Clinically significant depression appears to increase the risk of the onset of diabetes.

**Background:** Both diabetes and major depressive disorder have captured attention as chronic diseases emerging to be primary health challenges of the next century. Several longitudinal studies suggest that depression is a risk factor for the development of diabetes; however, those studies, as these authors point out, may have used inadequate measures of depression, such as self-reporting. Therefore, what was counted as "depression" may not have been diagnostically robust.

**Objective:** To better characterize the history and severity of depression of subjects in a population sample.

**Methods:** This study was part of a larger effort in Zaragoza, Spain, that longitudinally followed an adult population and documented the incidence and risk factors of depression and dementia. A potential sample was randomly selected and recruited from the general population. Subjects needed to be ≥55 years of age and without dementia at baseline. Only subjects from the study who were also without diabetes at baseline were included in the analysis. Participating subjects had baseline and then 2 waves of repeat interviews that included assessments of cognition and dementia, functional activity, personal and family medical history, and various co-varying health factors (ie, alcohol and tobacco use, body mass index, hypertension, etc). Depression was evaluated using a structured diagnostic interview that identified the level of severity of symptoms, characterized depression as first or recurring, and identified any pattern of use of antidepressants.

**Results:** Of the total sample of 3521 subjects, 379 (10.8%) were diagnosed with depression. In follow-up waves, the overall incidence of new cases of diabetes was significantly higher among depressed subjects (19.70 per 1000 person-years) compared to nondepressed subjects (12.36 per 1000 person-years). This association between having depression and the incidence of diabetes held when controlling for sociodemographic variables, diabetes risk factors, and antidepressant use. The diabetes incidence was interestingly, greatest among those with nonsevere and persistent depression and a history of depression. The overall impact on the risk of having clinically defined depression was to increase the likelihood of diabetes onset by 65%.

**Conclusions:** Having depression appears to confer an increased risk of diabetes.

**Reviewer's Comments:** The study specifically offered itself as a corrective trial to previous studies of the relationship between diabetes and depression by clarifying how depression is measured. However, it is precisely on this point that the study needed to provide more detail. Using a scale not commonly used in this literature and a limited description in the results made the gradations of "severe," "nonsevere," and "clinically significant" hard to judge. That being said, the paper will extend attention to this potentially important connection. (Reviewer-Gary S. Belkin, MD, PhD, MPH).

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**Keywords:** Major Depression, Diabetes

**Print Tag:** Refer to original journal article
The candidate genes identified in this study for the preferential antidepressant response of serotonergic versus noradrenergic medication continue to point to neurogenesis and inflammatory responses in depression.

Background: A systematic exploration of variation across the genome has the potential to detect genetic variants that may help in understanding the biology of antidepressant action, and better guide specific antidepressant selection in an individual patient with a greater likelihood of efficacy.

Objective: To report the findings from a genome-wide pharmacogenetic analysis of >500,000 common genetic variants. These variants were tested for association with a change in depression severity over a 12-week period after treatment with a serotonergic or noradrenergic antidepressant among subjects with moderate to severe depression.

Methods/Participants: The Genome-Based Therapeutic Drugs for Depression was a 12-week partially randomized open-label pharmacogenetic study with 2 active treatment arms. A total of 706 patients were included in the main analysis. The primary outcome measure was the 10-item Montgomery-Åsberg Depression Rating Scale. DNA was extracted and assayed for >610,000 single nucleotide polymorphisms and copy number variant markers. The participants were then randomized to either treatment with escitalopram or nortriptyline; there was no placebo group. Statistical analyses were conducted to determine if there were associations between genotype and outcome in the subjects treated with escitalopram and in those treated with nortriptyline.

