Cognitive deficits appear to be present years before the onset of schizophrenia, particularly in the areas of executive functioning.

**Background:** According to the neurodevelopmental model of schizophrenia, subtle behavioral, motor, and cognitive deviations are already apparent in childhood, years before the overt clinical symptoms of adult schizophrenia appear. In a recent meta-analysis, it was estimated that, on average, individuals who develop adult schizophrenia exhibit an 8-point deficit (0.5 SD) in their childhood IQ.

**Objective:** To report the findings of multiple cognitive assessments from childhood to early adolescence, before the onset of schizophrenia or depression, through the age of 32 years.

**Design:** This paper is from the ongoing group of Dunedin, New Zealand, cohort studies.

**Participants:** The subjects who developed recurrent depression were used as a comparison group with a different major mental illness.

**Methods:** Of the 1000 children in the Dunedin birth cohort, 3.5% met DSM-IV criteria for schizophrenia, and 13.4% met criteria for recurrent depression. The Wechsler Intelligence Scale for Children-Revised was administered to all cohort members at ages 7, 8, 11, and 13 years. The statistical analyses compared 3 mutually exclusive groups: cohort members diagnosed with schizophrenia (n=35), members diagnosed with recurrent depression (n=145), and healthy comparison subjects (n=556). Growth-curve models were then fitted to examine developmental change, relative to age, in specific cognitive functions from age 7 to 13 years.

**Results:** Lower childhood IQ predicted significantly increased risk of being diagnosed with schizophrenia or depression as an adult, even after adjustments for social class. There was no evidence of cognitive deterioration through the assessment end point of 13 years. However, future schizophrenia case subjects exhibited early and static cognitive deficits on the following 4 cognitive tests: information, similarities, vocabulary, and picture completion. The growth curves demonstrated that the deficits had already emerged by age 7 years and remained steady throughout puberty. In some contrast, the growth on tests measuring freedom from distractibility and visual-spatial problem-solving skills was developmentally slower, suggesting that there was an ongoing, and perhaps increasing, developmental lag in these areas. These deficits were not found in the recurrent depression group.

**Conclusions:** The developmental deficit model of schizophrenia—that there is an insult to the brain acquired or inherited in early development—is supported by these data, but there is also evidence of a developmental lag in working memory/executive functioning.

**Reviewer's Comments:** Recent research has demonstrated that processing speed is the most severely impaired function in chronic schizophrenia patients. The results of this study show that these changes begin in childhood through puberty, which raises questions as to how "treatable" the deficits are in adult patients with schizophrenia. (Reviewer-John G. Koutras, MD).

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Keywords: Schizophrenia, Cognitive Profiles, Executive Functioning

Print Tag: Refer to original journal article
Minocycline appears to have a beneficial effect on cognitive functioning and negative symptoms—some of the most debilitating and treatment-resistant symptoms in schizophrenia.

**Background:** The "glutamate hypothesis" links schizophrenia to a dysfunction in glutamatergic neurotransmission via N-methyl-D-aspartic acid (NMDA) receptors. Minocycline is a second-generation tetracycline that exerts antimicrobial and anti-inflammatory effects while having a distinct neuroprotective profile, via the glutamate hypothesis mechanisms. In one study, minocycline was even able to reduce cognitive disturbances induced by phencyclidine, an NMDA antagonist. Two open-label trials have demonstrated symptom reduction in patients with schizophrenia who were treated with minocycline as an adjunct to antipsychotics.

**Design/Objective:** This study is a double-blind, placebo-controlled, randomized trial of the effects of minocycline on executive function and the negative symptoms in early schizophrenia.

**Participants/Methods:** 54 subjects with schizophrenia who were within 5 years of their first exposure to antipsychotic treatment were entered into the study. The participants were randomly assigned to either minocycline or placebo in a 2:1 ratio. They entered the 22-week add-on phase with minocycline 200 mg/day or placebo being added to their atypical antipsychotic medication. The primary outcome measure was the Scale for the Assessment of Negative Symptoms (SANS). Secondary clinical outcome measures consisted of the Positive and Negative Syndrome Scale, and the Clinical Global Impressions (CGI) scale. Various subtests from the Cambridge Neuropsychological Test Automated Battery were used to assess working memory, cognitive shifting and flexibility, and cognitive planning.

**Results:** Minocycline was associated with a reduction in SANS and CGI scores. In contrast, the placebo treatment did not alleviate negative symptoms, with some measures actually deteriorating during the study. Minocycline was also associated with better executive functioning with study progression. Minocycline demonstrated improvement in social and occupational functioning as assessed on the Social and Occupational Functioning Assessment Scale. Surprisingly, patients in the placebo group also gained significantly more weight during the study than did patients in the minocycline group. Minocycline appears to improve clinical symptoms and cognitive performance compared to placebo.

**Reviewer's Comments:** The study also indicates that minocycline is well tolerated and safe for schizophrenia patients. There is a risk of a characteristic blue-gray hyperpigmentation associated with minocycline, which is most likely related to cumulative doses >70 g, takes >6 months to appear, and is not related to age or concomitant medication use. It is important to identify hyperpigmentation early, as it can take months to years to resolve. (Reviewer-John G. Koutras, MD).

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Keywords: Minocycline, NMDA/Glutamate, Cognitive

Print Tag: Refer to original journal article
Psychosis in childhood appears to reflect overlapping risk factors seen in adult schizophrenia and supports the view of this condition as a focus for study of the neurodevelopmental mechanisms of the onset of that disorder.

**Background:** When children experience hallucinations or delusions, what does that mean? When children report such symptoms, should they be considered part of a spectrum of neurobehavioral expression that unfolds into adult psychotic illness?

**Objective:** To evaluate the degree that the appearance of psychotic symptoms in childhood overlaps with the type of risk factors associated with schizophrenia; this was done as a way to support or question the idea that these symptoms capture, early on, a set of processes that later are etiologically related to schizophrenia.

**Methods:** Subjects were part of a longitudinal twin cohort of 2322 British children. The study began with home assessments and interviews in which there were 5-year-old twins. Follow-up assessments occurred at ages 7, 10, and 12 years. At age 12 years, the assessment included a clinical interview of the children to determine psychotic symptoms, as well as a structured interview with the parents concerning the child's behavior. Symptoms identified at age 12 could then be correlated with a full range of data gathered developmentally in previous assessments on family and child psychiatric treatment history, family and social conditions, pregnancy histories, child behavior at home and school, child neuropsychological performance at age 5, etc.

**Results:** Compared to children without symptoms, children with psychotic symptoms were more likely to have the following risk factors associated with schizophrenia: to have parents and family members with psychosis-spectrum disorders; to live in urban settings and within disadvantaged families; to have lower birth weights, lower IQs, impaired theories of mind, and more negative expressed emotions (less warmth); to be more likely to come from chaotic homes; to have been physically maltreated; to show externalizing behaviors as 5 year olds according to all informants; and to have engaged in anti-social activity and self-harm by age 12 years.

**Conclusions:** Children with self-reported psychotic symptoms show substantial overlap with the domains of social, psychiatric, and neuropsychological burdens seen as early risk factors and clinical harbingers of adult schizophrenia.

