Catatonia should be viewed as delirium — a potentially lethal syndrome with multiple etiologies that requires urgent intervention.

Objective: Catatonia was first delineated among psychiatric asylum patients in 1874. Although Emil Kraepelin identified catatonia in manic-depressive patients, it remained more tightly associated with the diagnosis of schizophrenia. Studies in the 1970s started to report catatonia as being prominent in patients outside of schizophrenia. Descriptions of malignant catatonia began to enter into the literature, and in 1980, the diagnosis of neuroleptic malignant syndrome was introduced. These reports further raised doubts about characterizing catatonia solely as a type of schizophrenia. Objective: To better understand the various presentations of catatonia, to describe some recent findings as to potential etiology, and to propose a possible treatment algorithm.

Methods: A thorough review of the literature citing 67 references.

Results: Per the authors, “Catatonia is a motor dysregulation syndrome with patients unable to move normally despite full physical capacity. Movements cannot be initiated or stopped and become repetitive, posture is frozen or oddly positioned, and actions become contrary to intent.” Stupor is a hallmark, and there is typically staring and a lack of response to pain. There is also an excited form of catatonia characterized as delirious mania, which is marked by restlessness, talkativeness, agitation, and frenzy. Malignant catatonia is a syndrome of acute onset, fever, abnormal blood pressures, tachycardia, and tachypnea, which can be life-threatening. Malignant catatonia was well described before the introduction of psychotropic agents. A recurrent form of periodic catatonia is described among patients with bipolar disorder, fluctuating between stupor and excitement, particularly during a mixed mood state or rapid cycling. More recently, catatonia has been identified in patients with paraneoplastic syndromes, such as associated with an ovarian teratoma in which N-methyl-D-aspartate receptor (NMDAR) antibodies are implicated in the pathophysiology. Catatonia has also occurred more frequently among patients with seizures or those who are mentally retarded and/or have an autistic spectrum disorder.

Conclusions: Catatonia should be its own syndrome with various potential etiologies (both psychiatric and other medical) and should be dissociated from schizophrenia as a formal diagnosis.

Reviewer’s Comments: The authors summarize treatment for catatonia as well, with a high priority placed on looking for other medical signs and symptoms which may point to physical etiologies rather than a mental disorder. The focus of treatment should be on intravenous lorazepam, beginning at 3 mg/day and increasing rapidly until effective resolution. For those who have a more persistent catatonia, consideration should be given to daily bilateral electroconvulsive therapy for 2 to 5 days. Antipsychotics are relatively contraindicated due to the risk of precipitating malignant catatonia. (Reviewer-John G. Koutras, MD).

© 2009, Oakstone Medical Publishing

Keywords: Catatonia

Print Tag: Refer to original journal article
The Apathy Evaluation Scale has questions for both the patient and the clinician to account for the impact apathy has on a patient’s insight and self-evaluation.

**Background:** Negative symptoms in chronic schizophrenic patients predict poor functioning. These symptoms are conceptualized as a syndrome composed of apathy, avolition, anhedonia, alogia, asociality, flat affect, and inattention. Apathy is defined as “…lack of motivation or goal-directed behavior not attributable to diminished level of consciousness, cognitive impairment, or emotional distress.” It is also found to be a common symptom in other disorders, such as Huntington disease and traumatic brain injury. Only 1 study has found apathy specifically to be related to poor functioning in schizophrenic patients.

**Objective:** To describe the relationship between apathy and functioning in first-episode psychotic patients.

**Methods:** 103 consecutive first-episode psychotic patients admitted to 3 hospitals in Norway between 2004 and 2006 were included in the study along with 62 randomly selected healthy controls. First-episode patients were used as the investigational group to limit the impact of treatment failure and social defeat in more chronically psychotic patients. Subjects were assessed with a battery of tests, most importantly the Apathy Evaluation Scale, as soon as they were clinically stable for the study group and at initiation of participation for the control group. The groups were subdivided into schizophrenia-spectrum, affective psychosis, and other psychosis groups and were compared across a range of variables.

**Results:** The study group reported significantly more apathy than the control group. Of the first-episode patients, 54% rated themselves as apathetic, while 53% of the clinicians also rated these patients as apathetic. Disorganized and depressive symptoms were significantly correlated with increased clinician-rated apathy. When all of the variables were combined in the analysis, lower premorbid adjustment in childhood and disorganization came out as most strongly linked to apathy. Finally, lower Global Assessment of Functioning scores (GAF-F) were significantly associated with apathy, negative and positive symptoms, and disorganization. **Conclusion:** Apathy was a prevalent symptom for first-episode psychotic patients, was significantly associated with lower functioning scores, and was less specific for schizophrenia than initially hypothesized.

**Reviewer’s Comments:** Interestingly, diagnosis, depression, and use of antipsychotic medications were not significantly associated with apathy in this study. Disorganization and poor premorbid social functioning were the major variables associated with apathy, and those with higher apathy scores tended to have lower GAF-F scores. The authors emphasize in their discussion, which I think is very important to remember, that apathy and negative symptoms remain very difficult to treat. Cognitive remediation and motivational techniques are growing in popularity, but the outcomes of these techniques are not yet clear. As a practitioner, it is important to be able to understand the negative symptom profile of your patients and be able to reasonably set expectations about improvement. (Reviewer-Elizabeth Ford, MD).
The 5 items on the Hoarding Rating Scale are clutter, difficulty discarding, excessive acquisition, distress, and impairment. Compulsive hoarding is not clearly understood from an epidemiologic or treatment perspective.

**Background:** Compulsive hoarding is defined as acquiring a large number of possessions that occupy living spaces and causes significant distress. It is associated with serious mental and medical health problems and family burden. Estimates of prevalence rates have varied based in part on measurement techniques. To date, there is no clearly effective treatment. Compulsive hoarding has a strong familial component, as evidenced by the majority of sufferers reporting a first-degree relative with similar problems. One of the best ways to sort out the influence of genetic and environmental factors on the prevalence of a disorder is to conduct twin studies.

