILIABILITY AND HERITABILITY OF SUBTYPES OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN A POPULATION SAMPLE OF ADOLESCENT FEMALE TWINS

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Attention deficit hyperactivity disorder (ADHD) is a highly heritable but clinically heterogeneous syndrome. Despite the almost universal reliance of current candidate gene and genetic linkage studies of ADHD on DSM-IV nosology, very little evidence has been presented regarding the relative heritabilities or familial specificities of DSM-IV ADHD subtypes. To examine the familiality and heritability of ADHD subtypes as defined by DSM-IV and by latent-class analysis (which assumes categorical rather than continuous latent variables), the authors studied a population sample of adolescent female twins drawn from the registry of all births recorded in the state of Missouri for the years 1968 through 1996. The researchers put forth the following hypotheses: (1) DSM-IV ADHD subtypes do not “breed true,” i.e., there is no tendency for particular subtypes to cluster exclusively in some families; and (2) latent-class ADHD subtypes do “breed true.”

The data consisted of parent reports on 4,036 female twins between the ages of 13 and 23 years (1,127 monozygotic pairs and 891 dizygotic pairs). The average age of the twins at the time of the parental interview was 14.9 years. Latent-class models were fitted to the parents’ responses about their offspring with regard to the 18 DSM-IV ADHD criterion A symptoms. Relative risk and odds ratios were used to assess within-subtype and between-subtype familiality and heritability of both DSM-IV and latent-class ADHD subtypes. Latent-class analysis was most compatible with the existence of three mild and three severe classes of ADHD symptoms in the general population. The three severe classes showed moderate overlap with the DSM-IV ADHD subtypes (inattentive, hyperactive/impulsive, and combined). The primarily inattentive and combined subtypes of DSM-IV ADHD co-clustered within families. The primarily hyperactive/impulsive DSM-IV subtype and the individual latent-class analysis subtypes did not co-cluster. Subtypes defined by both approaches were found to be highly heritable.

According to the authors, their results are most compatible with the presence of independent, familial forms of ADHD that are approximated by latent-class analysis and that are imperfectly operationalized by DSM-IV criteria. The findings suggest that the current DSM-IV ADHD subtypes may not be optimal for use as phenotypes in molecular genetic studies. (20 References) EAF
DEFICIENT INHIBITION AS A MARKER FOR FAMILIAL ADHD

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AM J PSYCHIATRY, 158:1884-90, November 2001

It is likely that attention deficit hyperactivity disorder (ADHD) is a multigenic and etiologically heterogeneous disorder. Some formulations of ADHD focus on deficits in various aspects of executive function, particularly deficient inhibition. Deficient inhibition produces secondary impairments in behavior, working memory, self-regulation of affect-motivation-arousal, internalization of speech, and reconstitution. These deficits underlie the behavioral abnormalities shown by ADHD individuals in everyday life and the impulsive and inattentive performances exhibited on a variety of laboratory tasks. The authors studied whether deficient inhibition, as measured by the stop-signal paradigm, denotes a familial subgroup of ADHD. The stop-signal paradigm is a laboratory task that requires a rapid ongoing motor response and the sudden cessation of that response following a specified signal (tone).

The study sample was composed of 54 ADHD children who were designated as having poor or good inhibition (on the basis of stop-signal paradigm performance) and 26 healthy comparison children (12 boys, 14 girls; mean age, 9.2 years). Of the ADHD children, 27 (24 boys, three girls; mean age, 9 years) had poor inhibition and 27 (24 boys, three girls, mean age, 9.3 years) had good inhibition. The two ADHD groups and the healthy group were compared with regard to family history of ADHD and exposure to neurobiological and psychosocial risk factors. Among the children with ADHD, those with poor and good inhibition did not differ in age, IQ, impairment, ADHD subtype, or comorbid diagnoses. However, the IQ of the children in the healthy comparison group was significantly higher than that of the ADHD children in the poor inhibition group and that of the ADHD children in the good inhibition group. No associations were found between family history of ADHD and either IQ or gender. Multinomial logistic regression indicated that the prevalence of ADHD was significantly higher in the families of ADHD children who exhibited poor inhibition (48.1%) than in the families of ADHD children who exhibited good inhibition (18.5%) or in the families of the healthy comparison children (7.7%). No significant differences emerged among the three groups in terms of neurobiological or psychosocial risk factors.

The authors conclude that deficient inhibition appears to delineate a familial subtype of ADHD. In the current study, psychosocial and neurobiological factors did not account for inclusion in the good inhibition group and did not act conjointly with inhibition to increase the risk for ADHD in the poor inhibition group. According to the researchers, their study demonstrates that cognitive measures, such as a laboratory measure of inhibition, can serve as phenotype markers for genetic analyses. (38 References)
DISSOCIATING ATTENTION DEFICITS IN CHILDREN WITH ADHD AND CONGENITAL HYPOTHYROIDISM USING MULTIPLE CPTs

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J CHILD PSYCHOL PSYCHIATRY, 42:1049-56, November 2001

Recent studies have suggested that children with different types of attention disorders also differ with regard to the kinds of errors they make on attention tasks. For example, children with attention deficit hyperactivity disorder (ADHD) consistently show an increased rate of commission errors (indicating difficulty with inhibitory control), whereas children with early-treated congenital hypothyroidism (CH) have problems with sustained and focused attention. In the present investigation, the authors attempted to determine whether children with ADHD and CH would produce different error patterns on continuous performance tasks (CPTs).

The study sample was composed of 43 children with ADHD (30 boys, 13 girls; age range, 7 to 12.8 years; mean age, 9.8 years), 35 children with CH (17 boys, 18 girls; age range, 6.9 to 12.9 years; mean age, 9 years), and 68 controls (32 boys, 36 girls; age range, 7 to 12.5 years; mean age, 9.9 years). The researchers used two variations of the CPT that differed in demands on inhibitory control and memory. One variation, the CPT: A-not-X task, required subjects to observe a continuous stream of letters shown at different rates on a computer screen and respond to all stimuli except “X.” The other variation, the CPT: AX task, required subjects to respond whenever a specified combination of letters, such as “A” followed by “X” appeared on the screen. On the CPT: A-not-X task, the results from one child with ADHD and two children with CH were eliminated because of technical difficulties. Nine children with ADHD, six children with CH, and four controls did not complete the CPT: AX task because of technical difficulties. On the CPT: A-not-X task, children with ADHD differed from controls in commission errors, signifying problems with inhibitory control; however, children with CH differed from controls in perceptual sensitivity or signal control. Although both the ADHD and the CH groups made more commission errors than the control group on the CPT: AX task, the ADHD group responded impulsively after seeing the first stimulus and thus did not adequately process the second stimulus, whereas the CH group responded correctly to the second stimulus but not to the first, suggesting a short-term memory deficit. Neither the ADHD nor the CH group differed from the control group in attentiveness or sustained attention.

According to the authors, the findings of the current study indicate that different groups of children with problematic attention may be affected in different ways. The present results also point to the utility of employing multiple CPTs in assessing the distinct deficits underlying different kinds of attention disorders. (39 References)
SEPARATING ATTENTION DEFICIT HYPERACTIVITY DISORDER AND LEARNING DISABILITIES IN GIRLS: A FAMILIAL RISK ANALYSIS

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AM J PSYCHIATRY, 158:1666-72, October 2001

Studies of referred and nonreferred children have consistently documented high rates of attention deficit hyperactivity disorder (ADHD) in children with learning disabilities and high rates of learning disabilities in children with ADHD. In the present investigation, the authors used familial risk analysis to examine the relationship between ADHD and learning disabilities in a group of girls who were between the ages of six and 18 years and in their first-degree relatives. They hypothesized that ADHD and learning disabilities in girls would be separate conditions transmitted independently and that their comorbidity would be due to nonrandom mating between parents.

The study sample was composed of the following three groups: female ADHD probands with a learning disability (N=21) and their parents and siblings (N=58); female ADHD probands without a learning disability (N=116) and their parents and siblings (N=303); and female comparison subjects without ADHD (N=113) and their parents and siblings (N=318). Rates of ADHD and learning disabilities were determined for the relatives in each of the three groups. Analyses revealed that the risk for ADHD was similarly high in the families of ADHD probands with and without learning disabilities; both the relatives of the ADHD children with learning disabilities and the relatives of the ADHD children without learning disabilities had significantly higher rates of ADHD than the relatives of the comparison children (24%, 20%, and 4%, respectively). Learning disabilities were significantly overrepresented in the first-degree relatives of the ADHD probands with learning disabilities (17%), as compared with the relatives of the ADHD probands without learning disabilities (8%) and the relatives of the comparison probands (4%). The authors examined the 58 relatives of the ADHD probands with a comorbid learning disability and compared the 13 relatives with ADHD and the 45 without ADHD. They found that the relatives with ADHD had a higher rate of learning disabilities than the relatives without ADHD (30.8% versus 13.3%). While this difference did not reach statistical significance, the fact that relatives with ADHD were over two times more likely than relatives without ADHD to have a learning disability suggests at least some degree of cosegregation between ADHD and learning disabilities. There was no evidence of nonrandom mating between spouses with ADHD and learning disabilities.

According to the authors, the present results provide support for the hypothesis that ADHD and learning disabilities are independent conditions. The current findings also raise the possibility that ADHD with a comorbid learning disability is a distinct familial subtype. (36 References)
INFLUENCE OF GENDER ON ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN REFERRED TO A PSYCHIATRIC CLINIC

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AM J PSYCHIATRY, 159:36-42, January 2002

There is a substantial discrepancy in the male-to-female ratio between clinic-referred (10 to 1) and community (3 to 1) samples of children with attention deficit hyperactivity disorder (ADHD). This discrepancy suggests that gender differences may be operant in the phenotypic expression of ADHD. In the current investigation, the authors systematically examined the impact of gender on the clinical features of ADHD in a group of children referred to a psychiatric clinic. They hypothesized that compared with ADHD in boys, ADHD in girls would be characterized by lower rates of comorbid disruptive behavior disorder, a preponderance of the inattentive subtype of ADHD, and less cognitive dysfunction.

The study sample was composed of 140 boys and 140 girls with ADHD and 120 boys and 122 girls without ADHD. Those without ADHD served as comparison subjects. All the boys and girls were between the ages of six and 17 years at the time of ascertainment. All the subjects were systematically assessed with structured diagnostic interviews and neuropsychological test batteries with regard to subtypes of ADHD as well as emotional, intellectual, interpersonal, school, and family functioning. Although the combined subtype of ADHD was found to be the most prevalent type in both boys and girls with ADHD, girls with ADHD were twice as likely as boys with ADHD to manifest the predominantly inattentive subtype of the disorder. Compared with boys with ADHD, girls with ADHD were less likely to have a learning disability in reading or mathematics, were less likely to manifest problems in school, and were more likely to participate in spare-time activities. In addition, girls with ADHD were at less risk than boys with ADHD for comorbid major depression, conduct disorder, and oppositional defiant disorder. A significant gender-by-diagnosis interaction was found for substance use disorders, which indicated that ADHD was a significantly weaker risk factor for substance use disorders in boys than it was in girls.

According to the authors, the findings of the current study suggest that the risk for ADHD-associated impairments may be similarly elevated in both boys and girls; however, the researchers note, gender-specific variations in baseline risks may result in different rates of psychiatric morbidity and dysfunction that may adversely affect the identification of ADHD in girls. (31 References) EAF
ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND PROBLEMS IN PEER RELATIONS: PREDICTIONS FROM CHILDHOOD TO ADOLESCENCE

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 40:1285-92, November 2001

While as many as 50% to 80% of children with attention-deficit hyperactivity disorder (ADHD) continue to meet diagnostic criteria for the disorder in adolescence (Barkley et al, 1990), little is known about the long-term effects of childhood ADHD on specific areas of adolescent adjustment, such as peer relationships. In the current investigation, the authors explored the association between childhood ADHD and adolescent peer functioning in terms of self-reported peer acceptance, parent-reported peer rejection, and both self- and parent-reported measures of the presence of friendship and the characteristics of the adolescents’ friends. Two hundred eleven adolescents (age range, 13 to 18 years) participated in the study: 111 with a history of childhood ADHD (proband group) and 100 with no such history (non-ADHD group).

While there was no difference between probands and non-ADHD adolescents in their self-perceptions of peer acceptance, there was a large and significant effect of ADHD history on parent-reported peer rejection; probands were reported to experience significantly more peer rejection than non-ADHD adolescents. Compared with the parents of non-ADHD adolescents, parents of probands reported that their children had fewer close friends. The non-ADHD group reported that their friends were more involved in conventional activities than did the proband group. Within the proband group, those who were more aggressive during childhood reported lower self-perceived peer acceptance in adolescence. Similarly, within the proband group, there were trends for more aggressive children to perceive less competence in their ability to establish close adolescent friendships and to have fewer close friends, according to parents’ reports. The long-term effects of ADHD on social functioning were more pronounced in those probands with persistent ADHD or conduct disorder in adolescence.

According to the authors, the current findings serve to extend our understanding of the functioning of adolescents with childhood ADHD beyond broad assessments of mental health to specific domains of social adjustment. The theory that children with ADHD outgrow the disorder is far from accurate, they conclude. Even those youths who no longer meet diagnostic criteria for ADHD in adolescence show impairment in their peer relationships. In light of the social sequelae of ADHD and the increased importance of peer group acceptance, friendships, and peer networks for adjustment, the researchers note, adolescence may be a particularly difficult time for youths with a history of ADHD. Standard medication regimens may not be sufficient to treat the social impairments common to ADHD. (33 References)
DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF SINGLE-DOSE AMPHETAMINE FORMULATIONS IN ADHD

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Stimulants are the drugs of choice for the pharmacological treatment of attention-deficit/hyperactivity disorder (ADHD), with methylphenidate being the most widely prescribed agent. Over the past few years, however, a mixture of 75% dextroamphetamine and 25% levoamphetamine (Popper, 1994) has been aggressively marketed under the trade name Adderall®. In the present study, the authors compared the efficacy and time course of single morning doses of Adderall, immediate-release dextroamphetamine sulfate, and extended-release dextroamphetamine (Spansules).