**Reviewer's Comments:** The study assessed children with respect to a set of known predictive factors of schizophrenia. However, showing greater likelihood than normal peers of having these risks does not mean they are on the neurodevelopmental pathway of schizophrenia. The overlap could be because of their similar association with risks for other things, especially since we do not know how many of these children later developed schizophrenia. (Reviewer-Gary S. Belkin, MD, PhD, MPH).

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Keywords: Childhood Psychosis, Prognosis

Print Tag: Refer to original journal article
Predicting Psychosis

Prediction of Psychosis in Adolescents and Young Adults at High Risk: Results From the Prospective European Prediction of Psychosis Study.

Ruhrmann S, Schultze-Lutter F, et al:

Arch Gen Psychiatry 2010; 67 (March): 241-252

The combined use of high-risk historical and prodromal symptom profiles and of certain cognitive disturbances provided substantial predictive value in prospectively identifying individuals who went on to have a psychotic illness over 12 months.

Background/Objective: A substantial amount of effort has gone into identifying features placing individuals at high risk for the development of psychotic illness, primarily schizophrenia. One approach uses features often described as capturing those at "ultra-high risk" (UHR). Persons qualifying as UHR fit a picture of having either brief, limited psychotic symptoms, attenuated positive symptoms (such as unusual thought content persecutory ideas, or perceptual abnormalities), or a combination of genetic familial risk and recent decline in functioning. Another approach involves 9 areas of cognitive disturbance captured by the acronym COGDIS. The European Prediction of Psychosis Study was developed to identify strategies that could maximize the early identification of individuals who would develop such illness and report the results of the value of doing so using both UHR and COGDIS criteria.

Methods: Individuals were recruited through information distributed through mental health as well as related-professional (eg, teacher) organizations, providers, newsletters, etc, alerting respondents to potential early warning signs of illness. Eligible subjects were screened through standardized structured scales and interviews that rate UHR and COGDIS criteria. In addition to screening, subjects at baseline received other symptom and diagnostic screens such as the Beck Depression Inventory, measures of positive symptoms, and a structured DMS-IV diagnostic interview. Assessments were repeated at intervals across the 18-month overall observation period.

Results: At 18 months, 37 of 245 subjects transitioned to psychosis. Subjects with a high-level cut-off score on the measure of attenuated psychotic symptoms were 4.81 times more likely to transition. Certain key variables across these criteria domains (positive symptoms, bizarre thinking, sleep disturbance, impaired functioning, and education) provided a prognostic index with a predictive value of 83.3%.

Conclusions: A combination of initial screening using COGDIS and UHR criteria, followed by the prognostic index, could much more effectively target individuals at likely risk for transition to illness.

Reviewer's Comments: As the authors acknowledge, what this layering of screening gains in predictive power, it loses in terms of fully capturing people at risk. It might be best suited as a research tool with which to identify individuals much more likely to transition in order to target studies on the effectiveness of preventive interventions and the mechanisms of disorder onset. (Reviewer-Gary S. Belkin, MD, PhD, MPH).

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Keywords: Prediction, Psychosis, Schizophrenia

Print Tag: Refer to original journal article
Bipolar disorder is associated with cognitive deficits in recall and verbal fluency that are unaffected by treatment with lithium.

**Background:** Cognitive blunting is listed as a common side effect of lithium, with patients complaining of psychomotor slowing, decreased attention and concentration, short-term memory problems, and decreased verbal fluency. There is some evidence, however, that bipolar disorder alone is associated with cognitive impairment suggesting that the disease, not the treatment, is responsible for these changes, and that lithium might be neuroprotective in the long run.

**Objective:** To examine the effects of lithium treatment on cognitive performance in euthymic patients with bipolar I disorder.

**Participants/Methods:** The authors recruited 20 subjects with bipolar disorder treated with lithium for at least 2 months, 20 patients with bipolar disorder who were unmedicated, and 20 control subjects. Bipolar patients were required to meet criteria for euthymia for 6 months before recruitment. All subjects completed a battery of neuropsychological tests evaluating executive function, attention, verbal fluency, verbal learning capacity, immediate and delayed recall, processing speed, and intelligence. The data were nonparametric; thus, the Kruskal-Wallis and Mann-Whitney U tests were used to compare neurocognitive performance between groups.

**Results:** Participants were aged 18 to 50 years, with 5 to 16 years of education. The median IQ was relatively low in each group (91.2 to 95.5). The bipolar group taking lithium demonstrated a later age at onset than did the bipolar group not taking lithium. The median lifetime lithium exposure was 5 years for the lithium-treated group and 6 months for the unmedicated group. Both medicated and unmedicated bipolar subjects demonstrated worse short recall, cued delayed recall, logical memory regression, and cued short and delayed recall in the associative memory test, with semantic assistance compared to the control group. No significant differences in cognitive performance were found between lithium-treated and untreated bipolar patients. Patients taking lithium demonstrated poorer function in the digits backward on the Wechsler Memory Scale compared to controls.

**Conclusions:** In this study, bipolar disorder itself, rather than lithium treatment, was associated with poorer performance on a range of neurocognitive tests. Executive function and processing speed were not altered by illness or lithium treatment. The authors hypothesize that patients with bipolar disorder have greater difficulty using semantic associations that facilitate information storage and recall.

**Reviewer's Comments:** This study was conducted in Columbia in adults with a lower-range IQ and often shortened education, limiting the generalizability of the results. Furthermore, bipolar patients in the study may have been "more stable" than the average population with this illness, based on the fact that they were either maintained on lithium monotherapy or no medication at all. Thus, these findings may not be relevant for bipolar patients who have experienced psychosis or who require more than one mood stabilizer to control their illness. Larger studies are needed to better assess the impact of bipolar illness and lithium treatment on cognitive function. (Reviewer-Charlotte O. Ladd, MD, PhD).

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Keywords: Lithium, Bipolar Disorder, Cognitive Function

Print Tag: Refer to original journal article
Medication Nonadherence Common in Bipolar Disorder

Clinical Features Associated With Poor Pharmacologic Adherence in Bipolar Disorder: Results From the STEP-BD Study.

Perlis RH, Ostacher MJ, et al:

J Clin Psychiatry 2010; 71 (March): 296-303

In bipolar patients, unstable mood, anxiety, low socioeconomic status, rapid cycling, and severe or chronic illness are associated with poorer medication adherence.

Background: Poor compliance with medication is a common obstacle in the treatment of bipolar disorder. Previous studies have suggested that psychiatric comorbidity, illness severity, and lower socioeconomic status are associated with decreased medication adherence.

Objective: The authors were interested in developing a risk stratification hypothesis of poor pharmacologic adherence in bipolar disorder and testing it in a large sample of patients. They utilized participants in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) trial to do so.