**Objective:** To estimate the percentage of monozygotic and dizygotic twins who have severe compulsive hoarding and to identify the contribution of genetic influences in the presence of the disorder.

**Methods:** 8313 monozygotic and dizygotic twins from the TwinsUK adult twin registry in the United Kingdom were mailed the self-report Hoarding Rating Scale. After surveys were returned, the twin analyses were done on the 4355 same-sex female monozygotic and dizygotic twins. Statistical analysis assumed that the larger the impact of genetics, the higher the concordance rate between monozygotic twins.

**Results:** Of the respondents, 2.3% reported severe hoarding, with a significantly higher percentage in men than women. In the twin studies, there was greater similarity in the monozygotic than dizygotic twins. Approximately 50% of the variance in hoarding was accounted for by genetic factors, with the other 50% explained by non-shared environmental factors and measurement error. **Conclusion:** Compulsive hoarding is largely heritable, at least in women, and is also influenced by non-shared environmental factors.

**Reviewer's Comments:** We have several things to think about regarding this article. First, the prevalence rate identified was much smaller than has been identified in earlier studies. This is likely because of less restrictive measurement techniques in the former studies. Second, the sample involved in the twin analyses only included Caucasian females (the TwinsUK study only included Caucasians). This clearly limits the generalizability of the findings to white women. Finally, a large percentage of the variance was attributed to non-shared environmental factors. This indicates that there may be some types of phenomena, like traumatic events, which predispose individuals to compulsive hoarding. Whatever the case, it is clear from this article that compulsive hoarding is not clearly understood from either an epidemiological or a treatment perspective. (Reviewer-Elizabeth Ford, MD).

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Keywords: Compulsive Hoarding, Genetics

Print Tag: Refer to original journal article
Mineralocorticoids are almost exclusively expressed in the prefrontal cortex and the hippocampus. In patients with depression, cortisol is elevated and binds to these mineralocorticoid receptors.

**Background:** Depression is associated with increased hypothalamus-pituitary-adrenal (HPA) axis activity that leads to elevated cortisol secretion and cognitive deficits. The theory behind this is that cortisol binds to mineralocorticoid and glucocorticoid receptors, which are clustered in the hippocampus and the prefrontal cortex, which are areas highly related to cognitive function. The research on this topic, however, is inconclusive and, at times, contradictory.

**Objective:** To examine the association between cognitive function and cortisol secretion in depressed patients versus healthy controls. One of the hypotheses was that patients would have higher cortisol levels and worse cognitive function than healthy controls.

**Methods:** This was a cross-sectional study. 52 moderately to severely depressed inpatients and outpatients who were medication-free for at least 5 days were recruited from a clinic in Germany. They were compared to a group of 50 healthy controls who were recruited via advertisements. The controls were medication-free for at least 3 months. Salivary cortisol measures were taken 4 times in 24-hours for each group. Neuropsychological testing was done to assess cognition focused on short-term and long-term verbal memory, psychomotor slowing, working memory, and selective attention.

**Results:** The depressed patients had higher salivary cortisol levels than the control group, especially in the morning. Although not significant, patients had lower scores than controls on verbal memory. They had significantly lower functioning than controls in terms of visuospatial memory, selective attention, and elements of working memory. **Conclusion:** Cognitive deficits and higher cortisol secretion seem correlated in depressed patients.

**Reviewer's Comments:** If cognitive impairment in depression is, in part or entirely, governed by cortisol, than we could consider treatments that normalize cortisol levels to improve cognition. The rare studies that have looked at this have not found consistent results. It is also unclear whether depression predisposes patients to cognitive impairment and elevated cortisol, or if patients with those symptoms are predisposed to depression. This is a bit of the chicken-or-the-egg scenario. I suspect that if a treatment could be designed that would decrease cognitive impairment in depression, the time to remission would also decrease. (Reviewer-Elizabeth Ford, MD).

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Keywords: Cortisol Secretion vs Cognitive Function

Print Tag: Refer to original journal article
Night eating syndrome should be listed as an “Eating Disorder Not Otherwise Specified” according to the current version of the Diagnostic and Statistical Manual (DSM) of the American Psychiatric Association.

**Background:** Night eating syndrome (NES) is not currently included in the Diagnostic and Statistical Manual (DSM) of the American Psychiatric Association. Five criteria have previously been proposed for a diagnosis to be included: (1) a significant number of empirical journal articles on the disorder must have been published in the past 10 years; (2) the criteria must include self-report measures, rating scales, and structured interviews; (3) research must demonstrate high interclinician correlations; (4) the disorder must have frequently occurring symptoms; and (5) the disorder can be distinguished from other similar disorders.

**Objective:** To review the literature on NES and argue for its inclusion as an Axis I disorder in the next version of the DSM.

**Methods:** The literature was reviewed, as well as information obtained from the First International Night Eating Symposium in 2008. The authors also propose 4 additional features that lend support for this syndrome as a separate diagnostic entity.

**Results:** In terms of the 5 initial diagnostic criteria, the authors describe support for each one. (1) In the past 10 years, 77 articles, mostly empirical, have been published on NES. Diagnostic criteria have been established by self-report weekly food and sleep diaries, rating scales, and structured interviews. (2) Using these tools, the 2 core criteria for the diagnosis are evening hyperphagia and ≥2 nocturnal awakenings with ingestions per week. (3) There have been studies where different clinicians have reached the same diagnostic ratings. (4) Evening hyperphagia and nocturnal awakenings with ingestions co-occur at a high rate. (5) The authors describe a number of ways that NES can be distinguished from the disorders with which it would most likely be confused (binge-eating disorder and sleep-related eating disorder). The four additional criteria that the authors report in support of DSM inclusion are prevalence (1.5%–5%), documented relationship to obesity, high prevalence of psychiatric comorbidity, and biological contributors.

**Conclusions:** The evidence, as described in the article, indicates that NES should be considered its own diagnostic entity.

**Reviewer’s Comments:** This article describes an interesting syndrome that is rarely reported, while also providing a closer look at how diagnoses might be included in the next version of DSM. Considering the importance of the DSM in terms of getting reimbursement for services, making disability claims, and providing a means with which mental health care providers can communicate effectively with each other, it is critical that practicing psychiatrists understand the process of how a diagnosis gets considered for inclusion. (Reviewer-Elizabeth Ford, MD).