Results: Regardless of which antidepressant was used, the outcome of treatment was associated with polymorphisms in 2 regions on chromosomes 1 and 10. The findings also showed that some previously unexpected regions may be more potent predictors of antidepressant response than functional candidate genes. For example, the uronyl-2-sulphotransferase gene, which is essential for neurogenesis and neuronal migration, was found to be specific to nortriptyline response. The apparent delayed onset of the pharmacogenetic effect on response after 4 weeks of treatment was consistent with a neurogenesis-related mechanism. For escitalopram, the marker for interleukin-11 (IL11) was found to have a suggestive level of significance for escitalopram responders. This finding is consistent with the role of inflammation in a subtype of depression and could explain the specific moderation by cytokines IL6 and IL11 of response to escitalopram.

Conclusions: A candidate gene involved in neurogenesis has been identified for the antidepressant efficacy of nortriptyline, although this finding requires replication.

Reviewer's Comments: Pharmacogenomic studies will change prescribing practices in the future. It is conceivable that genotyping individuals for specific, as yet unidentified, markers will help guide antidepressant selection. This may be a bold new frontier in psychiatry. (Reviewer-John G. Koutras, MD).

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Keywords: Genetic Scanning, SSRIs, Noradrenergic

Print Tag: Refer to original journal article
Self-reported depressive symptoms are common in new and expectant fathers and are correlated with maternal depression.

**Background:** Maternal depression is a common, profound contributor to the mental and physical health of developing children. Less attention has been paid to paternal depression.

**Design/Objective:** To perform a meta-analysis of data on paternal depression to clarify its prevalence and association with maternal depression.

**Methods:** Articles from January 1980 to October 2009 were identified from several search engines and the reference lists of review and retrieved articles. Only a priori studies that reported the number of depression cases in new or expectant fathers were included in the meta-analysis. The primary outcome measure was point prevalence of paternal depression. Data were analyzed using random effects models. The period of measurement was divided into 5 blocks: the first 6 months of pregnancy, the third trimester to birth, birth to 3 months’ postpartum, 3 to 6 months’ postpartum, and 6 to 12 months’ postpartum.

**Results:** 43 of 256 identified studies met inclusion criteria for the meta-analysis. More than 28,000 new and expectant fathers are represented in the meta-analysis. The majority of studies (40) used a self-reporting measure to identify depressed new and expectant fathers, while only 3 used structured or semistructured interviews. Most studies (30) recruited men from maternity or postpartum units. The overall estimate of paternal depression was 10.4% in the period between conception and 1-year postpartum. Time was a risk factor, with the 3- to 6-month postpartum period associated with the highest rate (25.6%) and the 0- to 3-month postpartum period associated with the lowest rate (7.7%). Nationality was also a risk factor, with fathers in the United States (14.1%) reporting a higher incidence than other countries (8.2%). Studies using self-reported data had a much higher rate of depression (11%) compared with clinician-rated studies (4.9%). Maternal depression was common in these studies (23.8%), again with the highest rate reported in the 3- to 6-month postpartum period. Maternal and paternal depression were significantly correlated ($r = 0.308$).

**Conclusions:** This meta-analysis of primarily self-reported measures demonstrates that expecting and new fathers frequently experience depressive symptoms, most commonly in the 3- to 6-month postpartum period. Mothers in this study were much more likely to report depression than in most studies, suggesting a selection or self-reporting bias.

**Reviewer’s Comments:** This meta-analysis must be interpreted cautiously because of the heavy reliance on self-reported depressive symptoms. The rate of paternal peripartum depression among the 3 interview-based studies was 4.9%, exactly the same as the 12-month prevalence of men this age, suggesting that self-reported measures overestimate the incidence of clinically significant depression. However, subsyndromal depressive symptoms may nonetheless have deleterious effects on well-being, marital satisfaction, and the ability to parent. Further prospective studies are sorely needed to clarify the prevalence, severity, and impact of paternal depression in conjunction with maternal health. (Reviewer-Charlotte O. Ladd, MD, PhD).