Design/Methods: The STEP-BD trial was a large, multicenter effectiveness study conducted in the United States; 4107 subjects entered the study and 3640 completed at least 1 follow-up visit. For the purposes of this study, subjects were divided into 2 cohorts (n=2000 and n=1869) to allow replication of univariate associations. Each week, patients were asked how many doses of their medication they missed, resulting in a percentage of nonadherence for each medication based on the number of milligrams missed. Poor adherence was defined as missing ≥25% of doses of any medication in the previous week. Results were analyzed by linear regression. Clinical outcomes were assessed with the Montgomery Asberg Depression Rating Scale, Young Mania Rating Scale (YMRS), and quality of life measures.

Results: Less than half of all participants reported 100% compliance (46.4%), 23.9% reported at least 20% nonadherence, and 29.6% reported nonadherence between 1% and 19% of visits. Patients reported poor adherence at an average of 12.8% of visits. In the first cohort, poor adherence was associated with younger age, unemployment, lower household income, Hispanic origin, rapid cycling, suicide attempt history, earlier age at onset, anxiety, and alcohol use. Clinical symptoms associated with nonadherence included irritability, depression, anxiety, and manic features. The only side effect associated with poor adherence was memory impairment (based on self report). The authors utilized a backward-elimination step-wise logistic regression model including only those factors with a \( P < 0.2 \) to examine the predictive value of these factors on nonadherence in the second cohort. Accuracy was 83.6%, sensitivity was 19.4%, specificity was 89.5%, and positive predictive value was 21%. The 12-month improvement in functional status and reduction in manic symptoms (measured by the YMRS) were lower among patients with poorer medication adherence in the first 3 months of treatment.

Conclusions: These results mirror previous studies showing that both clinical features and socioeconomic status affect medication adherence in bipolar disorder. The authors suggest that patients might be classified into "high versus low risk" categories; those in the high-risk groups might be followed up more closely for medication adherence.

Reviewer's Comments: Limitations of this study include use of self reporting to assess compliance, lack of blood levels to corroborate medication adherence, and lack of information regarding specific medication compliance. (Reviewer-Charlotte O. Ladd, MD, PhD).

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Keywords: Medication Compliance, Bipolar Disorder

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Pooled longitudinal data looking at the onset of depression and obesity indicate that rather than a causal relationship between the two, there appears to be a reciprocal relationship.

**Background/Objective:** Depression and obesity are highly prevalent health issues and present important public health challenges. There has been growing interest on how these 2 conditions might be related, that is, one causing or predisposing towards the other. There have been some longitudinal studies that might better clarify these relationships. This study enhances what we might learn from them by conducting a meta-analysis of the data from such prior work.

**Methods:** A computerized literature search was performed to identify longitudinal cohort studies of the relationship and appearance over time of depressive disorder, depressive symptom, being in an overweight condition, and body mass index (BMI)-defined frank obesity. Papers were scored in terms of their acceptability in terms of methodological rigor and design. Fifteen studies were included.

**Results:** Pooling the 15 studies created data for 58745 subjects. Baseline obesity significantly increased the odds of later development of depression (OR, 1.55). The relationship was stronger for diagnosed depressive disorder rather than just a change in level of measured depressive symptoms. For people >20 years of age, but not below it, being overweight also increased the risk of later depression (OR, 1.51). Having depression at baseline significantly increased the risk of later being obese (OR, 1.58), but interestingly, not of being overweight.

**Conclusions:** All things being equal, obesity and overweight appear to increase later risk of depression, and depression appears to increase later risk of obesity, but not overweight.

**Reviewer's Comments:** This apparent reciprocal relationship between depression and obesity adds complexity to the putative biological or psychological mechanisms that have been offered to explain one direction of the relationship or another. Also, the relationship between depression and later obesity, but not overweight, if replicated, might indicate some ways in which obesity is distinctly precipitated and sustained. (Reviewer-Gary S. Belkin, MD, PhD, MPH).

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Keywords: Obesity, Depression

Print Tag: Refer to original journal article
Obesity and diabetes appear to be associated with the later onset of Alzheimer's dementia, which may prove to be an added public health concern to our “obesity epidemic.”

**Background:** Established major risk factors for late-onset Alzheimer’s disease (AD) include advanced age beginning in the seventh decade, carriage of an apolipoprotein E epsilon4 (APOE4) allele, and a family history of AD. There have been conflicting reports of whether obesity and diabetes also increase the risk for development of AD.

**Objective:** To systematically review the literature regarding obesity and diabetes as potential AD risk factors, to quantify their associations with AD, and to identify mechanisms whereby they might increase the risk for AD.

**Methods:** The authors searched the PubMed database and included studies in the meta-analysis that reported separate risk statistics for AD by antecedent diagnosis or characterization of diabetes, metabolic syndrome, disorders of glucose or insulin levels, or body mass index (BMI) consistent with World Health Organization criteria for obesity.

**Results:** The meta-analysis yielded a highly significant pooled effect size for AD of 1.59 with obesity and of 1.54 with diabetes. A different meta-analysis combining all studies for obesity, diabetes, and abnormal glucose or insulin levels yielded a larger pooled effect size of 1.63. Taken together, the reviewed studies suggest that obesity and diabetes in mid-life and late-life increase the risk for AD and are consistent with AD pathogenesis beginning many years prior to the clinical onset of AD. The increased risk for AD due to obesity and diabetes appears to be independent of one another, other often comorbid vascular risk factors, and possibly also the APOE4 allele.

**Conclusions:** The results from this meta-analysis confirm a small but significantly increased risk for AD with obesity and diabetes.

**Reviewer’s Comments:** Obesity and diabetes being risk factors for vascular dementia seems readily comprehensible. However, the same cannot be said of the findings of this study, which demonstrate that these metabolic risk factors are also associated with AD, a disease involving the tau protein phosphorylation or amyloid precursor protein expression and processing. Potential causal mechanisms may be related to changes in adipose tissue physiology and in levels of systemic hormones, such as leptin, cortisol, estrogen, thyroid hormone, and growth hormone, and insulin-like growth factor affecting the hippocampus. Whichever the causal mechanism, or, more likely, multiple mechanisms, the implication of the findings in this meta-analysis are tremendous in regard to the potential for disease burden of Alzheimer’s in decades to come. Close to half of the U.S. population is either obese or has diabetes. (Reviewer-John G. Koutras, MD).

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Keywords: Obesity, Diabetes, Dementia, Alzheimer’s, Body Mass Index

Print Tag: Refer to original journal article
CBT Plus Activity Management Improves Outcomes for Low Back Pain

Group Cognitive Behavioural Treatment for Low-Back Pain in Primary Care: A Randomised Controlled Trial and Cost-Effectiveness Analysis.

Lamb SE, Hansen Z, et al:

Lancet 2010; 375 (March 13): 916-923

A CBT intervention for low back pain improves scores of reported pain and disability and appears cost-effective compared to other common treatment strategies.

Background/Objectives: Simple advice by a nurse for a patient with low back pain to remain active has proven more effective than general care by a primary care physician. But that intervention (as well as others, such as structured exercise, acupuncture, and manipulation) has only small to moderate effects for a short term (≤4 months). The clinical trial reported here was a large randomized controlled study comparing the use of a group format of cognitive behavioral therapy (CBT) added to advice for activity versus activity advice alone.