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Keywords: Night Eating Syndrome

Print Tag: Refer to original journal article
Although 65.2% of psychiatrists reported no formal training in weight management, they appear confident in their ability to help patients lose weight but are less confident in their patients’ ability to lose the weight.

**Background:** 30% of adults in the United States are obese. Those with severe mental illness are at a 3-times greater risk of death than the general population, in part because of increased heart disease. Issues of healthy eating and regular exercise are challenging in this population. Psychiatrists are becoming increasingly involved in treating obese patients and managing medication regimens that can cause or worsen obesity.

**Objective:** To identify the perceptions and practices of psychiatrists who treat obese patients.

**Methods:** A survey was mailed to a random sample of 500 psychiatrists in the U.S. who were part of the 2007 American Psychiatric Association roster. Items on the survey included questions about the Stages of Change model (precontemplation through maintenance), Self-Efficacy Theory, perceived barriers to care, and engagement in the 5As model for addiction treatment (ask, advise, assess, assist, arrange). Overall, 49% of the included surveys were returned, yielding a working sample of 237.

**Results:** Psychiatrists who were themselves of normal weight or underweight were more likely to change medications based on weight-gain potential for their obese patients than were those psychiatrists who were themselves obese. Although 65.2% reported no formal training in weight management for obese patients, >90% thought that this topic should be included more vigorously in residency training programs. In general, psychiatrists were confident in their ability to help patients lose weight but were less confident that their patients would actually lose the weight. Time constraints, poor patient compliance, lack of guidelines, limited training, and fear of offending patients were most commonly listed as perceived barriers. Those who perceived more barriers were significantly less likely to be involved in treating obesity. Those with formal training in weight management were significantly more likely to be involved in treating obesity. **Conclusion:** Although psychiatrists manage obese patients on a daily basis, the perceived barriers to weight loss and their own level of training in weight management significantly impact whether they are actively involved in weight loss interventions with their patients.

**Reviewer’s Comments:** The authors use these results to encourage more training on obesity and weight management in psychiatric residency programs. I could not agree more, and I think that medical schools should place a stronger emphasis there as well. I have noticed that residents and colleagues place too great an emphasis on changing psychiatric medications as a form of weight control, even when those medications are controlling psychiatric symptoms, than counseling and working with the patient on alternate methods, including changes in diet and exercise. While some psychiatric medications clearly cause weight gain, it seems that they are being blamed for what was an obesity problem long before they were introduced. (Reviewer-Elizabeth Ford, MD).

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Keywords: Obesity, Treatment Practices & Attitudes

Print Tag: Refer to original journal article
Exposure to political violence by Palestinian and Israeli adolescents is a powerful predictor of both social disruption and mental health symptoms, with similar patterns seen across nationalities.

**Objective:** To compare the prevalence of disorders and the burden of illness experienced by Palestinian and Israeli adolescents exposed to political violence and to assess the degree of impairment and symptoms.

**Methods:** Subjects included male and female adolescents aged 14 to 18 years who attended school in either Israel or the Gaza Strip. Participants were assessed with a range of instruments and surveys, including questionnaires obtaining sociodemographic circumstances, the Buss-Perry Aggression Questionnaire (classifies use and frequency of aggressive behaviors), the McMaster Family Assessment Device (describes structural and functional features of family support, expression, and interactions), symptom scales for post-traumatic stress disorder (PTSD), general symptom types and their severity (the Brief Symptoms Inventory [BSI]), and an assessment of social and peer interaction-functioning.

**Results:** 442 Israeli and 450 Palestinian children were evaluated. While both groups reported levels of symptomatology, these were significantly higher among Palestinians in terms of greater exposure to political violence, more symptoms on all BSI subscales (somatization, obsession-compulsion, interpersonal sensitivity, depression, anxiety, hostility, phobic avoidance, psychoticism, and paranoia), as well as total PTSD scores. They also reported significantly more problems in family and social functioning as well as higher levels of aggressive behavior. Controlling for nationality, relationships between political violence exposure and levels of mental health symptoms and PTSD symptoms were significant, and exposure was also a significant predictor of poor family and social functioning. Regression analysis found that the detrimental effects of violence operate similarly across groups. The greater the reported mental health symptoms, the greater reported problems in family function, social relationship difficulties, and aggression. Greater religious identification was associated with diminished reports of problems in family functioning, while lower socioeconomic status was associated with worse symptoms and familial and peer social functioning. Parental education mitigated family problems and level of PTSD symptoms.

**Conclusions:** Exposure to political violence by Palestinian and Israeli adolescents is a powerful predictor of both social disruption and mental health symptoms, with similar patterns of interaction between socioeconomics, violence exposure, symptom levels, and impaired social and family functioning across nationalities.

**Reviewer's Comments:** The dynamics of the interactions between social variables and violence exposure variables are hard to tease apart in a cross-sectional study like this. In the absence of efforts to end violence, targeting interventions, such as family supports, might mitigate the potential lifetime scars left by the exposure to violence. (Reviewer-Gary S. Belkin, MD).

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**Keywords:** Violence Exposure, Adolescents

**Print Tag:** Refer to original journal article
Low-income, parental psychopathology, and loss of a loved one appear to confer a significant risk for the development of serious emotional disturbances in children exposed to a hurricane disaster such as Hurricane Katrina.

Background: Typically, in the first 3 to 6 months after a hurricane, >50% of children exposed to the disaster exhibit symptoms of post-traumatic stress disorder (PTSD), disruptive behaviors, or other manifestations of psychological distress. The presence of diagnosable psychiatric disorders is lower but still elevated.

Objective: To identify factors that distinguish children who will develop chronic symptoms from those whose distress is more transient following a natural disaster.