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Keywords: Postpartum Depression, Paternal Depression, Maternal Depression

Print Tag: Refer to original journal article
Hormone fluctuations do not underlie the increased risk associated with perimenopause, but testosterone is independently associated with higher depression scores in this population.

**Background:** Previous studies have shown an increased risk of depression in perimenopausal and postmenopausal women. The etiology of this vulnerability is unclear. Studies investigating whether perimenopausal hormone fluctuations contribute to depression have been inconclusive, largely due to methodological limitations, including small sample size, cross-sectional design, and short duration.

**Objective:** In this study, the authors collected yearly samples of several hormones, including estradiol, follicle-stimulating hormone (FSH), estradiol (E₂), dehydroepiandrostosterone (DHEA), DHEA sulfate (DHEA-S), and testosterone. They then examined correlations with these hormones to depressive symptoms for 8 years in women entering perimenopause.

**Participants/Methods:** 3302 participants were part of the Study of Women's Health Across the Nation (SWAN), a multi-site, ethnically diverse study of menopause that lasted 8 years. Women ranged in age from 42 to 52 years and were either premenopausal or perimenopausal at study entry. Self-reported depression symptoms were measured with the Center for Epidemiological Studies Depression Scale (CES-D). Yearly levels of FSH, E₂, DHEA, DHEA-S, and testosterone were measured in the first few days of the follicular phase or an approximation thereof once menses had ceased. The primary outcome measure was a CES-D score ≥16.

**Results:** At baseline, higher depression scores were associated with African-American or Hispanic ethnicity, tobacco use, elevated body mass index, and being in early perimenopause. No association was found between any hormone level and depression score at baseline. As women progressed into perimenopause, they were 31% more likely to have a CES-D score ≥16 compared to premenopause. With menopause, this increased risk jumped to 79%. Over time, the log-transformed testosterone level was positively associated with having a CES-D score ≥16. Although no other hormone levels were associated with elevated depression scores throughout perimenopause, several other risk factors were associated with elevated CES-D scores, including Hispanic ethnicity, stressful life events, low educational attainment, and vasomotor symptoms.

**Conclusions:** Individual changes in FSH, E₂, DHEA, and DHEA-S were not associated with elevated depression scores in an 8-year time period in which most women entered menopause. The authors replicated their previous research showing an increased risk of significant depression symptoms as women progress through this phase of life. Psychosocial factors, such as life stress and poor social support, were much more highly correlated with depression than testosterone, whose association with CES-D scores was independent of menopausal status.

**Reviewer's Comments:** It is not surprising that single snapshots of gonadal hormones over time did not reveal an association with perimenopausal depression. The interplay between gonadal hormones and mood is highly individualized and likely exists downstream of the steroid receptors. It is more plausible that individual differences in steroid receptor responsiveness to these hormones underlie differences in vulnerability to depression in perimenopausal women. (Reviewer-Charlotte O. Ladd, MD, PhD).

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Keywords: Perimenopause, Depression

Print Tag: Refer to original journal article
A specialist intervention providing intensive resources to individuals early in their psychotic illness showed an impact on social functioning and hospitalization rates at 18 months, but did not sustain those gains as much as 5 years later.

**Background:** Efforts to gather a range of social, supportive, and psychopharmacologic interventions as early as possible in the course of psychotic illness have proliferated. Does this work? One such trial, the OPUS study, found a decreased use of hospital days by patients at 1 year but not 2 years. The Lambeth Early Onset (LEO) study found similar benefits at 18 months. The review that follows this one actually looks at those 18-month outcomes but does so in terms of cost-effectiveness.

**Objective:** The same group presents data on whether those clinical benefits persisted over time, sharing follow-up data from 3.5 to 5 years.