The sample was composed of 35 children (21 boys, 14 girls; age range, 6.9 to 12.2 years; mean age, 9.1 years) with a history of severe hyperactivity, impulsivity, and inattention; all met DSM-IV criteria for ADHD, combined type. Double-blind medications were administered for eight weeks, with each child receiving (in random order) two weeks of treatment with Adderall, immediate-release dextroamphetamine, dextroamphetamine Spansules, and placebo. Behavior ratings, locomotor activity measurements, and academic assessments were obtained over the eight-week period. Compared with placebo, all three stimulants exhibited robust efficacy on nearly all objective and subjective measures. Teacher ratings indicated that dextroamphetamine Spansules were significantly less effective in the morning than immediate-release dextroamphetamine, which did not differ significantly from Adderall. Objective wrist-mounted Actometers confirmed that Adderall was more effective than immediate-release dextroamphetamine for the first hour of morning classroom time and more effective than Spansules for the first two hours of morning classroom time. There were no drug-drug differences on measures of academic productivity (obtained nearly four hours after drug administration), but Adderall did not significantly increase the number of math problems attempted or completed relative to placebo, whereas Spansules had a robust effect on both measures. Parent behavior ratings and locomotor activity measures indicated improvements up to 12 hours after single doses of all three drugs.

In the current study, both immediate-release amphetamines (Adderall and dextroamphetamine) demonstrated an earlier onset of efficacy, while extended-release dextroamphetamine (Spansules) showed more sustained effects that were present on a wider range of measures. To truly define the utility of single-morning doses of amphetamines in the treatment of ADHD, the authors note, future studies should compare long-acting formulations with multiple doses of immediate-release preparations. (24 References)
METHYLPHENIDATE EFFECTS ON TASK-SWITCHING PERFORMANCE IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 40:1277-84, November 2001

Several researchers have argued that attention-deficit/hyperactivity disorder (ADHD) is associated with a deficit in executive control. Executive control processes encompass those cognitive functions that are concerned with the selection, scheduling, and coordination of the computational processes responsible for perception, memory, and action. The main goal of the present study was to examine the specificity of methylphenidate effects on the processes that support the ability to rapidly and accurately coordinate the performance of multiple tasks in children with ADHD.

Twenty children with ADHD (14 boys, six girls; age range, 8 to 14 years; mean age, 8.9 years) performed a task-switching paradigm while on and off medication. The paradigm involved switching between two different tasks: discriminating the value of a number presented on a computer screen and deciding how many numbers were present on the screen. Single-task control conditions were also performed. The children were tested in two experimental sessions conducted on two different days. A single dose of methylphenidate (range, 5 to 30 mg; mean, 15 mg) was administered 30 to 90 minutes prior to experimental testing. Ten children were unmedicated during the first session, and 10, during the second session. Analyses of variance indicated that methylphenidate selectively enhanced the children’s ability to rapidly and accurately switch between tasks and to focus attention on the currently relevant response set. Medication helped the children in selectively ignoring the incorrect response on response-incompatible trials (those trials in which the relevant and irrelevant task called for different responses); i.e., the children were able to reduce error rates when receiving methylphenidate. Medication did not significantly affect the children’s use of a cue to prepare for a task switch.

According to the authors, the present findings extend our knowledge of the influence of stimulant medication on the executive control processes of children with ADHD. These data also suggest that some aspects of executive control necessary for the coordination of multiple tasks, such as the preparation of a new task set, are relatively intact in children with ADHD. Further research will be needed to determine whether ADHD children’s ability to prepare for a subsequent task is dependent on explicit environmental cues (such as those used in the current study) or whether preparation can also be internally triggered (e.g., on the basis of the knowledge that that the task will change every four trials). (40 References)
DEVELOPMENTAL ASPECTS OF PSYCHOSTIMULANT TREATMENT IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 40:1441-7, December 2001

Presently, the most well-established pharmacological treatments for attention-deficit/hyperactivity disorder (ADHD) are the psychostimulants. Although a significant amount of attention has been directed toward the use of psychostimulants in children with ADHD, little is known about the dosing and efficacy of these drugs in teenagers with ADHD. In the present study, the authors examined the relationship between age and short-term clinical response to psychostimulant treatment in youths with ADHD and determined whether weight-corrected doses of optimized psychostimulant therapy varied as a function of patient age.

The study sample was composed of 177 patients with ADHD (143 males, 34 females): 83 were diagnosed with the inattentive subtype, and 94 were classified as having the combined subtype. Sixty-nine (57 males, 12 females) were between four and 7.99 years of age (mean, 6.35 years); 56 (45 males, 11 females) were between the ages of eight and 10.99 years (mean, 9.47 years), and 52 (41 males, 11 females) were between 11 and 17.59 years of age (mean, 13.64 years). Of the 177 patients, 111 were treated with methylphenidate, and 66 were treated with Adderall®. All the patients were evaluated at baseline and after receiving a week of treatment at each blinded, randomized dose level (placebo, 5 mg per dose, 10 mg per dose, and 15 mg per dose). At the end of the four-week trial, a “best dose” was assigned to each patient before the medication blind was broken. This best dose was determined on the basis of the results of rating scales, parent interviews, patient reports, teacher ratings, and clinical observations. The results indicated that methylphenidate and Adderall were of similar efficacy. Both medications proved to be as effective in teenagers as they were in children. However, the oldest youths benefited from the smallest weight-adjusted dose of medication, and the children who were between the ages of seven and 11 years were found to optimally respond to a lower weight-adjusted dose of medication than the youngest patients. In general, both medications were well tolerated.

According to the authors, the results of the current investigation suggest that psychostimulants are equally effective in treating children and adolescents with ADHD. Adolescents with ADHD, the researchers note, may not necessarily require more medication than younger children to achieve a similar therapeutic response. (21 References)
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Books Received for Review
COMORBIDITY, IMPAIRMENT, AND SUICIDALITY IN SUBTHRESHOLD PTSD

Randall D. Marshall, MD (Anxiety Disorders Clinic, Unit 69, New York State Psychiatric Institute, 1051 Riverside Dr., New York, NY 10032; e-mail: randall@nyspi.cpmc.columbia.edu); Mark Olfson, MD, MPH; Fredric Hellman, BS; Carlos Blanco, MD, PhD; Mary Guardino; and Elmer L. Struening, PhD

AM J PSYCHIATRY, 158:1467-73, September 2001

According to the authors, reliance on the categorical model of psychiatric disorders has led to neglected study of posttraumatic sequelae that fall short of meeting full criteria for posttraumatic stress disorder (PTSD). Subthreshold PTSD, defined in several different ways, has been found to be as common as full-blown PTSD and to be associated with substantial degrees of impairment. The purpose of the present investigation was to examine the relationships among PTSD symptoms, disability levels, and comorbid psychiatric disorders in a large data set collected on National Anxiety Disorders Screening Day 1997.

Of the 9,358 individuals who were screened for affective and anxiety disorders at 1,521 sites across the United States, 2,608 (27.9%) reported experiencing at least one PTSD symptom that persisted at least one month after the occurrence of a traumatic event. Of the total study group (N=9,358), 844 individuals (9%) met full screening criteria for PTSD, and 1,764 (18.9%) had from one to three subthreshold PTSD symptoms. Impairment, comorbid anxiety disorders, major depressive disorder, and rates of suicidality were determined and compared in individuals with no, one, two, three, or four (full PTSD) symptoms by means of a screening questionnaire. Regression analyses were used to evaluate the relative contribution of subthreshold PTSD and comorbid disorders to impairment and suicidal ideation. Impairment, number of comorbid anxiety disorders, and likelihood of meeting screening criteria for major depressive disorder increased significantly with each incremental increase in number of PTSD symptoms from one to four. The proportion of subjects stating that they had had suicidal thoughts in the last month also increased as the number of PTSD symptoms increased (9% of those with no PTSD symptoms, 13% of those with one symptom, 15% of those with two symptoms, 23% of those with three symptoms, and 33% of those with four symptoms). Individuals with subthreshold PTSD were at greater risk for suicidal ideation even after the authors controlled for the presence of comorbid major depressive disorder.

The current results indicate that substantially greater numbers of individuals experience disability after trauma than is suggested by simply considering rates of full PTSD. In light of the broad public health implications of these findings, the authors note, more efforts are needed to identify subthreshold PTSD symptoms in clinical populations, epidemiologic surveys, and treatment studies. (35 References)
CSF NOREPINEPHRINE CONCENTRATIONS
IN POSTTRAUMATIC STRESS DISORDER

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Norepinephrine is one of the major central nervous system (CNS) effectors of the human stress response. Despite evidence of hyperresponsive peripheral and CNS noradrenergic activity in individuals with posttraumatic stress disorder (PTSD), direct measures of CNS norepinephrine in PTSD have been lacking. The goal of the present investigation was to determine serial norepinephrine levels in patients with PTSD.

By means of an indwelling subarachnoid catheter, CSF samples were obtained serially over a six-hour period in 11 male combat veterans with chronic PTSD (age range, 23 to 49 years; mean age, 42 years) and eight healthy men (age range, 23 to 50 years; mean age, 41 years). The use of a flexible, indwelling subarachnoid catheter allowed the researchers to wait for the stress of the lumbar puncture procedure and spinal canal catheterization to resolve before sampling CSF. The norepinephrine levels obtained were therefore more reflective of baseline status than of a stress-induced state. Both the PTSD patients and the healthy men were administered the Structured Clinical Interview for DSM-III-R. Severity of the patients' PTSD symptoms was assessed with the Clinician-Administered PTSD Scale. CSF norepinephrine levels (obtained hourly) were found to be significantly higher in the PTSD patients than in the healthy men. The mean CSF norepinephrine level was 0.55 pmol/ml in the PTSD subjects and 0.39 pmol/ml in the normal subjects. In the patients with PTSD, mean CSF norepinephrine concentrations correlated positively with total Clinician-Administered PTSD scores. The correlation between mean CSF norepinephrine and the avoidance subscale of the Clinician-Administered PTSD Scale was positive and significant; nonsignificant positive correlations were observed for both the intrusion and hyperarousal subscales. However, no significant relationship was found between plasma norepinephrine concentrations and severity of PTSD symptoms.

According to the authors, the current data reveal not only that baseline CNS noradrenergic tone is higher in patients with chronic PTSD than in healthy comparison subjects but also that this pathophysiologic finding is directly related to the severity of the disorder's clinical manifestations. The elevated baseline CSF norepinephrine concentrations are consistent with a sustained hyperactivation of CNS fear-related neurocircuits in PTSD, even in the absence of a specific stressor. (34 References)
GENDER DIFFERENCES IN POSTTRAUMATIC STRESS DISORDER AFTER MOTOR VEHICLE ACCIDENTS

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AM J PSYCHIATRY, 158:1486-91, September 2001

Women have higher rates of posttraumatic stress disorder (PTSD) than men. To determine the extent to which this gender difference might be explained by known risk factors for the development of PTSD, the authors studied 122 subjects (64 men, 58 women; age range, 18 to 65 years) who had been involved in a serious motor vehicle accident and examined the following variables: prior trauma, PTSD, major depression, anxiety disorder (not including PTSD), and peritraumatic dissociation; current peritraumatic dissociation; and passenger injury. One month after the accident, all study participants were assessed with the Structured Clinical Interview for DSM-III-R and the Peritraumatic Dissociative Experiences Questionnaire-Rater Version.

At one month postaccident, 42 subjects (12 men, 30 women) were found to have developed PTSD. Women did not differ from men in meeting the overall reexperiencing criterion (criterion B) for a diagnosis of PTSD; however, women were at greater risk for two of the individual reexperiencing symptoms. Women were 3.79 times more likely than men to report intense feelings of distress when in a situation similar to the motor vehicle accident and 5.16 times more likely to report a physical reaction to memories of the accident. Women were 4.71 times more likely than men to meet the overall avoidance/numbing criterion (criterion C) for PTSD. Examination of individual criterion C symptoms indicated that women were 3.75 times more likely than men to report avoiding thoughts and situations associated with the accident; 3.65 times more likely to report loss of interest in significant activities; and 2.90 times more likely to experience a sense of a foreshortened future. Women were 3.83 times more likely than men to meet the overall arousal criterion (criterion D) for PTSD, and in terms of individual criterion D symptoms, women more often reported trouble sleeping, difficulty concentrating, and being easily startled. Gender differences in acute PTSD were not associated with prior trauma, prior PTSD, prior peritraumatic dissociation, prior major depression, prior anxiety disorder (not including PTSD), or passenger injury. However, peritraumatic dissociative symptoms at the time of the accident were associated with a significantly higher risk for acute PTSD in women than they were in men.

According to the authors, the present findings indicate that there may be fundamental neurobiological differences between women and men with regard to peritraumatic dissociation. (17 References)
EFFECTS OF GENDER AND ETHNICITY ON DUTY-RELATED POSTTRAUMATIC STRESS SYMPTOMS AMONG URBAN POLICE OFFICERS

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J NERV MENT DIS, 189:442-8, July 2001

Most studies of posttraumatic stress disorder (PTSD) in the general population have found that women and ethnic minorities (e.g., African-Americans and Hispanic-Americans) have higher rates of PTSD than men and European-Americans (i.e., non-Hispanic whites), respectively. To examine ethnic and gender differences in duty-related symptoms of PTSD, the authors studied a group of urban police officers. They obtained self-report measures of PTSD symptoms, peritraumatic dissociation, exposure to duty-related critical incidents, general psychiatric symptoms, response bias due to social desirability, and demographic variables. Assessment instruments included the Social Desirability Scale, the Critical Incident History Questionnaire, the Peritraumatic Dissociative Experiences Questionnaire, the Mississippi Scale-Civilian Version, and the Symptom Checklist 90-Revised.

The study sample was composed of 655 urban police officers (519 men, 136 women; mean age, 37.2 years). In terms of ethnicity, 313 (249 men, 64 women) were white (European-American), 158 (120 men, 38 women) were African-American, and 184 (150 men, 34 women) were Hispanic-American. Contrary to expectation, the authors found no gender differences with regard to PTSD symptoms. However, ethnicity was found to be a weak but statistically significant predictor of duty-related PTSD symptoms. This ethnicity effect was specific to PTSD symptoms in that no effect was found for general psychiatric symptoms once PTSD symptoms were accounted for. Hispanic-American police officers reported higher levels of PTSD symptoms than their African-American and European-American counterparts, whereas African-American officers were not significantly different from European-American officers in terms of the magnitude of PTSD symptoms. The researchers found that the ethnic difference remained even after they controlled for differences in social desirability and peritraumatic dissociation.