Methods: Data were collected regarding 797 children exposed to hurricane Katrina. Serious Emotional Disturbance (SED) was determined utilizing the Strength and Difficulties Questionnaire (SDQ), which included items to assess for conduct problems, hyperactivity-inattention, emotional symptoms, and peer problems. An additional item was included to assess the level of associated social impairment. The respondents were then asked 30 questions regarding exposure to hurricane-related stressors. These included serious risk of death, victimization due to lawlessness, victimization of a loved one, physical illness or injury caused by the storm, extreme physical adversity (such as sleeping on a cement floor and little food), extreme psychological adversity (such as inadequate toilet facilities, major property loss, income loss), and ongoing difficulties associated with housing. Race/ethnicity, socioeconomic status, parental psychopathology, and whether the family was living in a displaced setting were also examined.

Results: The estimated prevalence of SED based on the SDQ in the total sample was 14.9% and did not differ from pre-hurricane figures. However, 10% of the sample continued to experience impairing SED which was attributed to the hurricane. Estimated prevalence of hurricane-related SED (H-SED) was associated with low income in New Orleans but not in the remainder of the sample. Death of a loved one was most strongly related to H-SED in New Orleans, whereas physical adversity was most strongly associated with H-SED in the remainder of the sample from other areas. Parent psychopathology was associated with H-SED in both samples.

Conclusions: Parental psychopathology and low family income are associated with serious emotional disturbances in children at 18 to 27 months after being exposed to the hurricane Katrina disaster.

Reviewer's Comments: This fascinating study will surely be a model for future investigations, particularly regarding the systematic categorization of types of traumatic experiences within the disaster. (Reviewer-John G. Koutras, MD).

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Keywords: Natural Disaster, Mental Health, Adolescents

Print Tag: Refer to original journal article
Some part of the moon is visible for 29.53 days per lunar cycle. Still, no significant association has been shown between the frequency of aggravated assault and lunar cycles.

**Background:** There has long been an assumption that the moon and lunar phases influence human behavior, despite no clear evidence to support it. The gravitational pull of the moon on the earth and the relationship of lunar light to melatonin levels have been proposed as explanations. However, there is no consistent highly convincing data to date.

**Objective:** To explore any associations between the 4 phases of the moon and the incidence of aggravated assault, controlling for location of the offense (indoors vs outdoors) and gender of the offender.

**Methods:** 23,127 aggravated assaults filed with a regional police department in Bavaria, Germany, from 1999 to 2005 were included in the study. Each crime was linked to its respective lunar phase (absent moon, crescent moon, full moon, and decrescent moon). The number of crimes committed in the 2 days surrounding the full moon and the 2 days surrounding the absent moon were compared to the other 2 lunar cycles.

**Results:** 83% of the crimes were committed by men, and the mean age of the offender was 31 years. Of the crimes analyzed, 13.7% took place during the absent moon, 13.7% took place during the full moon, and 36% each for the other 2 phases. Half of the crimes were committed indoors and half were committed outdoors. During the crescent moon, there was a significantly smaller number of assaults committed outdoors. A significantly higher percentage of assaults were committed outdoors during the full moon and the decrescent moon. There was no significant difference in the rate of assaults based on the lunar phase in which they were committed.

**Conclusions:** This study did not identify a significant association between the frequency of aggravated assault and lunar cycles, although there was an increase in outdoor assaults during the full moon.

**Reviewer’s Comments:** When I was working in the psychiatric emergency department (ED), people would always comment on the increase in psychopathology during a full moon. I remember doing a literature search a few years ago and found results similar to those in this study: there was not any proof that a full moon actually influenced behavior. What it may do, which would be supported by the finding of more outdoor assaults in this study, is increase the amount of available nighttime light by which witnesses can observe others’ behaviors. This would increase both the arrest rate and the rate of people being brought to a psychiatric ED for bizarre behavior. (Reviewer—Elizabeth Ford, MD).

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Keywords: Assault, Lunar Phase

Print Tag: Refer to original journal article
A specific set of genotypes of the so-called \textit{NOS1} gene appears associated with certain cognitive deficits among individuals with schizophrenia as compared to normal controls.

\textbf{Background:} One gene suspected as having a significant role for risk of schizophrenia is the nitric oxide synthase 1 gene (\textit{NOS1}). \textit{NOS1} synthesizes nitric oxide (NO) throughout the nervous system. If there is a relationship between some polymorphisms of this gene and schizophrenia, how would those gene effects contribute to the appearance of the disease? One possibility may come from studies that relate NO production with cognition in human and animal models.

\textbf{Objective:} To determine the relative distribution of different \textit{NOS1} genotypes among patients with schizophrenia and controls, and to describe the association of these genotypes with the distribution of cognitive performance between these groups.

\textbf{Methods:} Two samples were studied. A sample from Ireland consisted of patients with verified DSM-IV diagnoses of schizophrenia and matched healthy controls. All were of Irish ancestry. A replication sample for comparing the consistency of result patterns contained subjects recruited in Germany as part of a previous study. This sample consisted of patients with objectively verified DSM-IV diagnoses and recruited, matched, healthy controls. All were of German descent. All subjects were assessed on a range of cognitive parameters using standardized neuropsychological testing instruments, including general IQ, episodic memory, working memory, and attention.

\textbf{Results:} In comparing carriers of what are classified as AA, AG, and GG genotypes of \textit{NOS1}, both samples found that the GG genotype underperformed with respect to verbal IQ and working memory. A post hoc analysis also showed full-scale and performance IQ underperformance in GG carriers in the German sample.

\textbf{Conclusions:} A gene variant associated with schizophrenia appears uniquely associated with certain features (working memory and verbal intelligence) of cognitive underperformance.

\textbf{Reviewer's Comments:} These findings raise interesting questions about how an ensemble of genes gives rise to a disorder such as schizophrenia. The apparent association between the GG genotype and certain domains of cognition could reflect the role of “cognitive reserve” as both a feature of the disease and as a developmental feature that leaves individuals at greater risk for its appearance. (Reviewer-Gary S. Belkin, MD).

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Keywords: Cognition, Genetics, \textit{NOS1} Genotypes

Print Tag: Refer to original journal article
A model of exploratory behaviors seen in people with bipolar mania or schizophrenia can be standardized to select for homologous mice behavior with which to more reliably establish animal models for research.