**Participants/Methods:** The initial study included 144 individuals who presented for psychiatric care in Lambeth, London, for a first or second episode of non-affective psychosis without prior treatment. Subjects were randomized to usual referral and treatment by existing community providers, or to be cared for by the LEO specialist group, which consisted of a range of 10 mental health professionals offering interventions such as low-dose medication trials, cognitive behavioral therapy, vocational rehabilitation programming, and family therapy—all using established protocols for this population. Key outcomes were rates of relapse and hospitalization, and changes in scores on social and vocational functioning, quality of life, and medication adherence. At 18 months, those who received the specialist group care had fewer admissions over the follow-up period, as well as a statistically greater amount of time spent employed (mean, 6.9 vs 4.2 months), quality of life scores, and likelihood of medication adherence. In order to conduct further follow-up, the original 144 patient sample had to be traced and contacted again.

**Results:** There was no difference in terms of time spent in psychiatric care, chance of an admission, the number of admissions or total bed days, or social, vocational, and quality of life measures between those who were initially cared for in the specialist treatment arm and those who were not. It was not clear if these results reflected controlling for whether a subject remained in the specialized care track (or for how long), as apparently they had been referred out to their general practitioner.

**Conclusions:** A longer follow-up of subjects from a study of the effects on outcomes of intensive service access early in psychotic illness showed that apparent gains from such services were not apparent after a longer follow-up.

**Reviewer’s Comments:** This was a generally puzzling study. It made clear that it did not have the statistical power to adequately assess its outcomes. It was not clear to the degree it did, or could, evaluate outcomes with respect to ongoing exposure to the intervention—that is, according to time spent in “specialty” care. (Reviewer-Gary S. Belkin, MD, PhD, MPH).

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Keywords: Early Intervention, Psychosis

Print Tag: Refer to original journal article
An early intervention of concentrated services for individuals with early psychotic illness showed a high likelihood of being cost-effective in terms of outcomes as to service use and enhanced functioning, at least at 18 months of care.

**Background:** The previous review was of a study that lends mixed endorsement to concentrating intensive arrays of outpatient care options as early as possible after the onset of psychotic illness. However, on top of “muddy waters” on the effectiveness of such strategies and the durations of apparent benefits is the added and less studied question of cost-effectiveness. Given the presumably greater amount of resources brought to bear to provide such care, are the benefits in terms of functioning or reduced need for acute care worth it? **Objective:** To look at cost-effectiveness based on the first set of 18-month outcomes, costs, and benefits of the Lambeth Early Onset (LEO) study. **Participants/Methods:** As described in the previous review, the initial LEO study included 144 individuals who presented with a first or second episode of schizophrenia, schizoaffective disorder, or delusional disorder. These patients did not have or continue with any treatment before study entry. Subjects were randomized to either usual care in the community, or care by an enhanced team of multiple providers. The authors evaluated the key outcomes of rates of relapse and hospitalization, changes from baseline to follow-up with respect to scores on social and vocational functioning, quality of life, and medication adherence. In addition, they captured detailed information about the costs of services used, and translated functional and vocational performance outcome measures into opportunity and vocational function benefits. Service use information and associated costs were obtained by a standardized format for clients to report and track the use of services, and information was also obtained through records and public service databases as part of the National Health Service in Britain. **Results:** Total costs were 11,685 British pounds in the early intervention group versus 14,062 British pounds for the standard care group. When costs were combined with vocational and quality-of-life scores, the probability estimate that the early intervention was highly likely to be cost-effective was 92%. This was done assuming that increments in quality of life had no value, and, of course, increased in probability as statistical models put increasing value to incremental improvement in those measures. **Conclusions:** For the period studied, the intensive service-early intervention showed a high likelihood of being significantly cost-effective compared to standard care. **Reviewer’s Comments:** The apparent cost-effectiveness of this intervention is hard to get too excited about given the findings of the previously reviewed effort showing that the benefits of this very intervention seemed to be lost after several years. Because of the issues identified in that work, it is hard to understand if the cause for that falling value reflects the course of illness, the lack of vigilance in continuing this intensity of service, or both. (Reviewer-Gary S. Belkin, MD, PhD, MPH).
Twelve-month selective serotonin reuptake inhibitor treatment leads to sustained benefits for panic-disordered patients 1 year after medication discontinuation.