According to the authors, the current data are of note because: (1) they replicate the results of a previous study in which higher rates of PTSD were found among Hispanic-American military personnel; and (2) they fail to replicate the well-established finding of higher levels of PTSD symptoms among civilian women. Further study is needed to determine whether a more careful assessment of Hispanic ethnicity or an assessment of PTSD symptoms relative to a police officer’s entire trauma history would reveal greater vulnerability to PTSD among Hispanic-American police officers. (30 References)
GENDER DIFFERENCES IN RISK FACTORS FOR TRAUMA EXPOSURE AND POST-TRAUMATIC STRESS DISORDER AMONG INNER-CITY DRUG ABUSERS IN AND OUT OF TREATMENT

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COMPR PSYCHIATRY, 42:111-7, March/April 2001

Some studies suggest that the rate of posttraumatic stress disorder (PTSD) in persons exposed to trauma may vary as a function of both gender and the nature of the traumatic event. Over the past two decades there has been a growing awareness of the comorbidity between PTSD and substance use disorders in the general population. The authors studied a group of drug users recruited from the street in order to examine the role of gender with regard to the following: (1) prediction of the nature of the traumatic event and PTSD symptoms; (2) patterns of substance use disorders in relation to trauma exposure and PTSD symptoms; (3) comorbidity of other psychiatric disorders with trauma exposure and PTSD; and (4) the temporal association of substance use disorder, exposure to trauma, and PTSD.

In all, 464 current drug abusers (mean age, 32.3 years) were assessed by means of the Diagnostic Interview Schedule for DSM-III-R and the Composite International Diagnostic Interview-Substance Abuse Module. Of the total sample, 166 subjects (109 males, 57 females) reported being exposed to a traumatic event at some time in their lives. Although men and women were exposed to traumatic events at the same rate, the type of events reported differed by gender. Women were significantly more likely than men to report rape as the primary qualifying trauma, but they were three times less likely than men to report physical assault. Of the 166 subjects who were exposed to a traumatic event, 30 individuals met criteria for DSM-III-R PTSD. Although gender was not a predictor of exposure to traumatic events, once exposed, women were more likely than men to meet criteria for PTSD. In terms of comorbidity, adult antisocial personality disorder, affective disorder, schizophrenia, and generalized anxiety disorder predicted exposure to a traumatic event. Once exposed, subjects who met diagnostic criteria for schizophrenia, generalized anxiety disorder, or a phobic disorder were more likely to develop PTSD than exposed subjects without these disorders.

Although polydrug use, drug injection, and a drug abuse/dependence diagnosis were predictive of exposure to trauma, they were not associated with progression to PTSD among the event-exposed. When the group of subjects who experienced trauma was considered as a whole, analyses showed that the onset of drug use preceded exposure to a traumatic event by seven years. While women experienced their first traumatic event four years after initial drug use, men were exposed to their first traumatic event approximately eight years after the onset of drug use. (25 References)
A LONGITUDINAL AND RETROSPECTIVE STUDY OF PTSD AMONG OLDER PRISONERS OF WAR

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AM J PSYCHIATRY, 158:1474-9, September 2001

One avenue for studying the long-term course of posttraumatic stress disorder (PTSD) is to examine cohorts of survivors who have lived with trauma for 50 years or longer, i.e., survivors of World War II, the Holocaust, and the Korean War. The authors used contemporaneously gathered longitudinal data and retrospectively gathered symptom reports to obtain a more complete picture of changing PTSD symptom levels among older survivors of remote trauma, namely, American former prisoners of war (POWs). For the longitudinal portion of the study, PTSD prevalence and symptom levels were reassessed in 177 community-dwelling World War II and Korean War POWs who had first been assessed four years earlier. For the retrospective portion, 244 community-dwelling World War II POWs were asked to provide symptom level reports in five-to-ten-year increments from the time of repatriation up to the time of the first data collection (early 1990s). The main assessment tool used was the Mississippi Scale for Combat-Related Posttraumatic Stress Disorder.

The authors found that PTSD prevalence and symptom levels increased modestly but significantly over the four-year measurement interval. At the first assessment, 47 subjects (27%) met or exceeded the Mississippi scale cutoff score for PTSD, whereas 60 subjects (34%) met or exceeded the cutoff score at the second assessment. Of the 177 subjects who participated in the longitudinal portion of the study, 19 were newly diagnosed with PTSD at the second assessment; six no longer met PTSD diagnostic criteria at the second assessment; 41 met PTSD criteria at both measurements; and 111 did not meet PTSD criteria at either measurement. Retrospective reports of feeling “seriously troubled” by PTSD symptoms since repatriation revealed symptom increases in the preceding two decades. Symptom levels were high immediately following discharge and for a few years after repatriation. PTSD symptoms then began a slow decline that lasted into the 1970s. The number of respondents who reported feeling “seriously troubled” by PTSD symptoms began to rise again in the 1980s, and this increase continued into the early 1990s. Long-delayed onset of PTSD symptoms was found to be rare.

According to the authors, clinicians should be aware of the possibility that older patients with trauma histories may be at risk for a re-emergence or intensification of PTSD symptoms as they move through their later years. On the other hand, older survivors of remote trauma who so far have not experienced significant PTSD symptoms are not likely to experience a long-delayed onset of the disorder. (47 References)
TR A U M A, SYMPTOMS OF POSTTRAUMATIC STRESS DISORDER, AND ASSOCIATED PROBLEMS AMONG INCARCERATED VETERANS

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PSYCHIATR SERV, 52:959-64, July 2001

The number of incarcerated persons in the United States is growing, and a substantial proportion of these individuals have psychiatric disorders. While the prevalence of posttraumatic stress disorder (PTSD) has been examined separately in incarcerated women, incarcerated men, and incarcerated male adolescents, the symptoms of psychological trauma have not been evaluated in jailed veterans. The authors examined exposure to trauma, PTSD symptoms, functional status, and treatment history in a group of incarcerated veterans.

A convenience sample of 129 jailed veterans (124 men, 5 women; mean age, 43.3 years) agreed to be interviewed as part of a clinical outreach program. The mean duration of incarceration prior to interview was 20.53 days. The participants completed the Life Event History Questionnaire, the Addiction Severity Index, and the PTSD Checklist-Civilian Version (PCL-C). Veterans who had scores of 50 or above on the PCL-C (designated as screening positive for PTSD) were compared with those veterans whose PCL-C scores were below 50 (designated as screening negative for PTSD). A total of 112 participants (87%) reported at least one lifetime traumatic event (mean number of events reported, 2.8). In all, 51 veterans screened positive for PTSD, and 78 screened negative. Participants who screened positive for PTSD reported significantly more total lifetime traumas than those who screened negative. The two groups also differed in their reporting of some specific traumatic events. Items on the Life Event History Questionnaire that assessed vicarious trauma ("witnessed death or injury," "witnessed a bad event happening to someone close") were most strongly associated with screening positive for PTSD. In addition, participants who reported a history of childhood trauma were more likely than those who denied childhood trauma to screen positive for PTSD. Compared with veterans who screened negative for PTSD, those who screened positive also reported more serious current legal problems; a higher lifetime use of alcohol, cocaine, and heroin; higher recent expenditures on drugs; more psychiatric symptoms; and poorer general health despite more previous psychiatric, medical, and substance abuse treatment.

According to the authors, the present results indicate that exposure to trauma and symptoms of PTSD are prevalent among incarcerated veterans. The researchers recommend the development of an improved treatment model that potentially could play a role in keeping jailed veterans with PTSD away from falling into a pattern of repeated incarcerations. (26 References) EAF
VIRTUAL REALITY EXPOSURE THERAPY FOR VIETNAM VETERANS 
WITH POSTTRAUMATIC STRESS DISORDER

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Posttraumatic stress disorder (PTSD) is one of the most disabling psychopathologic conditions affecting the veteran population. In the report presented here, the authors propose the use of virtual reality exposure (VRE) therapy as an alternative to typical imaginal exposure treatment for Vietnam combat veterans with PTSD. Virtual reality integrates real-time computer graphics, body-tracking devices, visual displays, and other sensory input devices, all of which are used to immerse a participant in a computer-generated virtual environment that changes in a natural way with head and body motion. The advantages of VRE include conducting exposure therapy without leaving the therapist’s office, exactly controlling exposure stimuli, and exposing the patient to less risk of harm or embarrassment.

In an open clinical trial, 10 male Vietnam combat veterans, all of whom met DSM-IV criteria for current chronic PTSD, were exposed to two virtual environments: a virtual Huey helicopter flying over Vietnam terrain (jungles, rivers, and rice paddies), and a virtual clearing surrounded by jungle. Treatment was typically delivered in 10 90-minute individual sessions conducted twice a week over a period of five to seven weeks, although the range was eight to 16 sessions (depending on the participant’s progress). A variety of clinician-rated and self-report measures were used to assess the patients at pretreatment, posttreatment, and three- and six-month follow-ups. At the six-month follow-up, results of the Clinician Administered PTSD scale (the primary outcome measure) indicated an overall statistically significant reduction from baseline in symptoms associated with specific reported traumatic experiences. All eight participants interviewed at the six-month follow-up reported reductions in PTSD symptoms ranging from 15% to 67%. Significant decreases were seen in all three symptom clusters (reexperiencing, avoidance, and arousal). Patient self-reported intrusion symptoms as measured by the Impact of Event Scale were significantly lower at the three-month follow-up than at baseline, but not at the six-month follow-up, although there was a clear trend toward fewer intrusive thoughts and somewhat less avoidance.

In the small sample of male Vietnam veterans studied here, the authors conclude, VRE therapy was well tolerated and led to significant reductions in PTSD and related symptoms. The patients appeared to become emotionally engaged in the exposures and seemed to believe that VRE therapy was of benefit to them. No patient decompensated as a result of exposure to the virtual environments. (29 References)
IMAGERY REHEARSAL THERAPY FOR CHRONIC NIGHTMARES IN SEXUAL ASSAULT SURVIVORS WITH POSTTRAUMATIC STRESS DISORDER
A Randomized Controlled Trial

Barry Krakow, MD (Sleep & Human Health Inst., 4775 Indian School Rd. NE, Ste. 305, Albuquerque, NM 87110; e-mail: bkrakow@salud.unm.edu); Michael Hollifield, MD; Lisa Johnston, MA, MPH; Mary Koss, PhD; Ron Schrader, PhD; Teddy D. Warner, PhD; Dan Tandberg, MD; John Lauriello, MD; Leslie McBride, BA; Lisa Cutchen, MA; Diana Cheng, MA; Shawn Emmons, PhD; Anne Germain, MPs; Dominic Melendrez, PSG-T; Diane Sandoval, BS; and Holly Prince, MA  JAMA, 286:537-45, August 1, 2001

Chronic nightmares occur frequently in patients with posttraumatic stress disorder (PTSD). The authors’ aim was to determine whether treating chronic nightmares with imagery rehearsal therapy (IRT) would reduce the frequency of disturbing dreams, improve sleep quality, and decrease PTSD symptom severity. IRT is a sleep-oriented treatment that focuses on nightmares within the framework of an imagery and cognitive restructuring paradigm.

The study sample consisted of 168 female sexual assault survivors with self-reported nightmares, insomnia, and posttraumatic stress symptoms. They were randomly assigned to a treatment group (IRT, N=88) or to a wait-list control group (N=80). The former received IRT over a series of three sessions; the latter received no additional intervention, but continued to receive any prior ongoing therapy. Assessment tools (administered at baseline and three- and six-month follow-ups) included the Nightmare Frequency Questionnaire, the Pittsburgh Sleep Quality Index, the PTSD Symptom Scale, and the Clinician-Administered PTSD Scale. In all, 114 participants completed at least one follow-up, and 77 completed both. When the authors compared baseline and follow-up scores (N=97-114), they found that IRT significantly reduced nights per week with nightmares and number of nightmares per week, improved sleep, and reduced PTSD symptoms. The controls showed small, nonsignificant improvements on the same measures. In a three-point analysis (N=66-77), improvements occurred in the IRT group at three months and were sustained without further intervention or contact between three and six months. An intent-to-treat analysis (N=168) confirmed significant differences between the IRT and control groups for nightmares, sleep and PTSD, with moderate effect sizes for treatment and small effect sizes for the control condition. PTSD symptoms decreased by at least one level of clinical severity in 65% of the IRT group, while symptoms worsened or did not change in 69% of the controls.

The authors conclude that IRT is a brief, well-tolerated treatment that appears to decrease chronic nightmares, improve sleep quality, and decrease PTSD symptom severity. (51 References)
SERTRALINE TREATMENT OF POSTTRAUMATIC STRESS DISORDER: RESULTS OF 24 WEEKS OF OPEN-LABEL CONTINUATION TREATMENT

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Posttraumatic stress disorder (PTSD) is typically associated with a high degree of chronicity, comorbidity, and psychosocial disability. While two large, placebo-controlled studies have confirmed the efficacy of sertraline in the acute treatment of PTSD, almost no prospective, long-term treatment trials have been reported. In the current study, 128 outpatients (95 women, mean age, 39.8 years; 33 men, mean age, 41.2 years) who met DSM-III-R criteria for PTSD and who had completed 12 weeks of double-blind, placebo-controlled, acute-phase treatment with sertraline were enrolled in a 24-week, open-label continuation phase. The mean duration of PTSD was 11.4 years for the women and 16.9 years for the men. During the 24 weeks of open-label treatment, the patients were evaluated and rated weekly for the first four weeks and then every two weeks thereafter. The primary efficacy parameters were the 17-item total severity score on the Clinician Administered PTSD Scale Part 2 (CAPS-2); the total score on the 15-item, patient-rated Impact of Event Scale; and ratings on the Clinical Global Impressions (CGI)-Improvement scale and the CGI-Severity of Illness scale. Treatment response was defined as a decrease of at least 30% in the CAPS-2 severity score (compared with acute-phase baseline score) and a CGI-Improvement score of 1 or 2.