Participants/Methods: Subjects were recruited from 56 general practices in England; all had visits within the prior 6 months for sub-acute low back pain of at least 6 weeks duration. Subjects were assessed with several standard scales and questionnaires evaluating low back pain disability, general ratings of pain and disability, and measures of overall self-rated quality of life. They also completed structured surveys that captured overall health care service use and costs attributable to their low back pain. Subjects were randomized to having a session of self-care and activity advice including printed materials or to having such a session in addition to being offered participation in a 6-session CBT group program. Repeat assessments were made at 3, 6, 9, and 12 months after randomization.

Results: 701 subjects were randomized. Sixty-three percent of subjects randomized to cognitive behavioral intervention met threshold levels of participation. Those more likely to participate also tended to have lower pain scores than those who were not. Overall, at 12 months, those randomized to CBT showed reduction in pain scores and disability scores of 13.8% and 13.4%, respectively, compared to 5.4% and 6.4%, respectively, for those randomized to the advice-only intervention. With respect to self-reported benefit from treatment, 31% of controls and 59% of those assigned to CBT reported recovery at 12 months. The calculated cost for each quality-adjusted life-year (QALY) attributable to the intervention was 1786 British pounds (approximately $2500. This compares to prior estimates of approximately 4200, 3800, 8700, and 3090 British pounds for each gain in QALY for acupuncture, exercise, manipulation, and postural intervention, respectively.

Conclusions: A group CBT intervention added to activity management advice for low back pain was relatively cost-effective and had significantly improved outcomes on reported pain, disability, and overall improvement compared to advice alone.

Reviewer’s Comments: This study provides support for the consideration of a psychological approach to reduce the consequences and severity of low back pain. However, the better condition of those who could actually follow-through with the intervention may self-select for those with a more psychologically and behaviorally loaded condition. (Reviewer-Gary S. Belkin, MD, PhD, MPH).

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Keywords: Cognitive Behavioral Therapy, Low Back Pain

Print Tag: Refer to original journal article
Office-Based Manualized ERP Works for Moderate OCD

Does the Therapy Manual or the Therapist Matter Most in Treatment of Obsessive-Compulsive Disorder? A Randomized Controlled Trial of Exposure With Response or Ritual Prevention in 118 Patients.

van Oppen P, van Balkom AJLM, et al:

J Clin Psychiatry 2010; March 23 (): epub ahead of print

Manualized OCD treatment is effective regardless of the therapist’s level of experience.

Background: A barrier to obsessive-compulsive disorder (OCD) treatment is the limited access to behavior therapists experienced with exposure response prevention (ERP) as well as the ability of therapists to travel to patients' homes to supervise ERP (henceforth termed therapist-controlled ERP). Objective: The next study sought to clarify the effectiveness of manualized ERP delivered in 4 different ways: therapist-controlled ERP delivered by experienced behavior therapists; therapist-controlled ERP delivered by master's students of clinical psychology; self-controlled ERP delivered by experienced behavior therapists (in the office only); and self-controlled ERP delivered by master's level students of clinical psychology (in the office only). The authors hypothesized that self-controlled ERP would be inferior to therapist-controlled ERP and that ERP delivered by students would be inferior to ERP delivered by experienced behavioral therapists, with poorer outcomes and higher dropout rates.

Participants/Methods: 118 out of 146 eligible individuals enrolled in the study and were randomized to 1 of the 4 treatment groups. The mean Yale-Brown Obsessive Compulsive Scale (YBOCS) score at baseline was 25 to 27 in each group, indicating moderate severity. All providers were supervised weekly and followed a 12-week ERP manual. Therapist-controlled ERP consisted of ten 90-minute weekly sessions in the patient's home or other naturalistic area and 2 hours of weekly assigned homework. Self-controlled ERP consisted of ten 30-minute sessions in the providers' office reviewing the patients' hierarchy and three 1-hour weekly ERP homework assignments. Pre- and post-YBOCS scores were used to assess treatment response in an intent-to-treat analysis.

Results: 101 patients completed at least 8 sessions of ERP. The mean baseline YBOCS score was higher among the 17 dropouts (29.8) compared with completers (25.6). There were no significant differences in treatment response between experienced versus inexperienced therapists or between therapist-controlled and self-controlled ERP, nor were there any significant interactions found between these 2 variables. Two-thirds of patients experienced at least a 5-point drop in their YBOCS score during treatment (treatment response), and roughly half experienced recovery defined as YBOCS <17 post-treatment.

Conclusions: None of the authors' hypotheses were confirmed. Manualized ERP was highly effective in treating moderate OCD in this Dutch population regardless of provider experience or who was controlling the ERP. The results suggest that OCD treatment could be disseminated much more broadly with the use of supervised therapists regardless of their experience.

Reviewer's Comments: These results are hopeful for broader dissemination of effective treatment for moderate OCD. The authors observed a 40% decline in YBOCS scores in 12 weeks, which is an impressive achievement. It is disheartening that patients with more severe OCD were more likely to drop out of treatment; thus, the utility of this treatment protocol may be limited to less severe OCD. (Reviewer-Charlotte O. Ladd, MD, PhD).

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Keywords: OCD, Exposure, Response, Prevention

Print Tag: Refer to original journal article
To detect malingering, consider seeking out a psychologist to perform standardized measures, such as the PST index of the SCL-90-R, if there is strong secondary gain involved in a patient’s presentation in order to detect malingering.

**Background:** Major depression, post-traumatic stress disorder (PTSD), and generalized anxiety disorder can be faked by simulating malingers. Studies have demonstrated that spurious compensation claims in personal injury and disability cases for PTSD are common, particularly when there are strong incentives to mangle. For example, the prevalence of faked PTSD has been estimated at 20% to 30% in veterans seeking disability compensation. Individuals can easily access the formal diagnostic criteria as well as various individual clinical presentations in various media. A number of tests of psychopathology have been developed that include validity scales designed to detect deceptive, bizarre, discrepant, or rare responding.

**Objective:** To assess the relative diagnostic validity of malingering indices from 2 measures of psychopathology in the detection of simulated malingering.

**Methods:** Participants were first-year psychology students in Australia, with a mean age of 25 years. The total sample consisted of 41 participants. The participants completed 2 measures of personality and psychopathology, the Personality Assessment Inventory (PAI) and the Symptom Checklist-90 Revised (SCL-90-R). The PAI has 4 standard malingering indices. One of the SCL-90-R global distress indexes, the Positive Symptom Total (PST), was used as an indicator of malingering. The PST provides an indication of a dramatizing presentation style indicative of faking badly. Participants were asked to believably fake psychological impairment on the PAI and SCL-90-R for a chance to win $100. To facilitate believable simulations, they were given a list of psychological symptoms to study before testing.

**Results:** Participants instructed to fake impairment for potential financial reward demonstrated significantly greater psychopathology than controls on the tests studied. These results suggest that malingering was successfully induced. Faked performances at levels suggestive of clinically significant psychopathology were apparent on all but 2 clinical scales. This finding suggests that the number and type of psychopathological disorders vulnerable to faking may be greater than previously demonstrated. The 2 types of psychopathology that were not successfully faked on the PAI were presentations of mania and antisocial features. In general, the PST was better at differentiating malingerers from nonmalingerers.