**Background:** Research on brain function, drug action, and neurodevelopment with respect to mental disorders often depends on animal models. But how good are these supposedly analogous animal models? Exploratory behavior, which is “the act of making the unknown known,” has been studied in many animal species and appears to be a fundamental function. A well-established paradigm has been developed to study this in mice. The Behavior Pattern Monitor (BPM) is an objective assessment of 3 features of exploratory behavior: the amount of motor activity, the sequential patterns or structure of the exploratory behavior, and exploring new stimuli.

**Objective:** To establish a human BPM (hBPM) by objectively tracking and measuring movement patterns in patients with bipolar mania or schizophrenia to see if their exploratory behaviors show unique “signature” patterns. These patterns were then compared to those of mice treated with amphetamines and mice with bred abnormalities in dopamine transporters.

**Methods:** Inpatients with bipolar mania or schizophrenia were observed with video monitoring, tracking motor activity, spatial patterns, acceleration of movement, and counts of exploratory events. Discernible patterns of movement were compared to those of controls and were sorted scores on mania and positive and negative symptom scales.

**Results:** Patients with bipolar mania had a unique pattern of exploration characterized by high exploration and motor activity. In contrast, patients with schizophrenia and healthy controls explored at a constant pattern. Predictability of movement was greater among patients with schizophrenia who had high negative symptoms as opposed to those who had higher scores on the BPRS manic symptoms domain, who engaged in more unpredictable movement patterns. Bipolar patients explored more intensely than did patients with schizophrenia or controls. Mice with selective dopamine transporter inhibition showed patterns of movement more similar to human patients with bipolar mania than did the amphetamine-treated mice.

**Conclusions:** Patients with bipolar mania demonstrate hyperexploration and increased motor activity compared to patients with schizophrenia and normal controls. Exploratory behavior studies reveal characteristics of bipolar mania were similar to those in a mice model of mania resulting from dopamine transporter inhibition but not to those in a mice model of amphetamine exposure.

**Reviewer's Comments:** This species comparison of a fundamental behavioral trait can perhaps lead to future animal analogues that allow study of underlying neurobiological features of mental disorders. (Reviewer-Gary S. Belkin, MD).

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Keywords: Schizophrenia vs Bipolar Mania, Exploratory Behaviors

Print Tag: Refer to original journal article
The risk of parole violations is two times higher among prison parolees with a dual diagnosis of a major psychiatric disorder and a substance use disorder than among those parolees with either a psychiatric illness alone or a substance use disorder alone.
Psychotherapy's Value Questioned for Refractory Depression

Cognitive Behavioral Analysis System of Psychotherapy and Brief Supportive Psychotherapy for Augmentation of Antidepressant Nonresponse in Chronic Depression: The REVAMP Trial.

Kocsis J, Gelenberg A, et al:

Arch Gen Psychiatry 2009; 66 (November): 1178-1188

Adding psychotherapy to antidepressant medication does not clearly provide added benefit for the treatment of resistant depression.

Background: In intent-to-treat analyses, approximately 50% of chronically depressed patients fail to respond to an adequate trial of antidepressant medication or psychotherapy, and an additional 20% do not obtain complete remission. Most studies have failed to demonstrate decisive advantages (moderate-to-large effect sizes) for combined medication and psychotherapy over medication alone.

Objective: To compare the efficacy of adding therapy (cognitive behavioral analysis system of psychotherapy [CASP] or brief supportive psychotherapy [BSP]) to antidepressant nonresponders or partial responders versus only continued medication management in the same population.

Methods: All participants completed phase 1, which lasted 12 weeks and involved pharmacotherapy options. Those who did not achieve remission were then entered into phase 2, which lasted for another 12 weeks. There were 491 phase-2 participants: 36% had chronic major depressive disorder (MDD), 30.9% had MDD with incomplete interepisode recovery, and 33.1% had double depression (chronic MDD and dysthymia). The phase-2 participants were randomly assigned to 1 of 3 treatment groups: medication only, CBASP and medication, or BSP and medication. The primary outcome measures were the Hamilton Scale for Depression (HAM-D) and the Clinical Global Improvement scale.

Results: No statistically significant differences emerged among the 3 treatment groups in the proportion of phase-2 remission (15.0%), partial response (22.5%), and no response (62.5%) or in changes in HAM-D scores.

Conclusions: The addition of either of 2 forms of therapy, one more specific for depression, did not demonstrate significant differences in outcome compared with pharmacotherapy alone in patients with depression refractory to antidepressants.

Reviewer's Comments: These studies which examine the potential benefit of combination psychotherapy and pharmacotherapy to pharmacotherapy alone in patients with depression often have somewhat disappointing results. However, clinicians should keep a couple of things in mind. First, remember that the patient in front of you is not the central tendency of a study but an individual. Second, remember that this individual may receive benefits from psychotherapy which may improve certain crucial symptoms of depression, such as suicidality, which are lost in total scores of measures, such as the HAM-D. (Reviewer-John G. Koutras, MD).

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Keywords: Major Depressive Disorder, Psychotherapy vs Medication

Print Tag: Refer to original journal article
Progression to Daily Use of Cannabis Hastens Psychosis Onset

**Association of Pre-Onset Cannabis, Alcohol, and Tobacco Use With Age at Onset of Prodrome and Age at Onset of Psychosis in First-Episode Patients.**

Compton MT, Kelley ME, et al:

Am J Psychiatry 2009; 166 (November): 1251-1257

Cannabis is the most commonly used illicit drug among people with schizophrenia. Progression to daily use of cannabis and tobacco increases the relative risk of onset of psychosis.

**Background:** In first-episode psychotic patients, cannabis abuse rates range from 15% to 65%, alcohol abuse rates range from 27% to 43%, and daily cigarette smoking rates range from 50% to 75%. Drug abuse typically begins prior to the onset of psychotic symptoms and there is evidence that cannabis abuse may be associated with an earlier onset of psychosis. A less richly explored topic is whether cannabis abuse is associated with an earlier age of onset of prodromal symptoms.