The results indicated that 92% of the patients who had responded to sertraline during acute-phase treatment maintained their response during the full six months of continuation treatment. In addition, 54% of the patients who failed to meet responder criteria during the acute-phase became responders during continuation therapy; 49% of the patients who converted to responder status did so within the first six weeks of continuation treatment. Over the 36-week course of acute and continuation therapy, 20% to 25% of the improvement in the CAPS-2 severity score occurred during the continuation phase of treatment. A high pretreatment CAPS-2 score (>75) predicted a longer time to response and a greater likelihood that response would occur after 12 weeks of treatment. Sertraline was found to be well tolerated, with only 8.6% of patients discontinuing the drug because of adverse events.

According to the authors, the current data indicate that the acute efficacy of sertraline is sustained in the vast majority of patients and that at least half of those who do not respond to acute treatment will eventually respond to continued treatment. (35 References)
BOOKS RECEIVED FOR REVIEW


DIGEST of NEUROLOGY and PSYCHIATRY

Abstracts and Reviews of Selected Literature in Psychiatry, Neurology, and their Allied Fields

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BOOKS RECEIVED FOR REVIEW
FLUOXETINE TREATMENT FOR OBSESSIVE-COMPULSIVE DISORDER IN CHILDREN AND ADOLESCENTS: A PLACEBO-CONTROLLED CLINICAL TRIAL

Daniel A. Geller, MD; Sharon L. Hoog, MD (Eli Lilly & Co., Lilly Corporate Center, Indianapolis, IN 46285; e-mail: [HOOG_S_L@Lilly.com]); John H. Heiligenstein, MD; Randall K. Ricardi, DO; Roy Tamura, PhD; Stacy Kluzyenski, MS; Jennie G. Jacobson, PhD; and the Fluoxetine Pediatric OCD Study Team

J AM ACAD CHILD ADOLESC PSYCHIATRY, 40:773-9, July 2001

Obsessive-compulsive disorder (OCD) occurs in as many as 2% to 4% of juveniles and, if left untreated, can severely impair academic, family, and social functioning. The authors conducted a 13-week, double-blind, placebo-controlled study for the purpose of assessing the efficacy and safety of fluoxetine in the acute treatment of child and adolescent OCD.

In all, 103 pediatric outpatients with OCD (49 males, 54 females; age range, seven to 17 years) were randomly assigned to receive either fluoxetine (N=71) or placebo (N=32). Dosing was initiated at 10 mg daily for two weeks and then increased to 20 mg daily. After four weeks of treatment, and again after seven weeks of treatment, nonresponders could have their dosage increased by 20 mg daily (up to maximum possible dosage of 60 mg daily). The primary measure of efficacy was improvement in OCD symptoms as measured by the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS). All analyses were intent-to-treat. Compared with placebo, fluoxetine was associated with a significant reduction in OCD severity as measured by total CY-BOCS score. The difference between fluoxetine and placebo tended toward significance at week 5 and was significant at all subsequent patient visits. Patients who recorded a 40% or greater reduction in their CY-BOCS score between baseline and endpoint were classified as responders. Thirty-five (49%) of the 71 patients in the fluoxetine group and eight (25%) of the 32 patients in the placebo group were classified as responders; this difference was significant. Clinicians rated 55% of the fluoxetine-treated patients as much improved or very much improved; only 18.8% of the placebo-treated patients were so rated by clinicians. The percentage of patients who completed the study was comparable in the two groups (69% [49/71] of fluoxetine-treated patients; 62.5% [20/32] of placebo-treated patients). The percentage of patients who discontinued treatment because of adverse events was similar in the fluoxetine group (8.5%, 6/71) and the placebo group (6.3%, 2/32).

In the pediatric population studied here, fluoxetine (20 mg to 60 mg daily) was well tolerated and was significantly more effective than placebo in the treatment of OCD. The current results are consistent with a growing body of evidence demonstrating the efficacy of fluoxetine for the treatment of OCD in children as well as adults. (29 References)
The objectives of the present study were threefold: (1) to compare the efficacy of contemporary cognitive-behavioral therapy (CBT) with that of traditional behavior therapy (exposure and response prevention [ERP]) in the group treatment of obsessive-compulsive disorder (OCD); (2) to investigate the degree to which CBT, relative to ERP, was effective in inducing cognitive change in participants with OCD; and (3) to identify predictors of treatment outcome in both CBT and ERP. Both CBT and ERP were conducted by two therapists working with groups of six to eight participants. Therapy was conducted for 12 consecutive weeks, with each session lasting 2.5 hours.

All subjects met DSM-IV criteria for OCD. A total of 76 participants began treatment, 34 in the CBT condition and 42 in the ERP condition. All subjects were assessed at pretreatment, posttreatment, and three-month follow-up. Of the 76 who started treatment, 33 were wait-listed for three months before therapy (control condition) for the purpose of assessing possible course effects. Participants in the delayed condition completed two pretreatment assessments, one at the beginning of the three-month waiting period and one at the end, immediately before beginning treatment. Participants were considered to have completed treatment if they attended at least seven sessions and completed the posttreatment interview assessment. In all, 63 subjects (33 men, 30 women; age range, 18 to 56 years; mean age, 35 years) were considered to be treatment completers, 31 in the CBT condition and 32 in the ERP condition. Of the 63 completers, 61 (97%) were available for the three-month follow-up assessment. Both treatment conditions were superior to the wait-list control condition in terms of symptom reduction, with ERP being marginally more effective than CBT by the end of treatment and again at the three-month follow-up. The percentage of completers who demonstrated clinically significant improvement (“recovered status”) at the conclusion of treatment was similar in the two therapy groups; however, at the three-month follow-up, significantly more ERP participants (45%) than CBT participants (13%) met criteria for recovered status. Only one of seven belief measures changed with treatment-related improvement; the extent of this cognitive change was similar in the CBT and ERP groups.

The authors conclude that both CBT and ERP are effective group treatments for OCD. They suggest that ERP may be more suitable when treating OCD patients in a group setting, while CBT (because of its complexity) may be more appropriate for individual treatment. (40 References)
INSIGHT AND RESISTANCE IN PATIENTS WITH OBSESSIVE-COMPULSIVE DISORDER

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PSYCHOPATHOLOGY, 34:62-8, March-April 2001

Recently, the role of insight in the diagnosis and treatment of obsessive-compulsive disorder (OCD) has received a great deal of attention. The authors evaluated the following: (1) the degree of insight and resistance present in a sample of OCD patients, with resistance being defined as the patients' efforts to combat their symptoms; (2) the clinical features and family history of patients with poor insight; and (3) the predictive value of poor insight with regard to response to treatment with serotonin reuptake inhibitors (SRIs). Assessment instruments included the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) and the 17-item Hamilton Rating Scale for Depression (HDRS).

The study sample consisted of 94 patients (47 males, 47 females; mean age, 30.6 years) who met DSM-IV criteria for OCD. Mean duration of illness was 7.7 years, and mean age at onset was 22.9 years. Seventy of these patients (34 males, 36 females; mean age, 31.6 years) were treated with an SRI in a 24-week open-label trial. While 79 patients (84%) were considered to have normal insight, 15 patients (16%) did not recognize obsessions and compulsions as unreasonable or senseless and were considered to have poor insight. Resistance was very low or totally absent in 49 patients (52%). In addition, 68 patients (72%) had little or no control over obsessions, and 61 (64%) were unable to exercise effective control over compulsions. Compared with the patients with normal insight, those with poor insight were significantly more likely to have higher scores on the Y-BOCS and the HDRS, a finding that indicated a greater severity of both obsessive-compulsive symptoms (Y-BOCS) and depressive symptoms (HDRS). In addition, patients with poor insight were significantly more likely to have a personal history of childhood psychiatric disorders and a family history of schizophrenia spectrum disorders (as seen in their first-degree relatives). Of the 70 patients (58 with normal insight and 12 with poor insight) who began SRI therapy, 50 (42 with normal insight and eight with poor insight) completed the 24-week trial. While 22 (52%) of the 42 patients with normal insight were classified as SRI responders, none of the eight patients with poor insight were found to be responders.

The present findings are in agreement with a growing body of evidence suggesting that the insight of OCD patients varies widely. While some patients appear to recognize fully the irrationality and senselessness of their obsessions and compulsions, others seem to believe strongly in the rightness of their obsessive ideas and compulsive behaviors. (40 References)
MEMORY DEFICITS IN PATIENTS WITH DSM-IV OBSESSIVE-COMPULSIVE DISORDER

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PSYCHOPATHOLOGY, 34:113-7, May-June 2001

Pathological doubting is considered to be a prominent feature of obsessive-compulsive disorder (OCD). Individuals with OCD are often uncertain as to whether or not they have performed a particular action, and this uncertainty may entail obsessional doubts that increase the desire to repeat the action. Some studies have found evidence to suggest that certain memory deficits may play an essential role in the emergence of doubts and, consequently, in the perpetuation of checkers’ rituals. Other reports have suggested that metacognitive factors, such as confidence in memory, may be as important as memory deficits in the emergence of obsessional doubting. In the present investigation, the authors examined mnestic functioning and self-perception of memory ability in OCD patients and normal controls.

The study sample was composed of 27 nondepressed OCD outpatients (14 males, 13 females; mean age, 38.9 years) and 27 normal control subjects (12 males, 15 females; mean age, 37.2 years). The patients met DSM-IV and ICD-10 criteria for OCD, displayed prominent behavioral checking rituals of at least one year’s duration, and scored 16 or higher on the Yale-Brown Obsessive-Compulsive Scale. They were drug free and had no other psychiatric disorders or major medical or neurological illnesses. According to DSM-IV and ICD-10 criteria, the normal controls were considered to be free of psychiatric illness. Measures of memory performance indicated that, compared with normal controls, OCD patients demonstrated significant deficits in intermediate and immediate nonverbal memory. The patients with OCD also displayed significant deficits in general memory and verbal memory. In terms of self-perception of memory, OCD patients reported having significantly less confidence in their memory ability than controls did. Within the patient group, no between-sex differences were found in the results of the objective measures of memory ability. With regard to self-ratings, however, female OCD patients (compared with male patients) had less confidence in their recall ability, reported less vivid memories, and expressed a greater desire for more vivid memories.

According to the authors, the present results indicate that obsessive-compulsive checkers display an actual deficit in mnestic functioning as well as a lack of confidence in memory ability. Limitations of the current study include the difficulty in clearly separating basic memory dysfunction from the more complex metacognitive function of an individual’s conscious assessment of whether a recollection is valid or not. (24 References)
REGIONAL CEREBRAL BLOOD FLOW ABNORMALITIES IN EARLY-ONSET OBSESSIVE-COMPULSIVE DISORDER: AN EXPLORATORY SPECT STUDY

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 40:347-54, March 2001

Recent epidemiological and clinical data suggest that obsessive-compulsive disorder (OCD) may be subtyped according to the age of onset of obsessive-compulsive symptoms (OCS). The aim of the present study was to determine whether the pathophysiology of OCD differs in individuals with early-onset and late-onset OCD. Using single-photon emission-computed tomography, the authors measured resting regional cerebral blood flow (rCBF) in 26 adult subjects who met DSM-IV criteria for OCD and 22 healthy controls with no history of psychiatric illness. Voxel-based rCBF comparisons were performed by means of statistical parametric mapping.

The control group (mean age, 31.9 years) was composed of 12 men and 10 women. Of the 26 subjects with OCD, 13 (eight men, five women; mean age, 31.2 years) had an early onset of OCS (<10 years of age), and 13 (seven men, six women; mean age, 33.1 years) had a late onset (>12 years of age). The mean age of OCS onset was 7.7 years (range, 4 to 10) in the early-onset group and 22.8 years (range, 13 to 38) in the late-onset group. Compared with OCD subjects in the late-onset group, those in the early-onset group showed decreased rCBF in the right thalamus, the left anterior cingulate cortex, and bilaterally in the inferior prefrontal cortex (p<.0005, uncorrected for multiple comparisons). Compared with the healthy controls, the early-onset OCD subjects had reduced rCBF in the left dorsal anterior cingulate cortex and the right lateral orbitofrontal cortex as well as increased rCBF in the right cerebellum. When the late-onset OCD subjects were compared with the healthy controls, the late-onset group showed reduced rCBF in the right lateral orbitofrontal region and increased rCBF in the left precuneus. In the early-onset subjects only, severity of OCS was found to be positively correlated with left orbitofrontal rCBF.

In the present investigation, the authors found functional differences between early-onset and late-onset OCD, in terms of both the location and direction of rCBF changes. According to the researchers, the current data provide preliminary evidence that the brain mechanisms implicated in OCD may differ according to the age at which symptoms are first expressed. Their findings also support the notion that individuals with early-onset OCD require a distinct clinical approach. (42 References)
DEVELOPMENTAL ASPECTS OF OBSESSIVE COMPULSIVE DISORDER:
FINDINGS IN CHILDREN, ADOLESCENTS, AND ADULTS

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To evaluate the developmental continuity of obsessive-compulsive disorder (OCD) across the life cycle, the authors examined the clinical correlates of OCD in three distinct groups. Findings from children and adolescents who had been referred to a pediatric OCD clinic were compared with published data on adults who had been enrolled in a major specialty OCD program. All subjects met DSM-III-R and DSM-IV criteria for OCD and underwent structured diagnostic interviews and clinical assessments conducted by OCD experts.

Of 101 pediatric subjects, 46 were under the age of 12 (OCD children), and 55 were 12 years of age or older (OCD adolescents). Among the adult sample (OCD adults), there were 560 with clinical symptoms and 60 with comorbid diagnoses. Both the child and adolescent groups showed a clear male preponderance (67% and 64%, respectively) that differed significantly from that of the adult sample (46%). Compared with adults (31%), children (63%) and adolescents (69%) had much higher rates of aggressive obsessions (including fears of catastrophic events, such as death or illness in self or loved ones). Religious obsessions were over-represented in adolescents (36%) compared with children (15%) and adults (10%), while sexual obsessions were under-represented in children (11%) compared with adolescents (36%) and adults (24%). In terms of compulsions, only hoarding was seen more often in children (30%) and adolescents (36%) than in adults (18%). Although the majority of subjects in all three groups had both multiple obsessions and multiple compulsions, these rates were significantly higher in children and adolescents than in adults (multiple obsessions: 93%, 96%, and 72%, respectively; multiple compulsions: 100%, 100%, and 58%, respectively). Poor insight was found to be more prevalent in OCD children (18%) than in OCD adolescents (6%) or OCD adults (6%). The rate of major depression was significantly lower in children (39%) than in adolescents (62%) and adults (78%). However, Tourette's disorder was more common in children (25%) than in adolescents (9%) or adults (6%). Separation anxiety disorder was significantly more common in children (56%) and adolescents (35%) than in adults (17%), while adults had significantly higher rates of substance abuse/dependence (16%) than adolescents (2%) or children (0%). Eating disorders were also more common in adults (8%) than in children (0%) or adolescents (2%).