**Conclusions:** These results demonstrate that a number of other conditions are susceptible to malingering in addition to the disorders that are already known to be susceptible.

**Reviewer’s Comments:** One other interesting finding in this study is that 2 types of psychopathology were not successfully faked, those of mania and antisocial features. The negative social stigma associated with these conditions may be particularly strong, acting as a deterrent against malingering despite instructions. (Reviewer: John G. Koutras, MD).

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Keywords: Malingering, Detection

Print Tag: Refer to original journal article
The majority of patients with a primary psychotic disorder have negative symptoms, which are highly associated with unemployment and disease severity.

**Background:** Negative symptoms of psychosis are poorly understood, difficult to treat, and highly disabling. The hope that second-generation antipsychotics would reduce this burden has been dashed, and there are no good pharmaceutical options currently in the pipeline.

**Objective:** The authors of the Cardiovascular, Lipid, and Metabolic Outcomes Research in Schizophrenia (CLAMORS) study investigated the prevalence of negative symptoms in stable outpatients receiving antipsychotic treatment for 1 of 3 primary psychotic disorders, schizophrenia, schizophreniform disorder, and schizoaffective disorder.

**Participants/Methods:** 1452 patients recruited from 91 outpatient treatment centers met inclusion criteria for the study, which included receiving 1 antipsychotic for >12 weeks. The Positive and Negative Syndrome Scale (PANSS) was used to assess clinical severity and the presence of 5 categories of negative symptoms: blunted affect; social withdrawal; emotional withdrawal; poor rapport; and verbal fluency. The authors defined the presence of a negative symptoms as any of these subscores >3. Patients were described as having a primary negative symptom if they also scored <3 for each positive symptoms, exhibited no extrapyramidal symptoms, scored <4 on anxiety and depression subscales, were taking ≤15 mg/d of haloperidol, and were not prescribed antiparkinsonian treatment. Psychiatrists documented clinical severity with the Clinical Global Impressions-Severity (CGI-S) scale.

**Results:** The majority of patients were diagnosed with schizophrenia (77%), followed by schizoaffective disorder (18.6%) and schizophreniform disorder (4.2%); they had been ill for a mean of 15.5 years with an average of 2.6 hospitalizations. Olanzapine was the most commonly prescribed antipsychotic (21.1%), followed by risperidone (18.5%), ziprasidone (16.5%), quetiapine (15.0%), amisulpride (14.7%), and haloperidol (13.9%). A majority of patients exhibited at least 1 negative symptom (57.6%), and a large minority (39.1%) exhibited all 5 negative symptoms. The most frequent negative symptoms were social withdrawal (45.8%) and emotional withdrawal (39.1%). Approximately 12.9% exhibited ≥1 primary negative symptoms (with few positive symptoms). Schizophrenia was most often associated with negative symptoms. The presence of negative symptoms was highly correlated with clinical severity and being unemployed. There were no drug differences associated with negative symptoms.

**Conclusions:** In this large, cross-sectional multisite study of stable outpatients, a majority of patients with a primary psychotic disorder exhibited at least 1 negative symptom, and 17.8% exhibited negative symptoms in the relative absence of positive ones. Patients with the most positive symptoms were less likely to display negative symptoms. Clinical severity and unemployment were highly correlated with negative symptoms. The dose of potent D2 antagonists was correlated with negative symptoms; however, the direction of this relationship cannot be determined.

**Reviewer’s Comments:** These are sobering findings for those living with or treating chronic primary psychosis. It is hoped that future studies focus on the development of pharmacotherapeutic options for addressing this disabling aspect of psychosis. (Reviewer-Charlotte O. Ladd, MD, PhD).

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Keywords: Psychosis, Negative Symptoms

Print Tag: Refer to original journal article
In utero antidepressant exposure is associated with subtle, clinically insignificant motor milestone delays in infancy.

**Background:** The effects of in utero antidepressant exposure on fetal and infant growth are well studied but controversial due to the lack of controlled studies and confounding factors. While there has been no association between prenatal antidepressant use and cognitive or behavioral outcomes long term, increasing evidence suggests that there may be subtle delays in infant motor function following in utero exposure to antidepressants.

**Objective:** To determine whether or not in utero antidepressant exposure alters infant milestone development up to 19 months of age.

**Participants/Methods:** Participants were selected from the National Danish Birth Cohort from 1996 to 2002 (n=101,042 pregnancies). This was a self-report, prospective survey; information was obtained via computer-assisted telephone interviews at 17 and 32 weeks gestation and at 6 and 19 months postpartum. Women taking psychotropic medications other than antidepressants were excluded from the study (n=741). Substance exposure (caffeine, alcohol, and tobacco) and socioeconomic status (SES) were assessed at the first prenatal interview. Dichotomous answers to 14 questions assessed passage of social, auditory, and motor milestones. Limited information on postpartum medication use, lactation, and depression were obtained in the 2 postnatal interviews. Data were analyzed by linear regression.

**Results:** Selective serotonin reuptake inhibitors were the most commonly prescribed antidepressant (n=348), followed by serotonin norepinephrine reuptake inhibitors and tricyclic antidepressants. Antidepressant use was associated with higher SES and education. Both antidepressant use and maternal depression were associated with alcohol and tobacco use, with the highest consumption in women with unmedicated depression. There was no association between prenatal antidepressant exposure and social or auditory milestone development. There was a significant association between motor function and antidepressant exposure, with delayed ability to sit and walk in infants exposed to antidepressants in utero. At 19 months, antidepressant-exposed children reportedly were less able to occupy themselves for 15 minutes than were nonexposed children.

**Conclusions:** Antidepressant exposure in utero was associated with a 16-day delay in sitting and a 29-day delay in walking compared to infants not exposed to antidepressants; these differences were within the normal range of development. More treated mothers than untreated mothers reported that their infants could not occupy themselves at 19 months. There were no differences noted for any other milestones.

**Reviewer's Comments:** This study adds to increasing data suggesting very subtle delays in fine and gross motor function associated with antidepressant exposure in utero. It is reassuring that these differences remained in the range of normal and that no differences were found in other milestones. The study is limited by the fact that information was obtained by self-report. Women with depression severe enough to require antidepressants during pregnancy may extend their negative cognitive distortions onto their children, under-reporting their child's ability and exaggerating deficits. (Reviewer-Charlotte O. Ladd, MD, PhD).

© 2010, Oakstone Medical Publishing

Keywords: Pregnancy, Antidepressants, Fetal Exposure, Milestone Development

Print Tag: Refer to original journal article
Neurocognitive functions appear to be heritable and associated with schizophrenia among African Americans.

**Background:** Neurocognitive deficits are a core feature of schizophrenia. Understanding the genetic mechanisms for these deficits and their heritability is also therefore considered a way to uncover a core pathway for the unfolding of risk and pathology of schizophrenia more generally. While heritability of cognitive deficits has been established in several studies, this has not been done among African Americans. The Project Among African-Americans to Explore Risks for Schizophrenia (PAARTNERS) is an 8-site collaborative study to look at identifying schizophrenia liability genes among a cohort of this population.