**Objective:** To identify whether cannabis, tobacco, and alcohol use prior to psychotic or prodromal symptoms is associated with earlier onset of those symptoms in an urban minority population.

**Methods:** 109 patients were recruited from 2 inpatient units at an urban public hospital and a psychiatric crisis center in Georgia. All patients had first-episode nonaffective psychoses (most were diagnosed with schizophrenia). Substance use data and information about age of onset of prodromal and psychotic symptoms was also collected. For the analysis, patients were grouped according to their substance use and the progression to increasing severity.

**Results:** Prior to psychosis onset, 40.6% of the sample used cannabis daily, 44.1% smoked tobacco daily, and 7.9% drank alcohol daily. Although there was no significant effect of cannabis or tobacco on the risk of onset of psychosis, those who drank alcohol weekly or daily had a later age of onset of psychosis. However, progression to daily use of cannabis and tobacco was significantly associated with the onset of psychosis, and even more strongly significant with the onset of prodromal symptoms. This relationship was stronger for female patients than for males.

**Conclusions:** Rapid progression to daily use of cannabis and tobacco is associated with a higher risk of initiation of psychotic and prodromal symptoms. However, because the association does not determine causality, it is also possible that approaching psychosis triggers increased cannabis or tobacco use.

**Reviewer's Comments:** This study highlights what I have found in clinical practice, working in an urban public-sector hospital — a large percentage of first-break psychotic patients smoke cannabis. The mechanism is not clearly known, but it likely relates to the effect of cannabinoids on neurotransmitters, such as dopamine and glutamate, in areas of the brain associated with schizophrenia. The explanation for the increased risk of onset of symptoms with nicotine is not as evident, although there is some evidence of a connection between nicotinic neurotransmitters and schizophrenia. (Reviewer-Elizabeth Ford, MD).

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Keywords: Psychosis, Substance Abuse

Print Tag: Refer to original journal article
Naltrexone Implant Superior for Reducing Heroin Use

Improving Clinical Outcomes in Treating Heroin Dependence: Randomized, Controlled Trial of Oral or Implant Naltrexone.

Hulse GK, Morris N, et al:

Arch Gen Psychiatry 2009; 66 (October): 1108-1115

Naltrexone implant proved better than orally administered naltrexone in reliably keeping naltrexone circulating in the bloodstream and in reducing opiate use.

Background: Naltrexone, an opiate antagonist, has been available for the treatment of opiate dependence for 25 years. Research has shown naltrexone to be of limited efficacy due to poor patient compliance. As with depot neuroleptics, an implant form of naltrexone would presumably result in more sustained use and exposure to the medication, and thus better outcomes.

Objective: To determine if the effectiveness of naltrexone for the treatment of opiate dependence is improved through the use of an implant form of the medication.

Methods: Patients were randomly assigned to receive oral naltrexone, oral placebo, naltrexone implant, or placebo implant. Eligible subjects were identified through a substance use treatment center in Perth, Australia, and included individuals with verified DSM-IV diagnoses of opiate dependence. Patients were monitored for blood naltrexone levels on days 1, 5, 28, and then every 28 days for 6 months. Patients were also monitored for frequency of opiate and other use using standard reporting measures every 28 days, and urine toxicology screens at day 15 and then every 28 days.

Results: 70 subjects participated in the study. Compared to other patients, those using the naltrexone implant were significantly more likely to have sustained levels of naltrexone in their bloodstream (2 ng/mL), were less likely to use opiates, and had a longer mean time to relapse among those who did return to opiate use (mean, 158 days with implant vs 115 days with oral medication). Opiate abstinence with urine validation was reported in 49% of patients with naltrexone implants and 21% of oral naltrexone users. Regular heroin use (≥4 days per wk of use) was reported by 17% of implant recipients versus 62% of oral users.

Conclusions: Naltrexone implants appear to predictably result in more medication exposure, in significantly reduced use of heroin in terms of likelihood of regular use, and in urine-confirmed abstinence.

Reviewer's Comments: This study reinforces the consideration to advise patients with opiate dependence to use an implant form of this medication. (Reviewer-Gary S. Belkin, MD).

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Keywords: Opiate Dependence, Naltrexone, Implant

Print Tag: Refer to original journal article
Issues such as loss of family farms and women entering the workplace are encountered in rural psychiatry in a way that is different from urban areas.

Background: This article describes a 12-year-old program in Ohio that has incorporated a rural psychiatry component into its psychiatric residency training program. The goals of the program are to increase cultural competency of residents related to issues in rural psychiatry, to teach them about the unique challenges of providing care in small communities with different boundary expectations, and to encourage careers with some time devoted to rural communities.

Methods: The program works through a partnership between the state office of mental health, Wright State University, and various agencies at rural sites within 60 to 90 miles of the medical school. It is part of the postgraduate year 2 (PGY-2) community psychiatry curriculum that includes 1 day/week on-site training and 3 hours of didactics. The resident is placed at a rural site and sees patients individually and with a faculty member for 8 hours. The faculty member works 2 to 3 days at the rural site.

Results: Residents in this program receive experience working with populations in transition (such as one shifting from a farming to a manufacturing culture) and learning about rural community views on substance abuse and mental health. Role diffusion and limited resources are also emphasized as important factors in care delivery. Residents treat the patients with empirically validated treatment algorithms and learn about cost-saving medication prescribing practices, such as samples, patient assistance programs through pharmaceutical companies, and generic prescribing. At the beginning of this program, no residents were choosing careers in rural psychiatry. Since the program’s inception, 14 of 50 residents have selected careers that involve at least some rural psychiatry care.

Conclusions: The rural psychiatric residency training program described in this article has been successful in educating residents and recruiting them into vastly underserved rural communities after residency.