The present results support a hypothesis of developmental discontinuity between juvenile and adult OCD and identify age-specific correlates of the disorder across the life span. (24 References)
OBSESSIVE-COMPULSIVE DISORDER AND TRAUMATIC BRAIN INJURY:
BEHAVIORAL, COGNITIVE, AND NEUROIMAGING STUDIES

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NEUROPSYCHIATRY NEUROPSYCHOL BEHAV NEUROL, 14:23-31, January 2001

Obsessive-compulsive disorder (OCD) is a rare sequela of traumatic brain injury (TBI). The goal of the present study was to evaluate behavior and cognition in patients who developed OCD after suffering a TBI. Using magnetic resonance imaging (MRI), a battery of neuropsychological tests, and structured psychiatric rating scales, the authors examined 10 adult patients (four men, six women; mean age, 30 years) who met DSM-IV criteria for OCD after suffering a mild (N=6), moderate (N=2), or severe (N=2) TBI.

Nine of the 10 patients had no family history of OCD, tics, or Tourette syndrome. Only four patients had a personal history positive for OCD or related psychopathological disorders; two patients had premorbid obsessional personality traits, and two others had developed posttraumatic stress disorder during adolescence but were symptom-free several years prior to TBI. Nine patients developed obsessive-compulsive symptoms and comorbid psychopathology, particularly generalized anxiety and symptoms of posttraumatic stress disorder, within the first month after the TBI. The tenth patient had posttraumatic stress disorder during the acute period but developed typical obsessive-compulsive symptoms eight months after the TBI. The global severity of OCD ranged from moderate to severe, and all 10 patients had multiple obsessions and compulsions. The most common obsessions were aggression and contamination, followed by symmetry/exactness, somatic obsessions, and sexual obsessions. The most frequently observed compulsions were checking, cleaning/washing, and repeating. Unusual features such as obsessional slowness (three patients) and compulsive exercising (three patients) were also noted. Comorbid psychiatric diagnoses were common and included posttraumatic stress disorder, anxiety with panic attacks, depression, and intermittent explosive disorder. When compared with 10 age- and sex-matched normal controls, the OCD patients were found to perform poorly on tests of general intelligence, attention, learning, memory, word retrieval, and executive functioning; these cognitive deficits were found to be more pervasive in the patients who displayed obsessional slowness. All OCD patients with mild TBI had normal MRI scans. However, focal contusions were found in the frontotemporal cortices, in subcortical structures (caudate nucleus), or in both regions in the patients with moderate and severe TBI.

The authors conclude that posttraumatic OCD has a relatively specific pattern of symptoms (even in patients with mild TBI) and is associated with a variety of other psychiatric disorders. (60 References)
THE RELATIONSHIP BETWEEN OBSESSIVE-COMPULSIVE DISORDER AND ANXIETY AND AFFECTIVE DISORDERS: RESULTS FROM THE JOHNS HOPKINS OCD FAMILY STUDY

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PSYCHOL MED, 31:481-7, April 2001

Individuals with obsessive-compulsive disorder (OCD) frequently experience additional diagnosable psychiatric disorders over the course of their lifetimes. In the blind, controlled family study presented here, the authors investigated the relationship between OCD and anxiety, affective, and substance use disorders. The study sample was composed of 80 adult OCD (case) probands and their 343 first-degree relatives, as well as 73 adult control probands and their 300 first-degree relatives. The subjects were examined by psychiatrists or psychologists by means of the Schedule for Affective Disorders and Schizophrenia-Lifetime Anxiety version. Two independent psychiatrists reviewed all clinical materials, and final diagnoses were made according to DSM-IV criteria, by a consensus procedure.

When the authors examined the lifetime prevalence rates of definite DSM-IV anxiety disorders, they found that the following specific anxiety disorders occurred significantly more frequently in the case probands than the control probands: generalized anxiety disorder (GAD), panic disorder, agoraphobia, separation anxiety disorder (SAD), and social phobia. Recurrent major depression and recurrent brief depressive disorder also occurred significantly more often in the case probands than the control probands. However, no significant differences were found between the two proband groups with regard to the frequency of bipolar disorder, dysthymia, alcohol dependence, or substance dependence. When the lifetime prevalence of these disorders in the first-degree relatives was examined, it was found that GAD, agoraphobia, panic disorder, SAD, and recurrent major depression occurred significantly more often in the relatives of the case probands than the relatives of the control probands. These disorders occurred more frequently if the relatives were diagnosed with OCD. Only GAD and agoraphobia occurred more frequently in case relatives independent of OCD. There were no significant differences between the two relative groups in terms of the prevalence of social and specific phobias, bipolar disorder, recurrent brief depression, dysthymia, alcohol dependence, substance dependence, or schizophrenia.

The results indicate that several anxiety and affective disorders frequently co-occur with OCD. These comorbidities may arise as a result of a common etiological pathway or as a complication of OCD. While GAD and agoraphobia appear to share a common familial etiology with OCD, the other anxiety and affective disorders, when comorbid with OCD, may emerge as a consequence of OCD or as a more complex syndrome. (24 References)
GILLES DE LA TOURETTE’S SYNDROME WITH AND WITHOUT OBSESSIVE-COMPULSIVE DISORDER COMPARED WITH OBSESSIVE-COMPULSIVE DISORDER WITHOUT TICS: WHICH SYMPTOMS DISCRIMINATE?

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J NERV MENT DIS, 189:219-28, April 2001

Stereotyped repetitive behaviors occur in Gilles de la Tourette's syndrome (GTS) and obsessive-compulsive disorder (OCD). The authors compared the distribution of obsessive-compulsive (OC) and Tourette-related impulsive behaviors in 14 GTS patients with OCD, 18 GTS patients without OCD, 21 tic-free OCD patients, and 29 control subjects. All subjects underwent a semistructured interview designed to assess GTS- and OCD-related repetitive behaviors. Each reported item was evaluated in terms of the presence of anxiety and goal-directedness. This information was subsequently used to define the repetitive behavior as an (anxiety-related) obsession or compulsion or as a (non-anxiety-related) OC-like behavior, i.e., an impulsion.

When GTS subjects with OCD were compared with GTS subjects without OCD, those with OCD reported higher frequencies of overall repetitive behavior; they also reported more overall compulsions, more overall Tourette-related impulsions, more counting behaviors, more mental play, and more repetitive actions. GTS patients with OCD and tic-free OCD patients reported similar frequencies of overall repetitive behavior. However, when the GTS subjects with OCD were compared with the tic-free OCD subjects in terms of defined obsessions, compulsions, and impulsions, the authors found that the GTS subjects with OCD reported more overall impulsions, more mental play, more echophenomena, and more touching behaviors. Although GTS subjects without OCD and tic-free OCD subjects reported similar frequencies of overall repetitive behavior, when these behaviors were defined as obsessions, compulsions, or impulsions, the GTS subjects without OCD reported fewer overall obsessions and compulsions and more overall impulsions. Compared with the tic-free OCD patients, the GTS patients without OCD reported more mental play, more echophenomena, and more touching behaviors. All the patient groups reported more overall repetitions than the control group.

The authors conclude that the distribution of symptoms seen in GTS patients with OCD appears to be similar to the distribution found in GTS patients without OCD but different from that seen in tic-free OCD patients. Specific non-anxiety-related impulsions seem to discriminate between GTS patients and individuals with tic-free OCD. (43 References)
PROSPECTIVE, LONGITUDINAL STUDY OF TIC, OBSESSIVE-COMPULSIVE, AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDERS IN AN EPIDEMIOLOGICAL SAMPLE

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J AM ACAD CHILD ADOLESC PSYCHIATRY, 40:685-95, June 2001

In clinical samples, tics, obsessive-compulsive disorder (OCD), and attention-deficit/hyperactivity disorder (ADHD) commonly co-occur. However, understanding the interrelatedness of these conditions is complicated by the fact that previous studies have focused only on cross-sectional samples of clinically referred subjects. In the present investigation, the authors examined the cross-sectional and longitudinal associations among these disorders in an epidemiological sample of children followed prospectively into early adulthood.

Structured diagnostic interview information was acquired on 976 children (age range, one to 10 years) who were randomly selected from families living in upstate New York in 1975. Reassessments were carried out eight, 10, and 15 years later. Although 776 families were reinterviewed in 1983, 1985, and 1992, a lack of complete information in 1985 and 1992 resulted in the availability of smaller numbers of subjects at those time points (760 in 1985 and 728 in 1992). At the initial assessment, psychiatric symptoms in the child were assessed by interviewing his/her mother. In 1983 and 1985, both mothers and subjects were interviewed. Only subjects were interviewed in 1992. Diagnostic prevalences were estimated at each time point. The associations among tics, OCD, and ADHD were assessed within and across time points, as were their associations with comorbid illnesses and demographic risk factors. The prevalence of tics and of ADHD declined across each time point, whereas the prevalence of OCD declined in late adolescence before increasing in early adulthood. In temporal cross-section, tics and ADHD symptoms were associated with OCD symptoms in late adolescence and early adulthood (after demographic features and comorbid psychiatric symptoms were controlled). In prospective analyses, the presence of tics in childhood and early adolescence predicted an increase in OCD symptoms in late adolescence and early adulthood. ADHD symptoms in adolescence predicted more OCD symptoms in early adulthood, and OCD in adolescence predicted more ADHD symptoms in adulthood. The associations between tics and ADHD were unimpressive in temporal cross-section and not significant in prospective analyses. The authors found that tics, OCD, and ADHD shared numerous complex associations with demographic and psychopathological risk factors. ADHD was associated with lower IQ and lower social status, whereas OCD was associated with higher IQ.

In the sample studied here, tics and OCD were found to be significantly associated, as were OCD and ADHD. (75 References)
BOOKS RECEIVED FOR REVIEW


Abstracts and Reviews of Selected Literature in Psychiatry, Neurology, and their Allied Fields

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SCREENING THE PUBLIC FOR DEPRESSION THROUGH THE INTERNET

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Depression is a common psychiatric disorder associated with high levels of disability, impaired functional status, and high use of medical services. Despite increased public screening, many individuals with depression remain undetected or untreated. The purposes of the present study were to determine whether an Internet-based depression screening test would be useful in detecting individuals with depression, to compare this test with other public efforts in the U.S. population, and to estimate the costs of such a project.

The online screening test was adapted from the Centers for Epidemiological Studies Depression (CES-D) scale, a well-validated 20-question instrument that assesses symptom severity. The test was placed on Intelihealth, a large online health information portal. Individuals who completed the test received feedback regarding the probability of their having depression. Those who scored in the moderate range (CES-D score of 16 to 22) were instructed to seek further advice from a health professional or to retake the test later. Participants whose CES-D scores were above 22 were told there was a high probability that they were suffering from clinical depression; they were advised to seek treatment and were asked to complete a survey of attitudes and preferences that could be printed and taken to a health professional. Responses were collected anonymously, and demographic characteristics of the participants were compared with those of the U.S. population as well as with those of individuals who had participated in previous community screenings. Over the eight-month study period, the depression screening test was completed 24,479 times. Women and individuals 45 years of age and younger were significantly more likely than men and those over the age of 45 years to meet the criteria for depression. African Americans, Hispanics, and Asian Americans were less likely than whites to have a positive depression score. In all, 14,185 participants (58%) were identified as having a high probability of depression (CES-D score above 22); of these, 6,641 (47%) had never been treated for depression. The proportion of younger individuals who participated in the Internet screening was larger than that in previous public screenings, but was still lower than that in the U.S. population. The present sample contained a lower proportion of minorities than that found in the U.S. population (16.6% vs 28.3%). Sunk costs (those incurred at startup and not affected by future actions) totaled $9,000, while additional marginal costs needed to maintain the program came to $3,750.

The authors conclude that the Internet provides a continuously available, inexpensive, easily maintained platform to anonymously screen the public for depression. (47 References)
THE USE OF COMPLEMENTARY AND ALTERNATIVE THERAPIES TO TREAT ANXIETY AND DEPRESSION IN THE UNITED STATES

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Community surveys conducted over the past decade report that more than one-third of Americans use complementary and alternative medicinal treatments in any given year. To examine the use of such therapies for the treatment of anxiety and depression in the United States, the authors carried out a nationally representative telephone survey of 2,055 respondents. It was conducted between November 1997 and February 1998 and was designed to elicit information on the use of 24 complementary and alternative therapies (e.g., relaxation techniques, hypnosis, herbal medicines, megavitamins, homeopathy, massage, acupuncture, dietary modifications, aromatherapy) for treating specific chronic conditions. Because data on six of the respondents were missing, analyses were based on the remaining 2,049 respondents.

A total of 9.4% of the respondents (N=193) reported that they had experienced “anxiety attacks” at some time during the 12 months prior to the interview; 7.2% (N=148) reported suffering from “severe depression” in the past 12 months. In all, 38.8% (N=75) of the respondents with anxiety attacks also reported severe depression. A total of 56.7% of those with anxiety attacks and 53.6% of those with severe depression reported using complementary and alternative therapies to treat these conditions during the previous 12 months. However, only 20% of those with anxiety attacks and 19.3% of those with severe depression visited a complementary or alternative therapist. In all, 65.9% of the respondents seen by a conventional mental health professional for anxiety attacks and 66.7% of those seen by a conventional provider for severe depression also availed themselves of complementary and alternative therapies to treat these conditions. The perceived helpfulness of complementary and alternative therapies in treating anxiety and depression was found to be similar to that of conventional therapies.