**Objective:** The study used web-based neuropsychological testing methods to gather an unusually large set of data on neurocognition among probands with schizophrenia, their immediate family members, and healthy controls in order to look in a uniquely large sample at both the heritability of cognitive features (eg, to see if relatives are at greater risk for similar deficits) and its relationship to risk for schizophrenia itself.

**Methods:** 610 patients with schizophrenia or schizoaffective disorder, 928 of their biological relatives, and 334 comparison subjects completed a computerized neuropsychological battery that assessed 10 cognitive performance domains that included abstraction and mental flexibility, attention, working memory, verbal memory, face memory, spatial memory, language, spatial processing, sensorimotor processing, and emotion processing.

**Results:** Patients showed less speed and accuracy in most domains tested compared to their relatives, who in turn, performed significantly less well than normal controls. The most highly correlated heritability was for accuracy of abstraction/flexibility, verbal memory, face memory, spatial processing, and emotion processing.

**Conclusions:** According to the authors, “Neurocognitive functions in African-American families are heritable and associated with schizophrenia.”

**Reviewer's Comments:** This work, as the authors point out, provides further support for basing gene-mapping studies on performance in the 10 listed cognitive performance domains. (Reviewer-Gary S. Belkin, MD, PhD, MPH).

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Keywords: Neurocognition, Genetics, Schizophrenia, African Americans

Print Tag: Refer to original journal article
Background: Recent studies have indicated that the so-called "broad phenotype" of early-onset bipolar disorder, which lacks euphoria/expansive mood and an episodic course, is more likely a developmental subtype of either attention-deficit hyperactivity disorder (ADHD) or unipolar depression. However, studies have so far demonstrated remarkable symptom stability and impairment in youth diagnosed with prepubertal onset of bipolar disorder, whether broadly or narrowly defined, justifying the need for intervention.

Objective: To compare the efficacy and safety of second-generation antipsychotics (SGAs) and mood stabilizers (MSs) in youth and adults diagnosed with a manic or mixed episode, focusing on clinically meaningful outcomes such as effect sizes (ES), numbers needed to treat (NNT), and numbers needed to harm (NNH). Only double-blind, randomized, placebo-controlled trials (DB-RPCTs) are included.

Methods: A Medline/PubMed literature search was conducted. The authors then conducted a "comparative analysis" calculating ES and/or NNT/NNH. The authors identified 9 DB-RPCTs in pediatric patients, 8 of which were industry sponsored. Five of these studies compared SGAs versus placebo and 4 studies compared MSs versus placebo. In adults, 23 DB-RPCTs were identified, 22 of which were industry sponsored. Fourteen studies compared SGAs versus placebo, and 9 studies compared MSs versus placebo. All pediatric and adult patients were diagnosed with bipolar I disorder, mixed or manic episode.

Results: Compared to MSs, pooled ES were significantly higher with SGAs. This was true in youth as well as adults. However, after removing MS studies with topiramate (not approved for mania), SGAs had larger ES than MSs only in youth. In fact, individual medications did not differ from each other within or across age groups, except for significantly lower ES with topiramate than with other MSs in adults. In terms of adverse effects, SGAs were associated with more weight gain relative to placebo than MSs in youth, but not in adults. However, when topiramate was excluded, weight gain did not differ between SGAs and MSs, even in youth.

Conclusions: Compared to adults, youth are more likely to respond to SGAs than MSs, more likely to experience weight gain, and less likely to experience akathisia.

Reviewer's Comments: This article is not a meta-analysis and also not a review, but rather one of those in-between articles termed a quantitative review or, in this instance, a "comparative analysis." I urge the reader to look at this comprehensive article if further interested in the specific medication studies included, etc. (Reviewer-John G. Koutras, MD).
Bizarre behavior and social isolation are significant features that describe the heightened risk of relapse among patients with longer durations of untreated schizophrenia.

**Background/Objectives:** It is widely taught that the longer the duration of untreated illness (DUI) in schizophrenia, the harder it is to treat, or more specifically, the harder it is for someone on maintenance treatment after first-episode recovery not to relapse. This idea is originally attributed to the Northwick Park Study of First Episodes reported in 1986. However, as the authors here argue, that study left more ambiguous than later commentaries would suggest, the question of whether the relationship between DUI and shorter time to relapse was due to features of the patient, the illness, or the period of lack of treatment itself.

**Methods:** The authors re-examined data on the 120 first-episode subjects of the Northwick study that recovered from that episode and then were randomized to placebo or maintenance treatment. Time to relapse was an outcome of that study. The authors looked more specifically at estimates of onset, clinical features, and sociodemographic conditions as these were varyingly collected through use of the Present State Examination (PSE), a World Health Organization structured sociodemographic and history interview and other symptom rating scales, and the Disability Assessment Schedule (DAS). All these were widely accepted and valid tools in use at the time.

**Results:** Bizarre behavior and being unemployed emerged as the most significant predictors of time to relapse, with bizarre behavior at first treatment being the largest predictor. Indeed such behavior (threatening, unusual, and strange actions in the community, etc) was the strongest predictor of early relapse, stronger than being assigned to placebo.

**Conclusions:** Social isolation and bizarre behavior (the latter in particular) may be the predominant confounding reasons linking DUI and risk of relapse. This raises the prospect that the features of one's illness, not the DUI itself, are what pose a relapse risk.

**Reviewer's Comments:** The authors’ interpretation of these data regarding DUI being a confounder of a more primary relationship between illness features and relapse risk is (as was the original conclusions drawn about the original study that they challenge here) an interpretation. The authors’ discussion and justification of this interpretation was disappointingly hard to follow yet highly qualified. As with much of the work on how to improve outcomes based on how we treat illness early on, uncertainty and frustration is likely to remain. 
(Reviewer-Gary S. Belkin, MD, PhD, MPH).

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Keywords: Relapse, Schizophrenia, Untreated Illness, Risk Factors

Print Tag: Refer to original journal article
Intranasal Oxytocin May Offer New Hope for Tx of Autism Spectrum Disorders

Intranasal Oxytocin Improves Emotion Recognition for Youth With Autism Spectrum Disorders.


Biol Psychiatry 2010; 67 (April 1): 692-694

Intranasal oxytocin increases emotion recognition in adolescents with autistic spectrum disorders.

**Background:** Autism spectrum disorders are characterized by deficits in emotion perception that are both socially impairing and difficult to treat. Patients with these disorders have difficulty processing social cues and interpreting facial expressions; these deficits are associated with altered amygdala activation in neuroimaging studies. Oxytocin is a neuropeptide that coordinates pair bonding and maternal-infant bonding in mammalian species. In preclinical and clinical studies, it increases peer recognition and improves emotion recognition.

**Objective:** The authors investigate their hypothesis that exogenous oxytocin may reverse deficits in emotion recognition seen in autistic children.