Reviewer's Comments: This is not a clinical research article, but it is important in describing a training program that encourages career choices in underserved rural areas. It sounds like a very successful and well-received program, with funding support and collaboration from multiple agencies. I was struck by the similarities between the issues described pertaining to rural care and those that I experience as an inner-city public psychiatrist: emphasis on cost-saving prescribing methods, pressures to see large numbers of patients, and validated treatment protocols. I would have liked to have learned more about isolation as a mental health provider in a rural community because this seems like a striking difference between urban and rural public psychiatry. (Reviewer-Elizabeth Ford, MD).
Adjunctive Aripiprazole -- More Is Not Better

A Multicenter, Randomized, Double-Blind, Placebo-Controlled, 16-Week Study of Adjunctive Aripiprazole for Schizophrenia or Schizoaffective Disorder Inadequately Treated With Quetiapine or Risperidone Monotherapy.

Kane JM, Correll CU, et al:

J Clin Psychiatry 2009; 70 (October): 1348-1357

Aripiprazole augmentation of inadequately treated monotherapy with quetiapine or risperidone is no more effective than adding placebo, intensifying the skepticism related to the common practice of polypharmacy with antipsychotic medications.

Background: Although antipsychotic polypharmacy is common, it is not well supported by evidence. Clozapine augmentation perhaps has the best evidence to support it, but those studies are also mixed. The authors of this study considered it at least somewhat logical, given the complementarity of its higher D2, %-HT1A, and 5-HT2A affinity compared to quetiapine, and its potential to optimize D2 occupancy in combination with risperidone, to think that augmentation of inadequately treated patients on either drug might benefit from the addition of aripiprazole.

Objective: To determine if the addition of aripiprazole to risperidone or quetiapine improves the efficacy for the treatment of schizophrenia or schizoaffective disorder.

Methods: Patients were stable outpatients with chronic schizophrenia or schizoaffective disorder, but all had inadequate responses to their treatment with risperidone or quetiapine by investigator judgment, (CGI scores of 4-6). Patients were randomly assigned to augmentation with placebo or aripiprazole and were followed up for 16 weeks. Outcome measures involved serial assessments using a wide battery of symptom and quality of life/functional scales at baselines and at weeks 2, 4, 6, 8, 12, and 16, as well as metabolic and physical examination parameters.

Results: 177 subjects received augmentation with risperidone, and 146 received augmentation with quetiapine. Baseline characteristics, such as PANSS scores, were similar between groups. Other than decreases in prolactin among those on risperidone, there were no significant differences in psychiatric symptoms, metabolic parameters, or weight change between those augmented with aripiprazole versus those with placebo.

Conclusions: The addition of aripiprazole to the treatment regimen for patients with insufficient response to quetiapine or risperidone did not lead to significant improvement compared to those augmented with placebo.

Reviewer's Comments: This study adds to a gap between evidence and practice, with respect to polypharmacy. Continued prospective studies like this may be needed to reinforce some consistent assistance to clinicians working with very hard-to-treat patients with this disorder, if practice is to change. (Reviewer-Gary S. Belkin, MD).

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Keywords: Aripiprazole Augmentation, Schizophrenia

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Conduct disorder and so-called callous-emotional traits may be affected by different degrees in terms of genetic and environmental (negative parental disciplinary behavior) loading.

**Background:** Conduct disorder and conduct problems have long been linked to parental negative discipline. So-called “callous-emotional trait” is a temperament category that is also measurable and is related to antisocial behavior. Through monozygotic twin studies, this trait appears to have both a heritable component and environmental risk factors.

**Objective:** To determine if negative parental discipline is associated with conduct problems and callous-unemotional traits from childhood to early adolescence.

**Methods:** Subjects were part of a longitudinal twin pairs study in England and Wales starting with individuals born in the mid-1990s. Part of the follow-up of this cohort included teacher and parent ratings of behavioral problems of children at ages 7 and 12 years using the Strengths and Difficulties Questionnaire (SDQ). Using a validated structured interview, parental use of negative discipline strategies was assessed when the child was age 7 years. Callous-emotional traits were assessed using specific test items from the SDQs (4 items) and the Antisocial Screening Device (3 items). These kinds of questions included ratings of level of concern or responsiveness the child had to the judgment or needs/reactions of others, which were rated by teachers and parents. The study was thus able to look at both cross-sectional and longitudinal relationships between discipline type and both conduct problems and callous traits.

**Results:** Data were available for 2254 twin pairs. Within twin pairs, the twin receiving more negative discipline at age 7 years had more conduct problems but not more callous traits at age 12 years. This held true even when controlling for levels of conduct problems at age 7 years.

**Conclusions:** Negative parental discipline is a non-shared environmental risk factor for conduct problems during the transition to early adolescence, but it is not a non-shared environmental risk factor for callous-unemotional traits.

**Reviewer’s Comments:** Conduct disorder is not simply troublesome, it is a huge public health problem. This work supports other evidence of some disjuncture between the causal connection and risk association of callous temperament and conduct. The callous temperament is apparently more heritable and shared by twins, with parental disciplinary exposure modifying more so the risks of a child proceeding to a pattern of conduct problems in early adolescence. This underscores the focus of interventions that work to coach and assist parenting and enhance parenting skills. (Reviewer-Gary S. Belkin, MD).

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Keywords: Parental Discipline, Conduct, Callous Temperament

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**Secure Attachment Protects Child With At-Risk Genotype**

*Interplay of Genes and Early Mother–Child Relationship in the Development of Self-Regulation From Toddler to Preschool Age.*


The gene-environment interaction of serotonin transporter genotype and security of attachment appears to affect the ability to self-regulate.

**Background:** Individual differences in the capacity for self-regulation have been strongly implicated in many aspects of adaptive development and psychopathology. The 5-HTTLPR polymorphism (gene for serotonin transporters) has 2 common alleles, the short (s) and the long (l). Individuals who are either homozygous for the short allele (ss) or heterozygous (sl) have been found to be at risk for emotional and behavioral maladaptive outcomes. Being homozygous for long (ll) is believed to be protective. Secure attachment relationships in the mother-child dyad presumably confers resiliency to individuals who carry “at risk” alleles, thereby promoting normal development (“maternal buffering”).