The data suggest that the majority of U.S. residents who suffer from self-defined anxiety attacks or severe depression use some form of complementary or alternative therapy to treat these conditions. Thus, individuals with these conditions are considerably more likely to use complementary and alternative therapies rather than conventional medical or mental health treatments. Asking patients about their use of complementary and alternative treatments could prevent adverse effects and maximize the usefulness of any such therapies subsequently proven to be effective. (36 References)
EFFECTIVENESS OF ST JOHN’S WORT IN MAJOR DEPRESSION
A Randomized Controlled Trial

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Extracts of St John’s wort (Hypericum perforatum) are used widely to treat depression. Although more than two dozen clinical trials have been conducted with this herbal treatment, most of these studies have significant design flaws and do not enable meaningful interpretation. The purpose of the present report was to compare the efficacy and safety profile of a standardized extract of St John’s wort with that of placebo in outpatients with major depression.

Between November 1998 and January 2000, a randomized, double-blind, placebo-controlled clinical trial was conducted in 11 academic medical centers throughout the United States. The sample was composed of 200 adult outpatients (67% female; 85.9% white; mean age, 42.4 years) with a diagnosis of major depression and a baseline Hamilton Rating Scale for Depression (HAM-D) score of at least 20. The participants completed a one-week, single-blind run-in of placebo and then were assigned randomly to receive (for a period of eight weeks) either St John’s wort extract (N=98; 900 mg/day for at least four weeks, with the dosage increased to 1,200 mg/day for the remainder of the trial if there was no adequate response by week 4) or placebo (N=102). The primary outcome measure was rate of change on HAM-D scores over the eight-week trial period. Secondary measures included the Beck Depression Inventory (BDI), Hamilton Rating Scale for Anxiety (HAM-A), Global Assessment of Function (GAF) scale, Clinical Global Impression-Severity (CGI-S) scale, and CGI-Improvement (CGI-I) scale. The random coefficient analyses for the HAM-D, HAM-A, CGI-S, and CGI-I all showed significant effects for time but not for treatment or time-by-treatment interaction. Analysis of covariance showed nonsignificant effects for BDI and GAF scores. The proportion of participants achieving an a priori definition of response did not differ between groups. The number of participants whose illness remitted was significantly higher in the St John’s wort group than in the placebo group, but the rates obtained in the full intention-to-treat analysis were very low (14.3% [14/98] vs 4.9% [5/102], respectively). St John’s wort appeared to be safe and well tolerated. Headache was the only adverse event that occurred more often with St John’s wort than with placebo (41% [39/95] vs 25% [25/100], respectively).

In the present study, the authors conclude, St John’s wort was not effective in the treatment of major depression. (58 References)
PREVENTING RECURRENT DEPRESSION USING COGNITIVE THERAPY WITH AND WITHOUT A CONTINUATION PHASE
A Randomized Clinical Trial

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ARCH GEN PSYCHIATRY, 58:381-8, April 2001

Patients who recover from recurrent major depressive disorder (MDD) face an 80% recurrence rate in the absence of prophylactic treatment. Cognitive therapy (CT) could play a role in the prevention of relapses and recurrences (even after discontinuation of treatment) if patients learn the skills associated with CT and continue to use these skills to reduce symptoms effectively. In the study presented here, the authors compared the effects of CT with and without a continuation phase in CT responders who remained at high risk for relapse and recurrence because of a history of recurrent unipolar depression.

In all, 156 patients (age range, 18 to 65 years) who met DSM-IV criteria for MDD entered a 20-session trial of acute-phase CT (A-CT). After completion of the acute phase, 84 unmedicated responders (i.e., no MDD and a 17-item Hamilton Rating Scale for Depression score of 9 or less) entered an eight-month experimental phase and were randomly assigned to either 10 sessions of continuation-phase CT (C-CT) or a control condition (evaluation only). Follow-up lasted an additional 16 months. A clinician blind to assignment evaluated relapse and recurrence. Of the 84 randomized patients, 76 (90%) completed the eight-month experimental phase or had a relapse or recurrence. There was no significant difference between the number of patients who completed C-CT (39/41, 95%) and the number who completed the control condition (37/43, 86%). Sixty responders entered the follow-up phase; of these, 55 (92%) completed 16 months of follow-up or experienced a relapse or recurrence. Over the eight-month experimental phase, C-CT reduced relapse estimates significantly more than the control condition (10% vs 31%). Over 24 months, a period that included the CT-free follow-up, age of onset and quality of remission during the late phase of A-CT each interacted with condition assignment to influence durability of effects. Among patients with early-onset MDD, those who received C-CT were significantly less likely to experience a relapse or recurrence than those who did not receive C-CT (16% vs 67%). Patients who had an unstable remission during late A-CT were significantly more likely to experience a relapse or recurrence without C-CT than with C-CT (62% vs 37%).

The present results suggest that C-CT is worthy of further evaluation and that it appears to offer patients with recurrent MDD safe, tolerable, and effective prevention for an extended period. (38 References)
A RANDOMIZED TRIAL OF RELAPSE PREVENTION OF DEPRESSION IN PRIMARY CARE

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ARCH GEN PSYCHIATRY, 58:241-7, March 2001

Despite high rates of relapse and recurrence, few primary care patients with recurrent or chronic depression receive continuation and maintenance-phase treatment. The authors of the present investigation compared the efficacy of a low-intensity relapse prevention program with that of usual primary care in a sample of high-risk primary care patients with recurrent major depression or chronic depression. The researchers attempted to determine whether the relapse prevention intervention would be associated with improved adherence to antidepressant medication and less depressive symptoms over a one-year period and whether the intervention program would result in fewer relapses and/or recurrences of major depression during this 12-month span.

The study sample was composed of 386 patients who suffered from recurrent major depression or dysthymia and who had largely recovered after eight weeks of antidepressant treatment by their primary care physicians. The subjects were randomly assigned to a relapse prevention intervention (N=194) or usual primary care (N=192). Over a one-year period, patients in the intervention group received two primary care visits with a depression specialist and three telephone visits; the program was geared toward enhancing adherence to antidepressant medication, recognizing prodromal symptoms, monitoring symptoms, and developing a written relapse prevention plan. Patients’ adherence to antidepressant medication and depressive symptoms were assessed at three, six, nine, and 12 months after randomization by a telephone survey team blinded to randomization status. Of the 194 patients assigned to the intervention program, 188 (96.9%) made at least one visit to the depression specialist, and 181 (93.3%) made both visits. Compared with patients who received usual primary care (controls), those in the intervention group demonstrated significantly greater adherence to adequate dosages of antidepressant medication for 90 days or more within the first six-month period and also were significantly more likely to refill medication prescriptions during the 12-month follow-up period. Over follow-up, patients in the intervention program had significantly fewer depressive symptoms than the controls, but they did not experience fewer episodes of relapse/recurrence.

Compared with usual primary care, the authors conclude, the relapse prevention program described here was associated with a significant improvement in adherence to antidepressants as well as a significant decrease in depressive symptoms. (37 References)
SWITCHING VERSUS AUGMENTATION: A PROSPECTIVE, NATURALISTIC COMPARISON IN DEPRESSED, TREATMENT-RESISTANT PATIENTS

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As many as 30% of depressed patients fail to respond to an adequate antidepressant trial, and of those who do respond, an estimated 20% experience a relapse during the first 12 months of maintenance therapy. Thus, treatment resistance occurs in roughly half of the patients who begin antidepressant therapy. Using a naturalistic, open-label design, the authors compared the efficacy of switching antidepressants with that of augmenting them in depressed patients who did not respond to an initial adequate drug trial. The researchers also attempted to determine whether the likelihood of response decreased in a second trial of switching or augmentation.

The study sample was composed of 74 treatment-resistant, depressed outpatients. Of these, 38 (16 men, 22 women; age range, 18 to 83 years; mean age, 42.5 years) had their antidepressant switched, and 36 (13 men, 23 women; age range, 26 to 62 years; mean age, 41.1 years) had their antidepressant augmented. Short- and long-term outcomes of switching and augmentation were assessed by means of the Clinical Global Impressions scale and the Global Assessment of Functioning scale. In the acute phase of the study, 37 (50%) of the 74 subjects responded to one of the two interventions for treatment-resistant depression; of the 38 patients who were switched to a second antidepressant, 17 (44.7%) met criteria for a positive response, as did 20 (55.6%) of the 36 patients whose antidepressant was augmented. Of the 17 patients whose antidepressant was switched and who had a positive response during the acute phase, three dropped out prior to the six-month follow-up; 10 (71.4%) of the remaining 14 acute responders maintained their positive response for at least six months. Of the 20 patients who had a positive response to augmentation, four dropped out and two discontinued their regimen; 10 (71.4%) of the remaining 14 subjects maintained a positive response over six months of follow-up. Among the patients who did not respond to an initial switch or augmentation, 18 underwent a second trial; nine (50%) of these patients responded, yielding a response rate identical to that of the first trial.

The present results suggest that for patients who do not respond to an initial antidepressant trial, augmentation may be a somewhat more effective intervention than switching antidepressants. However, the authors state, larger, controlled studies are needed to confirm this conclusion. It remains unclear whether the likelihood of response decreases with each subsequent trial, but the current data indicate that a relatively high percentage of patients will continue to respond. (48 References)
REEMERGENCE OF SEXUAL DYSFUNCTION IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER: DOUBLE-BLIND COMPARISON OF NEFAZODONE AND SERTRALINE

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J CLIN PSYCHIATRY, 62:24-9, January 2001

Several different classes of antidepressants have been associated with sexual adverse effects. The authors conducted a multicenter, double-blind, randomized trial in which they compared the effects of nefazodone and sertraline on the reemergence rates of sexual dysfunction in depressed patients who had previously experienced sexual dysfunction during sertraline treatment. Specific types of substance-induced sexual dysfunction were examined, and depressive symptoms were also monitored.

In all, 105 patients were screened for entry into the study; all had a DSM-III-R diagnosis of major depression and were experiencing sexual dysfunction attributable to sertraline therapy (100 mg/day). After a one-week washout period during which sertraline treatment was suspended, patients entered a seven- to 10-day single-blind lead-in phase during which they received placebo only. After the single-blind placebo phase, those who were no longer experiencing substance-induced sexual dysfunction were randomly assigned to receive double-blind therapy with either nefazodone (400 mg/day) or sertraline (100 mg/day) for eight weeks. Of 75 randomized patients, three had major protocol violations and were excluded from the sexual function and efficacy (antidepressant response) portions of the analysis. Nearly three times more sertraline-treated patients (76%, 25/33) than nefazodone-treated patients (26%, 10/39) experienced a reemergence of substance-induced sexual dysfunction (ejaculatory and/or orgasmic difficulty). In addition, patients treated with nefazodone were more satisfied with their sexual functioning than were those treated with sertraline. Both treatment groups demonstrated a similar and sustained improvement in depressive symptoms. The overall incidence of adverse reactions was similar in the two groups. Nine sertraline-treated (26%) and five nefazodone-treated (12%) patients discontinued therapy because of adverse events. Within the group who discontinued treatment because of adverse reactions, five sertraline-treated patients but only one nefazodone-treated patient did so because of reported sexual dysfunction.

The current data indicate that nefazodone treatment is associated with a lower incidence of sexual dysfunction than sertraline therapy. The present results suggest that depressed patients with antidepressant-induced sexual dysfunction may be switched to nefazodone therapy with continuation of antidepressant response, but with significantly less risk of substance-induced sexual dysfunction. (21 References)
INCREASED PREVALENCE OF NEGATIVE LIFE EVENTS IN
SUBTYPES OF MAJOR DEPRESSIVE DISORDER

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COMPR PSYCHIATRY, 42:57-63, January/February 2001

While it is well known that depressed patients experience more negative life
events than normal subjects, there is little information available on the
relationships (if any) between negative life events and specific subtypes of
depression. To address this issue, the authors examined the frequency of
negative life events in 115 patients with major depressive disorder (MDD) and 60
normal controls with no psychiatric history.

Of the MDD patients, 76 (66%) reported experiencing at least one negative life
event in the year prior to the onset of depression; only 18 controls (30%)
reported experiencing at least one negative life event in the year prior to
interview. Significantly more patients than controls experienced at least two
negative life events during this period (24% vs 8%). Patients reported marital
difficulties, other personal problems, and medical events significantly more often
than controls. Patients and controls did not differ in the severity they (or the
interviewer) attributed to their negative life events. The two groups did not differ
significantly with regard to the frequency of positive life events, although the
control group tended to report the occurrence of at least one positive event and
the occurrence of two positive events more often than the patient group. Younger
MDD patients (<50 years of age) experienced four negative life events
significantly more often than older MDD patients (>50 years). A similar pattern
emerged when the following subgroups were compared: patients experiencing
their first depressive episode (FDE) and those with recurrent depression (RDE);
mildly or moderately depressed patients and severely depressed patients; and
patients with melancholic and nonmelancholic depression. FDE patients
experienced four negative life events significantly more often than RDE patients.
Nonmelancholic patients reported four life events significantly more frequently
than melancholic patients. Mildly or moderately depressed patients reported the
occurrence of three or four negative life events significantly more often than
severely depressed patients. Other patient and illness characteristics such as
gender, early parental loss, family history of depression or other mental
disorders, psychotic features, suicide attempts, and chronicity were not related
to increased prevalence of negative life events.

The current results suggest that there is a subset of depressed patients who
are especially prone to experience a cluster of negative life events. This subgroup
(patients under the age of 50 and suffering from their first, mild-to-moderate,
nonmelancholic depressive episode) may be at increased risk for relapse and
poor prognosis. (17 References)
MEDICAL ILLNESS, PAST DEPRESSION, AND PRESENT DEPRESSION: A PREDICTIVE TRIAD FOR IN-HOSPITAL MORTALITY

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AM J PSYCHIATRY, 158:43-8, January 2001

There is a growing body of evidence indicating that depression is associated with a higher mortality rate in medically ill patients. The authors attempted to determine (1) whether major depressive disorder diagnosed according to DSM-IV criteria modified for the medically ill would predict in-hospital mortality more accurately than major depressive disorder diagnosed according to inclusive DSM-IV criteria, and (2) whether a history of depression and a current diagnosis of depression would predict mortality independently of severity of physical illness.