**Participants/Methods:** 16 male subjects, aged 12 to 19 years and with either Asperger's Disorder or Autistic Disorder, were recruited for this double-blind, crossover, randomized controlled trial. Participants received either 18 IU (12- to 15-year-old subjects; n=11) or 24 IU (16- to 19-year-old subjects; n=5) of intranasal oxytocin or placebo 1 week apart. Forty-five minutes after administration of drug/placebo, Reading the Mind in the Eyes Test-Revised (RMET) was presented. This test assesses the individual's ability to read subtle facial cues around the eyes to determine emotional state. This is the most commonly used assessment of emotion recognition in autistic patients.

**Results:** Oxytocin improved performance on the RMET for 60% of the subjects. Improvement was limited to easier items on the test, with approximately a 15% to 20% improvement in the percentage of correct responses ($P<0.001$). The most commonly reported side effect was feeling tired.

**Conclusions:** Pretreatment with intranasal oxytocin modestly improved performance in a test of emotion recognition among adolescents with either Asperger's Disorder or Autism Disorder. Failure to read social cues is a core feature of these illnesses for which there is no current pharmacologic treatment. The authors hope that these preliminary results may lead to future investigations of oxytocin for the treatment of autism spectrum disorders.

**Reviewer's Comments:** Although the improvements in emotion recognition were modest and presumably temporary, this study provides much needed hope for both parents and physicians in the future treatment of autism spectrum disorders. Future studies should examine the duration of benefit following administration of oxytocin and the breadth of benefit in other social interactions. (Reviewer-Charlotte O. Ladd, MD, PhD).

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Keywords: Autism Spectrum Disorders, Oxytocin, Emotion Recognition, Social Cognition

Print Tag: Refer to original journal article
The CUPIT holds promise for use as a screening instrument for those individuals encountered in primary care and mental health settings who report occasional cannabis use.

**Background:** It has been estimated that clinicians would detect >80% of drug users if they limited their initial screening questionnaires to marijuana. A number of cannabis-specific screens have been developed internationally. However, these screens are not sensitive to risky (pre-dependent) cannabis use and are not intended for generalist settings. Yet, cannabis users typically start with occasional use and are unlikely to present to other specialized clinical settings, such as mental health settings.

**Objective:** To describe the empirical construction and the initial validation of the Cannabis Use Problems Identification Test (CUPIT), a brief self-report screen developed to expedite detection of currently and potentially problematic cannabis use.

**Methods:** The authors pooled candidate questions through reviewing currently available interview instruments and scales as well as developing their own. The candidate questions addressed: cannabis consumption amount and frequency; dependence (withdrawal symptoms and preoccupation); psychological (regrets); health effects (ie, respiratory); energy/motivation; memory effects; and abuse/harmful use (social/occupational/legal consequences). Then 212 cannabis users were recruited. The participants participated in taking the CUPIT and also underwent comprehensive clinical interviews, structured DSM-IV interviews, and other validated instruments (such as the Brief Symptom Inventory 18); the data were then analyzed.

**Results:** All items on the CUPIT loaded well above the minimum for interpretive purposes. The first component of the CUPIT is comprised of 5 consumption (amount, frequency use) variables, with the remaining 5 suggesting impaired control over use. The second component is comprised of 6 items of consequences or problems caused by cannabis use. One-week test-retest reliability estimates of CUPIT items were all in the ranges deemed excellent. Optimal cutoff scores were then determined for sensitivity versus specificity.

**Conclusions:** The CUPIT is a highly acceptable, reliable, and valid brief cannabis screener for use across community settings and consumers of all ages.

**Reviewer's Comments:** The CUPIT not only assesses currently diagnosable cannabis abuse/dependence but also potentially problematic use among respondents. The 16 final CUPIT items measure risky use, dependence/using behavior, health, and social problems. It requires a reading level of approximately 7 to 8 years of schooling and takes about 5 minutes administration time. It is self- or other-administered, and rapidly scored and interpreted, thereby greatly increasing its generalizability. It is available at http://ncopic.org.au/assets/downloads/workforce/cannabisinfo/assessment-tools/cannabis-use-problems-identification-test.pdf. (Reviewer-John G. Koutras, MD).

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Keywords: Cannabis Screening, Abuse, Dependence

Print Tag: Refer to original journal article
Diet Quality May Be a Factor in Psychiatric Disorders in Women

Association of Western and Traditional Diets With Depression and Anxiety in Women.

Jacka FN, Pasco JA, et al:

Am J Psychiatry 2010; 167 (March): 305-311

Higher rated diet quality appears to be associated with significantly decreased risk of reporting a score-measured excess of impairing depression and anxiety symptoms.

Background/Objective: Diet and nutrition have been explored for their association to mood disorders. Such an association is hypothesized given that they affect other physiological processes also associated with mood and emotional changes such as inflammation, brain plasticity, stress response, and oxidative processes. The study reported here used data gathered as part of a longitudinal study of women looking at osteoporosis risk. That study gathered detailed information about diet, as well as a psychiatric diagnostic evaluation and a scale of well-being and psychiatric symptoms, the General Health Questionnaire (GHQ-12).

Methods: A large epidemiological study in Australia followed a cohort of women for biennial assessments that included gathering detailed information about diet, health conditions, physical activity and alcohol consumption, sociodemographic data, etc. Data on 1127 women were available for analysis at 10-years follow-up. The dietary assessment allowed the calculation of a quality rating of the strength of categorization of a person's diet as traditional (vegetables, fruit, beef, lamb, fish, whole-grains), western (processed meats, sugar, flavored drinks, pizza), and modern (fruits, salads, fish, beans, nuts, yogurt). Overall quality was based on weighted ratings of use of diet features considered more healthy (eg, points assigned for having 2 fruit servings per day, 4 vegetable servings, etc) using a validated scoring algorithm.

Results: After adjusting for confounders (eg, age, health conditions, education), each standard deviation (SD) increase in the factor score for a western diet was associated with a 0.17 SD increase in mean GHQ-12 score. A 1.0 SD increase in score for a traditional pattern was associated with a 35% reduced odds for major depression or dysthymia and 32% for anxiety disorders. Positive diet quality ratings were also significantly associated with improved GHQ-12 scores in a dose-response relationship.

Conclusions: Both western diets and poorer quality diet scores were significantly related to the risk of depression and anxiety disorders, and with GHQ-12 scores, with the latter related to diet quality in a dose-response fashion.

Reviewer's Comments: This study provides some empirical support and certainly prompts further interest in the connection between diet and psychiatric morbidity. Of course, and especially because of its cross-sectional design, the study and this question involve highly confounding phenomenon. While the authors did control for a range of other variables that might be related to mood, lifestyle, and diet, features of lifestyle clearly impact both diet and mood. It will be a continuing challenge of further research and potential recommended interventions to singularly relate this observed association as a unique function of the diet itself. (Reviewer-Gary S. Belkin, MD, PhD, MPH).

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Keywords: Diet, Depression, Anxiety, Women

Print Tag: Refer to original journal article
It is important to ascertain the level of insight in BDD in order to have a better clinical sense of severity and possible refractoriness to SSRIs.