**Objective:** To examine whether secure attachment moderates the genotype on children’s capacity for self-regulation.

**Methods:** Mothers of 89 children agreed to participate, but 88 were successfully genotyped. There were 13 ss homozygotes, 47 sl heterozygotes, and 28 ll homozygotes. The children’s quality of attachment was assessed at 15 months utilizing the Strange Situation in which a stranger is introduced to the child in a standardized routine. There were 48 secure and 40 insecure children. The children were then exposed to tasks which were designed where the children needed to deliberately suppress a dominant response and instead perform a subdominant response: delaying (waiting to eat candy), slowing down gross and fine motor activity, suppressing/initiating activity to a signal, lowering voice, and effortful attention. These tasks were administered at ages 25, 38, and 52 months.

**Results:** Girls, overall, had higher scores on the self-regulatory composite. Among children who were ss homozygous, those who were insecurely attached demonstrated poor regulatory capacities in the tasks, but those who were securely attached developed regulatory capacities as good as children who were ll homozygous. There was no effect on attachment security for ll homozygotes: these children more consistently demonstrated good self-regulation.

**Conclusions:** Secure attachment served as a buffer against risk otherwise conferred by the child’s serotonin transporter genotype, thereby allowing for the development of better self-regulation.

**Reviewer’s Comments:** I recently reviewed a meta-analysis that questioned the validity of the 5-HTTLPR association with risk for depression in those with a history of maltreatment. However, as demonstrated in this study, this genotype may more accurately be associated with dimensional components of emotional self-regulation, which may lead to various anxiety and depressive symptoms. These symptoms may not be easily categorized into current diagnostic nosology, such as major depressive disorder. (Reviewer-John G. Koutras, MD).

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Keywords: Serotonin Transporter Gene, Childhood Development

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Exposure to a general universally applied program to sixth graders and their families to strengthen overall family issues and social skills was associated with a reduction in substance use 6 years later.

**Background:** Interventions to prevent later health outcomes are called “universal” when they are applied indiscriminately across individuals in a population who might have quite varied risk factors for a target condition. Such interventions may also be more likely to provide those who use them with more general kinds of capacities or protections that might impact a range of behaviors or risk factors, and thus outcomes. This has been the thinking behind interventions that support families to be enabled to sustain more prosocial and communicative practices, which can affect parenting practices that might enhance positive youth behavioral repertoires, their exposure to different risk peer groups, and their own social skills, all of which might impact exposure to a number of risks.

**Objective:** To determine if such “protective shield” approaches impact substance use risk at some time after the intervention, supporting the idea that such efforts enhance ongoing basic supports and capacities.

**Methods:** 22 Iowa public schools were randomly assigned to participate in the Iowa Strengthening Families Program (ISFP) or a control condition. The Program is a competency training prevention intervention that coached parents in appropriate disciplinary and behavior management strategies, instructed children in peer resistance and peer relationship skills, and provided joint family sessions with activities to promote problem solving, conflict resolution, etc.

**Results:** ISFP participation in sixth grade was associated with reduced use of illicit substances in twelfth grade, with a 49% relative rate of reduction. ISFP exposure reduced the rate of increase across adolescence, a blunting of “rate of use” that appeared to be a mitigating factor protecting against twelfth-grade risk of use.

**Conclusions:** Participation in a general family and social skills competency training program in sixth grade was associated with reduced risk of illicit substance use by twelfth grade, blunting the rate of increase in use across adolescence.

**Reviewer's Comments:** From a public mental health point of view, I would have liked to see the authors broaden their gaze in terms of the range of impacts and mechanism of the impact of such an approach. It would be interesting to see if such a universal “shield of protection” approach to health prevention had other beneficial mental health outcomes, such as depression or other disorders, and also the degree that any such possible impact was also involved in mediating other risks. (Reviewer-Gary S. Belkin, MD).

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Keywords: Universal Intervention, Substance Abuse, Children

Print Tag: Refer to original journal article
Telephone-delivered care management may be a useful intervention modality to treat cardiac patients who are depressed after undergoing coronary artery bypass surgery.

**Background:** As many as 50% of patients after coronary artery bypass surgery (CABG) report depressive symptoms in the perioperative period. These cardiac patients with depressive symptomatology have increased rates of rehospitalization and death after cardiac surgery, independent of cardiac status, medical comorbidity, or extent of surgery. Several treatment trials for depression have been conducted in cardiac populations, but the results have not been robust in terms of reducing symptoms or cardiovascular morbidity.

**Objective:** To report the main findings of Bypassing the Blues, the first randomized trial of a collaborative care strategy involving a nonphysician care manager for treating depression after an acute cardiac arrest.

**Participants:** 453 post-CABG patients.

**Methods:** 302 participants scored positive on a depression screening instrument which involved 9 items from the Patient Health Questionnaire. The remaining 151 patients were assigned to a comparison group without depression. At 2, 4, and 8 months after CABG, participants completed the 36-item short form of the Mental Health Component Scale (MCS), and the 17-item Hamilton Rating Scale for Depression (HRS-D). The 302 depressed patients were then randomly assigned in a 1:1 ratio to the treatment intervention or usual care. The treatment intervention was coordinated by a nurse care manager who conducted telephone interviews, provided education about depression and its effect on cardiac disease, and described treatment options. Treatment options included a workbook to enhance patient understanding and ability to “self-care” for depression, initiation or adjustment of antidepressants coordinated with the primary care physician, or referral to a local psychiatrist or psychologist.

**Results:** From baseline to the 8-month follow-up, a reduction of ≥50% in mood symptoms was reported by 50% of intervention patients and by 29.6% of patients in the usual care group. Men were more likely to use the workbook, and women were more likely to use pharmacotherapy. There were no significant differences observed between groups in rehospitalization rates for cardiac causes.

**Conclusions:** The telephone-delivered collaborative care model for depression after CABG appears to improve depressive symptoms.

**Reviewer’s Comments:** The patients were not blinded in this study, and it is unclear who administered the depression rating measures and whether they were blinded to the type of treatment received. Therefore, it is difficult to understand the true efficacy of this intervention. Also, this study now joins a long line of work that puzzlingly reduces depression but does not have a similar level of impact on cardiac outcomes (measured here in rehospitalization rates). (Reviewer: John G. Koutras, MD).

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Keywords: Coronary Bypass Surgery, Perioperative Depression

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