Of 392 patients consecutively hospitalized for the treatment of medical illnesses, 241 (157 males, 84 females) were interviewed within the first three days of admission, and 151 were excluded. Data on demographic and medical variables as well as history of psychiatric disorders were obtained from the medical chart and during the psychiatric interview, which included the administration of the Schedule for Affective Disorders and Schizophrenia. DSM-IV diagnoses of major and minor depressive disorder were made according to criteria that included all symptoms regardless of etiology and according to criteria modified for the medically ill (hopelessness, depression, and anhedonia were used as the qualifying affective symptoms; depressive symptoms were eliminated if easily explained by medical illness, treatment, or hospitalization). The Charlson combined age-comorbidity index was used to measure severity of illness. The primary outcome measure was death during index hospitalization. When patients were diagnosed according to the modified criteria, 15 were assigned a diagnosis of major depressive disorder, and 25 were considered to have a minor depressive disorder. When the inclusive set of criteria were used, 24 patients received a diagnosis of major depressive disorder, and 19 were assigned a diagnosis of minor depression. Of the 241 study patients, 20 (12 males, eight females) died while in the hospital. A modified diagnosis of major depression better predicted mortality than a diagnosis based on inclusive criteria. A past history of depression and the Charlson combined age-comorbidity index predicted in-hospital mortality, but demographic variables, pain, discomfort, length of stay, medical diagnoses, and minor depression did not. In the final multivariate logistic regression model, severity of illness (as measured by the Charlson combined age-comorbidity index), a current modified diagnosis of major depressive disorder, and a history of depression were independent predictors of in-hospital death.

The data show that depression (independent of severity of physical illness) predicts death in medically ill patients. (25 References) EAF
DEPRESSION AND CARDIAC MORTALITY
Results From a Community-Based Longitudinal Study

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ARCH GEN PSYCHIATRY, 58:221-7, March 2001

Depression may be a potential risk factor for subsequent cardiac death. The authors examined and compared the effect of depression on cardiac mortality in community-dwelling individuals with and without cardiac disease. The sample was composed of 2,847 men and women (age range, 55 to 85 years; mean age, 70.5 years) who were evaluated for a period of four years. Major depression was defined according to DSM-III criteria, while minor depression was defined by Center for Epidemiologic Studies-Depression Scale scores of 16 or higher. After adjustments were made for demographics, smoking, alcohol use, blood pressure, body mass index, and comorbidity, the effects of minor and major depression on cardiac mortality were examined separately in the 450 subjects with a confirmed diagnosis of cardiac disease and in the 2,397 subjects without cardiac disease.

The cardiac mortality rate for the total sample was 15.3 per 1,000 person-years. As expected, this rate was much higher in subjects with cardiac disease (53.1 per 1,000 person-years) than in those without cardiac disease (8.3 per 1,000 person-years). Among the subjects without cardiac disease at baseline, the crude cardiac mortality rate per 1,000 person-years was 7.7 in those who were not depressed, 16.2 in those with minor depression, and 22.3 in those with major depression. After adjusting for all confounding variables, the authors found that among the subjects without cardiac disease at baseline, those with minor depression were 1.5 times more likely than those who were not depressed to have a cardiac death (95% Confidence Interval [CI], 0.9-2.6), and those with major depression were 3.9 times more likely than those who were not depressed to have a cardiac death (95% CI, 1.4-10.9). Among the 450 cardiac patients, the crude cardiac mortality rate per 1,000 person-years was 47.1 in those who were not depressed, 72.4 in those with minor depression, and 126.8 in those with major depression. Compared with the fully adjusted relative risk (RR) of cardiac mortality in nondepressed cardiac patients, the RR was 1.6 (95% CI, 1.0-2.7) in cardiac patients with minor depression and 3.0 (95% CI, 1.1-7.8) in cardiac patients with major depression.

The results of the present investigation indicate that minor depression and (most strongly) major depression place community-dwelling cardiac patients as well as individuals free of cardiac disease at an increased risk for cardiac mortality. (38 References)
BOOKS RECEIVED FOR REVIEW


From the Editor

This issue of the *Digest of Psychiatry and Neurology* marks a major turning point. After 68 years of publication, the *Digest* is discontinuing its “hard copy” format and will be published in electronic form, available at this website. When the *Digest* began, it filled a unique need. We are proud of the global reach and the impact our publication has had; at one time, the *Digest* mailing list included 25,000 subscribers, with its readership extending not only throughout the United States and Canada but also to Europe, India, Australia, New Zealand, South America, and many other regions of the world. Over the years we have heard frequently from readers in third-world countries for whom the *Digest* was the primary source of continuing medical education. We gave it away for free whenever asked.

In the years since its inception, however, with the advent of new publishing technologies, a myriad of competing newsletters has appeared. As our subscriptions have steadily declined, we have had to reconsider the *Digest’s* role. In our new electronic format, we will appear quarterly. While each issue will be somewhat shorter than in the past, we hope to provide greater value by focusing each on a single theme. As always, each review will consist of a concise synopsis, without any editorializing and drawn from the leading peer-reviewed English-language journals. By publishing on the Institute of Living/Hartford Hospital website, we will maintain two additional traditional values: global and free access.

As you will note, our first electronic edition focuses on schizophrenia. This is in keeping with The Institute of Living’s Schizophrenia Initiative, a major programmatic focus on schizophrenia that features the development of our Schizophrenia Research Center and augmented programs and services for individuals with this devastating disorder, including special programs in Cognitive Remediation.

All of us at The Institute of Living hope you will find the new *Digest of Psychiatry and Neurology* to be as useful as the old.

Harold I. Schwartz, M.D.
Psychiatrist-in-Chief and
Vice President, Behavioral Health
The Institute of Living/Hartford Hospital
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CAUSES OF THE EXCESS MORTALITY OF SCHIZOPHRENIA

Steve Brown, MRCPsych (Mental Health Group, Univ. of Southampton, Royal South Hants Hosp., Brinton’s Terrace, Southampton SO14 0YG, U.K.; e-mail: sb15@soton.ac.uk); Hazel Inskip, PhD; and Brian Barraclough, DM  BR J PSYCHIATRY, 177:212-7, September 2000

While studies of schizophrenic patients consistently show higher levels of natural and unnatural mortality, the precise causes of this excess mortality are not well understood. In the study presented here, the authors examined the mortality of a community cohort of 370 schizophrenic subjects (213 men, 157 women) initially recruited in 1981 and followed for a period of 13 years. The researchers studied the circumstances of each death and attempted to identify the reasons for any excess mortality. Person-years-at-risk by age and gender were calculated and multiplied by the appropriate mortality rates for England and Wales, in order to obtain the expected number of deaths. The number of deaths observed divided by the number of deaths expected and multiplied by 100 yielded a standardized mortality ratio (SMR).

At the 13-year follow-up, only 13 of the subjects were untraceable; 79 subjects had died (58 from natural causes, 19 from unnatural causes, and two from unknown causes). The SMR for all age groups was above the average for the general population and fell with increasing age. The SMR for all causes of death was 298, a three-fold increase over the expected value. Mortality was higher (but not significantly so) in males, in the unemployed, in the unmarried, and in those from lower social classes. The SMR for natural causes was 232, which was twice the expected value. Death from natural causes accounted for 63% of the excess mortality; 80% of these deaths were from neoplastic, circulatory, or respiratory disease. In addition, the SMRs for cerebrovascular disease, diabetes, and epilepsy were greatly increased. The SMR was significantly elevated in smokers and in those with smoking-related diseases. The SMR for lung cancer was twice the expected value. The SMR for unnatural causes was 1,273; this figure was 12 times the expected value. Death from unnatural causes accounted for 33% of the excess mortality. Of the 19 schizophrenic subjects whose deaths were considered to be unnatural, 14 had committed suicide, three had suffered accidental deaths, and two had died from undetermined causes. The unnatural deaths occurred in the early years of follow-up (six in year 1 and 13 by the end of year 3).

According to the authors, the present findings suggest that most of the excess mortality of schizophrenia can be explained by known mechanisms and therefore should be susceptible to currently available interventions. The researchers conclude that some of the excess mortality of schizophrenia could be lessened by reducing patients’ smoking and exposure to other environmental risk factors and by improving the management of medical diseases, mood disturbances, and psychoses. (33 References)  EAF
TEMPOROLIMBIC VOLUME REDUCTIONS IN SCHIZOPHRENIA

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ARCH GEN PSYCHIATRY, 57:769-75, August 2000

Temporal lobe structures and circuitry modulate cognition and emotion. Neuroanatomic studies of schizophrenic patients have reported temporolimbic abnormalities. However, most magnetic resonance imaging (MRI) studies have evaluated small samples composed primarily of men with chronic schizophrenia. In the present investigation, the authors’ goal was to evaluate sex differences in segmented temporal lobe subregions with reliable parcelation methods, relating volume with clinical and neurocognitive parameters.

The study sample was composed of 100 schizophrenic patients (58 men, 42 women; 39 neuroleptic naive, 61 previously treated) and 110 healthy control subjects (51 men, 59 women). The participants were right-handed and between the ages of 18 and 45 years. All underwent MRI scanning, with gray and white matter volumes of temporolimbic (hippocampus and amygdala) and neocortical (superior temporal gyrus and temporal pole) regions being examined. Symptoms, functioning, and neurocognition were assessed concurrently. Assessment tools included the Scale for Assessment of Negative Symptoms, the Scale for Assessment of Positive Symptoms, the Hamilton Depression Scale, the Premorbid Adjustment Scale, the Quality of Life Scale, and a standardized battery designed to measure abstraction-flexibility, attention, verbal memory, spatial memory, verbal abilities, and spatial abilities. MRI results revealed that hippocampal gray matter volume was reduced in both schizophrenic men (7%) and schizophrenic women (8.5%). However, sex differences were observed with regard to the amygdala; while the schizophrenic men showed a decrease in volume (8%), the schizophrenic women exhibited an increased volume (10.5%). MRI of the temporal pole showed decreased gray matter in both male (10%) and female (8.5%) schizophrenic patients. Superior temporal gyrus volume was substantially decreased in male patients (11.5%); however, in female patients (4%) the decrease did not exceed that seen for the whole brain. For the most part, brain volumes were not found to be correlated with clinical measures, although higher hippocampal volumes were associated with better memory performance in all groups, and cortical volumes were associated with better memory performance in healthy women.

The authors conclude that schizophrenia is associated with reduced gray matter volume in temporolimbic structures. These abnormalities are evident in patients with first-episode schizophrenia and are more strongly correlated with cognitive performance than with symptom severity. (68 References)
DEPRESSIVE SYMPTOMS IN STABLE CHRONIC SCHIZOPHRENIA: PREVALENCE AND RELATIONSHIP TO PSYCHOPATHOLOGY AND TREATMENT

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SCHIZOPHR RES, 45:47-56, September 29, 2000

The authors examined the prevalence and correlates of the depressive syndrome in a community sample of 120 outpatients with stable, chronic schizophrenia (78 men, 42 women; age range, 21 to 65 years; mean age, 41.5 years). Assessment instruments included the Brief Psychiatric Rating Scale (BPRS), the Hamilton Depression Rating Scale (HDRS), the Clinical Global Impression Severity scale (CGI-S), the Scale for the Assessment of Negative Symptoms (SANS), the Extrapyramidal Symptom Rating Scale (ESRS), the Barnes’ Akathisia Scale (BAS), the Significant Others Scale (SOS), and the Beck Depression Inventory (BDI).

Of the 120 schizophrenic patients, 16 (13.3%) attained a score of 17 or higher on the BDI and were considered to be moderately or severely depressed. There were no significant differences between the 16 depressed patients and the 104 nondepressed patients in terms of age, sex, marital status, alcohol consumption, antipsychotic dosage, anticholinergic dosage, negative symptoms (as assessed by the SANS), or extrapyramidal symptoms (as rated on the ESRS). A correlation approaching significance was found between akathisia (as measured by the BAS) and depression. Compared with the nondepressed group, the depressed group had significantly higher scores on the CGI scale and significantly higher mean total BPRS scores. When the BPRS was divided into six factors, the depressed patients had significantly higher scores on the anxiety/depression factor, the hostility/suspiciousness factor, the positive symptom factor, and the thought disturbance factor. No correlation was found between the presence of depression and the anergia factor or the activation factor. When individual BPRS items were examined, significant differences were found for hostility, suspiciousness, depression, guilt, and anxiety. An association was found between depression and higher scores on the SOS, i.e., patients who perceived themselves as lacking in social support were more likely to be depressed. A significant association was found between scores on the HDRS and the SANS and also between scores on the HDRS and the ESRS.

According to the authors, the present results indicate that persistent depressive symptoms in stable schizophrenic patients living in the community are related to the degree of persistent positive psychotic symptoms, to patients’ perceptions of social support, and (weakly) to the degree of akathisia, but not to other aspects of antipsychotic treatment. (56 References) EAF
OBSESSIVE AND COMPULSIVE SYMPTOMS IN SCHIZOPHRENIA:  
A RANDOMIZED CONTROLLED TRIAL WITH 
FLUVOXAMINE AND NEUROLEPTICS

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J CLIN PSYCHOPHARMACOL, 20:410-6, August 2000

A possible relationship between obsessive-compulsive (OC) symptoms and schizophrenia has been of interest for over 100 years. Until recently, however, the presence of comorbid OC symptomatology in psychotic patients has been neglected, even though there is evidence to suggest that patients with schizophrenia and OC symptoms tend to have a more chronic course of illness, a higher frequency of social and occupational impairment, and a poorer long-term outcome. The aim of this eight-week, open, randomized, controlled study was to evaluate the efficacy of combined pharmacotherapy (fluvoxamine, a serotonin reuptake inhibitor [SSRI] plus standard neuroleptics) for the treatment of OC symptomatology in schizophrenic patients and to compare its efficacy with that of neuroleptic treatment alone.

The sample was composed of 30 inpatients (22 men, eight women) who met DSM-IV criteria for schizophrenia and who had prominent OC symptoms. Fourteen patients (10 men, four women; age range, 27 to 64 years; mean age, 38.8 years) were randomly assigned to eight weeks of treatment with conventional neuroleptics and fluvoxamine (100 to 200 mg/day). The other 16 patients (12 men, four women; age range, 25 to 48 years; mean age, 35.5 years) received standard neuroleptic treatment only. Patients were assessed at baseline and endpoint with the Yale-Brown Obsessive Compulsive Scale (Y-BOCS), the Positive and Negative Syndrome Scale (PANSS), and the Clinical Global Impression (CGI) scale. Side effects were assessed weekly. All patients completed the eight-week trial. The results indicated that all patients responded to the combined treatment. None of the patients experienced an acute exacerbation at the end of the study. A considerable reduction in PANSS (34.3%) and Y-BOCS (29.4%) scores was noted, and CGI scores decreased moderately in both treatment groups. The fluvoxamine/neuroleptic combination was well tolerated, and no acute dystonic reactions or other serious medical complications occurred. Side effects occurred during both regimens of treatment, but they were generally mild or moderate in intensity and were nearly resolved before the end of treatment.