**Background:** In those with body dysmorphic disorder (BDD), the preoccupation with a perceived or minor defect in one’s appearance consumes, on average, 3 to 8 hours daily. Although not part of the diagnostic criteria, individuals with BDD perform compulsive behaviors to examine, improve, or hide their perceived defect. Insight into these bodily preoccupations is often impaired; BDD patients hold these beliefs with strong conviction. Patients who have a delusional intensity qualify for an additional diagnosis of delusional disorder, somatic type. Both delusional and nondelusional variants of BDD may reflect 1 single disorder, with the degree of insight varying along a continuum. Delusional patients have greater impairment in occupational or academic functioning than do nondelusional patients. Pharmacotherapy trials consistently indicate that selective serotonin reuptake inhibitors (SSRIs) are often efficacious in treating both delusional and nondelusional variants of BDD.

**Objective:** This Australian sample of BDD patients compares demographics, clinical features, and treatment response between patients classified as delusional and nondelusional.

**Participants/Methods:** 65 patients with BDD were administered the following measures: Body Dysmorphic Disorder Questionnaire; Dysmorphic Concern Questionnaire; Self-Rating Depression Scale; Social Interaction Anxiety Scale; BDD Yale-Brown Obsessive-Compulsive Scale; and the Clinical Global Impressions (CGI) Scale. The patients were then treated with a standardized pharmacological protocol; citalopram or escitalopram were the first-line choice, and if poorly tolerated, then venlafaxine was the second-line choice. An adjunctive atypical antipsychotic (quetiapine) was used if the response to the SSRI was suboptimal.

**Results:** 60% of the patients were classified as currently delusional and 40% as nondelusional. The 2 groups did not differ on most demographic characteristics, although delusional patients were less likely to be female or employed. There were no significant differences between delusional and nondelusional patients in relation to the age of BDD onset and duration. Delusional patients had more severe BDD symptoms on the standardized measures and less improvement on the CGI. In terms of psychiatric comorbidity, there were no significant differences in comorbidity between the 2 groups. Overall, fewer delusional patients responded to treatment than nondelusional patients.

**Conclusions:** BDD appears to occur within a spectrum of insight, with delusional patients having a more severe form of the disorder. (Reviewer-John G. Koutras, MD).

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Keywords: Body Dysmorphic Disorder, Insight, SSRIs, Delusional, Nondelusional

Print Tag: Refer to original journal article
ADHD persists in >60% of girls into adulthood, and they are also at significantly higher risk for mood and anxiety disorders.

Background/Objective: Almost all of the available literature on follow-up studies of attention-deficit hyperactivity disorder (ADHD) is limited to studies of boys, so there is a scarcity of follow-up studies of girls with ADHD. This research group previously reported on a 5-year follow-up study of girls with ADHD into mid-adolescence, which demonstrated a significantly higher risk for disruptive behavior and mood, anxiety, and addictive disorders in adolescence. However, there is no information available on whether these and other similar findings extend into adulthood. This study is an 11-year longitudinal study of psychiatrically and pediatriically referred girls with and without ADHD followed into adulthood. The primary goal of the study was to estimate the burden of psychopathology associated with ADHD in young adulthood.

Participants/Methods: 96 girls with ADHD and 91 comparison girls participated in the 11-year follow-up, with an average end-of-study age of approximately 22 years. The participants were administered the Structured Clinical Interview for DSM-IV (SCID) supplemented with modules from the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Epidemiologic Version (K-SADS-E). The authors decided a priori that major depression would be diagnosed only if it was associated with severe impairment. However, the same standard was not held for bipolar disorder, as the diagnosis could be made even if there was moderate impairment.

Results: At the 11-year follow-up, 62% of the ADHD girls retained the diagnosis of full or subthreshold ADHD. The risk of all 6 composite lifetime diagnostic categories was higher in the ADHD group than in the comparison group; hazard ratios were 7.2 for antisocial disorders, 6.8 for mood disorders, 3.5 for eating disorders, 3.2 for developmental disorders, 2.7 for substance, and 2.1 for anxiety disorders.

Conclusions: In girls, there appears to be a strong association between ADHD and lifetime risks for antisocial, mood, anxiety, development, and substance abuse disorders.

Reviewer's Comments: A comparison of prevalence estimates between this study and the authors' study of boys with ADHD reveals a similar persistence of ADHD into adulthood, as well as a similar pattern of risk for comorbid disorders, except: higher rates of antisocial disorder in boys (13% in boys vs 6% in girls), higher rates of major depressive disorder in girls (20% in boys vs 8% in boys), as well as anxiety disorders (agoraphobia 25% in girls vs 3% in boys) and social phobia (20% in girls vs 4% in boys). The ADHD girls were also at higher risk for eating disorders. (Reviewer-John G. Koutras, MD).

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Keywords: ADHD, Comorbidity, Females, Adulthood

Print Tag: Refer to original journal article
The probability of recovery from a mood episode in bipolar I illness is significantly less for cycling episodes, mood episodes with severe onset, and patients with greater cumulative morbidity.

**Background/Objective:** Bipolar I mood cycles appear to have been well studied in terms of their variations over a course of illness, the relationship between characteristics of timing, and features of mood cycles in terms of outcomes, etc. The authors of the study described here, however, remark that much of the work in terms of the dynamics and impact of different mood episode features and frequency has relied on “survival analysis,” which analytically takes as its unit of measure a single episode per studied subject. Using a large, longitudinal sample with observation of subjects up to 25 years and using more recent statistical analytic methods that could look at mixed effects of multiple episodes, the authors revisited some of these questions as to the probability of recovery over time as a function of multiple mood episodes over time.

**Participants/Methods:** 219 subjects from 5 U.S. academic medical centers with structured interview-validated diagnoses of bipolar I were followed with a range of assessments, including the Longitudinal Interval Follow-up Evaluation every 6 months for 5 years and then annually. That evaluation was designed to capture weekly changes in scale-rated severity and type of symptoms and functioning level. This allowed identification of mood episode length, recurrence, remission, and clinical features.

**Results:** Bipolar mood episodes lasted a median of 13 weeks, with >75% of subjects recovering from a given episode within 1 year of onset. The likelihood of recovery, however, was significantly less for an episode of severe onset (eg, significant impairment and/or psychosis) and for those with greater “cumulative morbidity” (ie, number of cumulative years spent ill). Recovery was most difficult for major depressive, as opposed to manic, hypomanic, or minor depressive episodes, although recovery from a cycling episode had the least likelihood of recovery.

**Conclusions:** The probability of recovery from a mood episode in bipolar I illness is significantly less for cycling episodes, episodes with severe onset, and level of comorbidity.

**Reviewer’s Comments:** While much of this information is not surprising (ie, that more cumulative exposure and severe and depressive episodes are harder to come out of), the finding of cycling episodes as indeed more difficult in this respect than even depressive episodes, bolsters, the argument that these episodes may indeed validate the concept of such episodes as an entity that the authors argue should support inclusion as a specific subtype in the DSM-IV. (Reviewer-Gary S. Belkin, MD, PhD, MPH).

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Keywords: Bipolar Disorder, Mood Episodes, Duration, Frequency

Print Tag: Refer to original journal article