According to the authors, the existence of OC symptomatology in schizophrenic patients appears to represent one of the most severe forms of psychopathology and probably deserves to be considered as a separate clinical entity. The current results indicate that combined SSRI/neuroleptic therapy for this highly treatment-resistant group of patients is warranted and appears to be effective and well tolerated. (58 References)
FAMILY CHARACTERISTICS OF DEFICIT AND NONDEFICIT SCHIZOPHRENIA IN THE ROSCOMMON FAMILY STUDY

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SCHIZOPHR RES, 45:57-64, September 29, 2000

People with schizophrenia vary greatly with regard to treatment response, course of illness, environmental risk factors, clinical features, and biological correlates. This degree of variation raises the possibility that schizophrenia is a syndrome rather than a single disease with a uniform underlying pathophysiology. Several studies have suggested that the deficit syndrome of schizophrenia serves as a marker of a meaningful subgroup within this disorder. To assess differences in the family history of deficit and nondeficit schizophrenic groups, the authors utilized data from the Roscommon Family Study (Kendler et al., 1993), a population-based study that approximated a treated-incidence sample.

Of 133 probands who met DSM-III-R criteria for schizophrenia or simple schizophrenia, 22 were classified as having the deficit syndrome and 111, the nondeficit syndrome. In this sample, the lifetime prevalence of the deficit syndrome within schizophrenia was 16.5%. In all, 91% (20/22) of the deficit subjects were male, as compared with 63% (70/111) of the nondeficit subjects. Within the families of the deficit probands, those relatives without a diagnosis of a chronic psychotic disorder had a pattern of greater deficit-like symptoms than the relatives of the nondeficit probands, with significantly diminished emotionality/social interest, as well as magical ideation. The relatives of the deficit probands had a nonsignificantly higher mean social anhedonia score. The social isolation of the relatives was a significant predictor of deficit status in the probands. Differences in relative risks for selected diagnoses in the relatives of the deficit and nondeficit probands were not significant. The relative risk for schizophrenia (with covariates) in the relatives of the deficit probands was 1.75 times that of the risk in the relatives of the nondeficit probands. In the relatives of the deficit group, the relative risk was 1.54 for nonaffective psychoses and 1.24 for all schizophrenia spectrum disorders (nonaffective psychoses plus schizotypal and paranoid personality disorders). Compared with the relatives of the nondeficit probands, the relatives of the deficit probands had a relative risk for affective illness (unipolar and bipolar) of 0.65 and a relative risk for alcoholism of 1.06.

According to the authors, the current results provide further evidence that schizophrenic patients with the deficit syndrome exhibit clinical and neurobiological characteristics that differentiate them from other schizophrenic individuals. (50 References)
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NITHSDALE SCHIZOPHRENIA SURVEYS 20
Cognitive Function in a Catchment-Area-Based Population of Patients with Schizophrenia

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BR J PSYCHIATRY, 177:348-53, October 2000

It is now generally accepted that cognitive deficits are core aspects of schizophrenia. In this study, the first of its kind, the authors assessed cognition in a catchment-area-based population of schizophrenic patients and examined the relationship between cognitive and community functioning.

A 1998 census conducted in Nithsdale, an area in southwest Scotland, identified 182 patients (96 males, 86 females) with schizophrenia. Of these, 34% were outpatients, 20% were day patients, 14% were inpatients, 17% were seen mainly by a community psychiatric nurse, and 15% had contact only with a general practitioner. No patient had received electroconvulsive therapy in the preceding 12 months. Informed consent was obtained for all subjects prior to participation. Cognition was assessed by means of the National Adult Reading Test (NART), the Mini-Mental State Examination (MMSE), the Rivermead Behavioural Memory Test (RBMT), the Executive Interview (EXIT), and the Initial Letter Verbal Fluency Test (FAS). Social disability and community functioning during the previous two-week period were evaluated by means of the Health of the Nation Outcome Scales (HoNOS). Cognitive assessments were obtained from 138 of the 182 patients. Of these, 72 were men (age range, 23 to 76 years; mean age, 46 years), and 66 were women (age range, 20 to 90 years; mean age, 51 years). The mean premorbid IQ as measured by the NART (completed by 132 patients) was 98. Results of the MMSE (completed by 138 patients) indicated that 15% of the patients demonstrated significant global cognitive impairment. In all, 81% of the patients exhibited memory impairment as assessed by the RBMT (completed by 135 patients). On the EXIT, which was completed by 137 patients, 25% showed evidence of executive dyscontrol. Finally, 49% of the schizophrenic patients exhibited impaired verbal fluency, as measured by the FAS (completed by 136 patients). Scores on the functional impairment subscale of the HoNOS correlated with all measures of cognitive impairment.

According to the authors, their results indicate that cognitive dysfunction, particularly memory impairment, is a core disability in the majority of patients with schizophrenia. Such cognitive impairment appears to have a major impact on patients’ daily lives and is likely to limit their functioning in the community. The researchers conclude that cognitive evaluation and remediation should become important approaches in the management of individuals with schizophrenia. (32 References)
THE ROLE OF COGNITION IN VOCATIONAL FUNCTIONING IN SCHIZOPHRENIA

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The ability to work is markedly impaired in patients with schizophrenia, with estimates of unemployment in this group ranging from 70% to 85%. Several studies have found that cognitive functioning, rather than clinical symptoms, appears to be a major determinant of occupational functioning in schizophrenic subjects. Using comprehensive assessments of psychopathology and neuropsychological functioning, the authors of the present investigation examined the relationship between neurocognitive functioning and occupational status in 31 schizophrenic patients (19 men, 12 women) who were participating in a vocational rehabilitation program and whose work status had been stable for at least one year. The subjects were assigned to one of three groups on the basis of vocational status. Eight patients (seven men, one woman; mean age, 32.1 years) were assigned to the full-time group (working a minimum of 30 hours per week or enrolled as a full-time student); 13 patients (six men, seven women; mean age, 38.5 years) were assigned to the part-time group (working between one and 29 hours per week or enrolled as a part-time student); and 10 patients (six men, four women; mean age, 38.4 years) were assigned to the unemployed group (not working and not in school).

A univariate analysis of variance indicated that compared with patients in the part-time group and the unemployed group, those in the full-time group were significantly better educated, had more positive symptoms (delusions, hallucinations, and disorganized thinking), were more likely to be treatment-resistant, were more likely to be receiving an atypical antipsychotic medication, and were engaged in more cognitively complex work tasks. When an analysis of covariance (controlling for education) was performed, the results showed that the full-time group performed significantly better than the unemployed group on measures of executive functioning, working memory, and vigilance; the full-time group also performed significantly better than the part-time group on measures of vigilance and executive functioning. Although univariate analysis revealed no significant relationship between negative symptoms (affective flattening, alogia, avolition, and anhedonia) and employment status, a multiple regression analysis indicated that negative symptoms, level of education, and executive functioning differentiated the groups.

The current data confirm the importance of cognitive functioning as a predictor of occupational functioning in patients with schizophrenia. In this study, as well as in a previous report (Meltzer & McGurk, 1999), the authors found that specific areas of cognitive functioning (executive functioning, working memory, verbal learning and memory, and vigilance) are significantly associated with vocational functioning in schizophrenia. (32 References)
RANDOMIZED CONTROLLED TRIAL OF THE USE OF COMPENSATORY STRATEGIES TO ENHANCE ADAPTIVE FUNCTIONING IN OUTPATIENTS WITH SCHIZOPHRENIA

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Schizophrenia is often characterized by deficits in adaptive functioning that range from difficulties in performing basic activities of daily living to problems in maintaining competitive employment. Cognitive adaptation training is a novel psychosocial treatment approach designed to improve adaptive functioning. This approach utilizes a manual-driven series of compensatory strategies that are based on neuropsychological, behavioral, and occupational therapy principles. These compensatory strategies are environmental adaptations designed to bypass neurocognitive impairments, and they include the use of signs, labels, and electronic devices that are designed to cue and sequence appropriate behavior. In the study reported here, the authors examined the effect of cognitive adaptation training on schizophrenic outpatients recently discharged from a state psychiatric facility.

Forty-five patients (34 men, 11 women; mean age, 37.12 years) with a DSM-IV diagnosis of schizophrenia (N=38) or schizoaffective disorder (N=7) were randomly assigned to one of three treatment conditions: standard medication follow-up (N=15); standard medication follow-up plus cognitive adaptation training (N=15); or standard medication follow-up plus a condition designed to control for therapist time and provide environmental changes unrelated to cognitive deficits (N=15). The trial was carried out over a period of nine months, with comprehensive assessments being conducted every three months by raters who were blind to treatment condition. At the end of the nine-month study period, significant differences were found between the three treatment groups in levels of psychotic symptoms, motivation, and global functioning. Overall, patients in the cognitive adaptation training group had higher levels of improvement than those in the other two treatment groups. The three groups also had significantly different relapse rates over the course of the nine-month trial; relapse rates were 13.33% for the cognitive adaptation training group, 67.67% for the group in which therapist time and environmental changes were controlled, and 33.33% for the group that received standard follow-up only.

The current report appears to be the first randomized, controlled study to demonstrate the benefit of compensatory strategies for outpatients with schizophrenia. The use of compensatory strategies may add to the growing repertoire of interventions designed to help schizophrenic patients lead more productive and satisfying lives. (19 References)
THE PSYCHOSOCIAL OUTCOME OF ADOLESCENT-ONSET SCHIZOPHRENIA: A 12-YEAR FOLLOWUP

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To address the psychosocial consequences of adolescent-onset schizophrenia, the authors examined the educational/occupational functioning and social adjustment of a sample of young adults who had initially been treated for schizophrenia in adolescence (age range at index admission, 11.5 to 17.9 years; mean, 16 years). Of 96 patients (55 males, 41 females) consecutively admitted to a university teaching hospital between 1976 and 1987, 65 (38 males, 27 females) were available for reassessment. The average time interval between the first inpatient episode and the follow-up interview was 11.8 years (range, 10 to 15 years). The mean age of the patients at follow-up was 27.8 years (range, 23 to 32 years).

At follow-up, 54 (83%) of the 65 reassessed patients had had at least one further inpatient-treated episode; 36 (55%) had been hospitalized at least three times over the course of the follow-up interval. At follow-up, only 17 subjects (26%) had left the mental health care system; 48 (74%) were still receiving some form of psychiatric treatment. When educational/occupational outcome was examined, it was found that 12 subjects (18%) had left school without receiving a diploma, and almost half of those who started a program of occupational training did not complete it. At follow-up, 16 (25%) of the subjects were not working at all, and 30 (46%) were working with considerable difficulties, either employed in the sheltered labor market or occupied in a clinical setting. In all, 49 subjects (75%) were still financially dependent, either being supported by their parents or receiving public assistance. Of the 64 subjects for whom social disability data were available, 42 (66%) were classified as having serious, very serious, or maximum social disabilities. No significant gender differences were found in any area of functioning at follow-up. Overall, rates of severe impairment in subjects who received no treatment at follow-up were low (educational/occupational impairment, 18%; social disability, 31%), as compared with those in subjects who were still receiving some form of treatment (71% and 77%, respectively). History of treatment (longer duration of inpatient stay, more than two inpatient episodes) was found to be predictive of lower vocational functioning at follow-up. Severity of positive symptoms and occurrence of more than two inpatient episodes in the early course of illness predicted social disabilities in young adulthood.

The authors conclude that the long-term outcome for many patients with adolescent-onset schizophrenia is characterized by poor social adjustment, severe functional impairment, and a high degree of socioeconomic dependence. (48 References)
ADULT OUTCOMES OF CHILD- AND ADOLESCENT-ONSET SCHIZOPHRENIA: DIAGNOSTIC STABILITY AND PREDICTIVE VALIDITY

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The author attempted to establish the predictive validity of a diagnosis of schizophrenia in childhood and early adolescence by examining diagnostic continuity into adult life and comparing social and symptomatic outcomes of child- and adolescent-onset schizophrenia with those of nonschizophrenic psychoses. A total of 110 patients who presented to the Maudsley Hospital in London between 1973 and 1991 with a first-episode psychosis of child- or adolescent-onset (mean age at onset, 14.2 years) were followed up an average of 11.5 years after initial contact. Adequate follow-up data were obtained for 93 of these patients, 51 with a first-episode diagnosis of DSM-III-R schizophrenia and 42 with nonschizophrenic psychoses (23 affective, 12 schizoaffective, and seven atypical). Consensus best-estimate DSM-III-R diagnoses were made at follow-up, and course and outcome were assessed by raters blind to first-episode diagnosis.

Of the 51 patients assigned a diagnosis of schizophrenia in adolescence, 41 received the same diagnosis in adulthood (positive predictive value=80%). Of the 23 patients given a diagnosis of affective psychosis in adolescence, 19 were assigned the same diagnosis in adulthood (positive predictive value=83%). However, schizoaffective psychosis had a positive predictive value of only 33%, with only four of the 12 schizoaffective adolescents receiving the same diagnosis in adulthood. None of the seven patients diagnosed with atypical psychosis in adolescence were assigned the same diagnosis at follow-up. A diagnosis of schizophrenia in adolescence predicted a greater likelihood of a severe, unremitting course of illness. Only 12% of those assigned a diagnosis of schizophrenia in adolescence were in complete remission for most of the follow-up period, as compared with 52% of those diagnosed with nonschizophrenic psychoses in adolescence. Subjects with adolescent-onset schizophrenia spent less time living independently than those with nonschizophrenic psychoses. In adulthood, almost half of the subjects with adolescent-onset schizophrenia had very limited social contacts; those diagnosed with a nonschizophrenic psychosis in adolescence were much less socially impaired.

The author concludes that the diagnosis of DSM-III-R schizophrenia in childhood and adolescence has good predictive validity. The high level of diagnostic stability suggests etiological continuity with adult schizophrenia, with onset in childhood and adolescence being associated with a particularly malignant course and outcome. (35 References)
BOOKS RECEIVED FOR REVIEW