**Background:** The treatment of panic disorder using cognitive behavioral therapy (CBT) involves desensitization to feared bodily sensations that mimic or precede a panic attack, relearning a sense of safety through this process. Some researchers believe that this learning process is context dependent, such that a response to CBT provided with antidepressant therapy may not remain robust without medication.

**Objective:** The authors of the next hypothesis sought to test this "context-safety hypothesis" by comparing the persisting effects of year-long CBT or selective serotonin reuptake inhibitor (SSRI) monotherapy with combined CBT and SSRI in panic-disordered patients before and after discontinuation of treatment.

**Participants/Methods:** 150 patients with panic disorder were randomized to 1 of 3 treatments: CBT, SSRI, or CBT plus SSRI administered at 11 treatment sites in the Netherlands. Each treatment lasted approximately 1 year and was then tapered and discontinued. Clinicians chose between 5 SSRIs: paroxetine, sertraline, fluvoxamine, citalopram, and fluoxetine. CBT was administered by supervised students or experienced psychotherapists. Primary outcome measures were the clinician-rated Hamilton Anxiety Rating Scale (HARS) and the coping scale of the Panic Appraisal Inventory (PAI), a self-report of confidence in managing future panic attacks. Remission was defined as the absence of panic attacks for at least 2 weeks and minimal anticipatory anxiety and agoraphobia. Data were collected before treatment, after treatment, and at 2 follow-up points in the year after discontinuation of treatment.

**Results:** The retention rate in the 2-year study was 65%. Paroxetine, sertraline, and fluvoxamine were the most commonly prescribed antidepressants. The mean number of CBT sessions and psychopharmacology sessions were 19 and 12, respectively. After 9 months of treatment, SSRI treatment with and without CBT was superior to CBT monotherapy in HARS score. This difference abated in subsequent follow-up assessments. PAI coping scores decreased with all 3 treatments equally over time. There was no treatment effect on remitter status at any time point. Half of the sample had agoraphobia, which predicted poorer PAI scores after treatment. Daily benzodiazepine use also predicted poorer PAI scores after treatment.

**Conclusions:** The use of SSRIs either alone or in combination with CBT led to a faster response than CBT alone, which caught up after 1 year of treatment. There was no drop-off in primary outcome measures after antidepressant discontinuation, contrary to the authors’ hypothesis. Thus, both clinician- and patient-reported anxiety scores remained low even after treatment was discontinued, arguing against the so-called "safety-context hypothesis." Daily benzodiazepine use predicted poorer prognosis and should be avoided whenever possible in panic disorder.

**Reviewer’s Comments:** These results are reassuring to patients who seek rapid relief from panic symptoms that they may not be reliant on persistent antidepressant treatment to sustain gains after initial treatment. Larger studies are needed to replicate these findings. (Reviewer-Charlotte O. Ladd, MD, PhD).

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Keywords: Panic Disorder, Treatment, Cognitive Behavioral Treatment, SSRIs

Print Tag: Refer to original journal article
Does DCS Enhance Learning by Activating Hippocampal Neurocircuits?

The N-Methyl-D-Aspartate Receptor Co-Agonist D-Cycloserine Facilitates Declarative Learning and Hippocampal Activity in Humans.

Onur OA, Schlaepfer TE, et al:

Biol Psychiatry 2010; 67 (June 15): 1205-1211

A single 250 mg dose of D-cycloserine hastens declarative learning in healthy adults while increasing activity in the cornu ammonis region of the hippocampus.

Background: D-cycloserine (DCS) is a partial agonist for the glycine regulatory binding site of the N-methyl-D-aspartate (NMDA) receptor, making it a potentially safe modulator of NMDA-associated learning. DCS has been shown to enhance extinction in a number of anxiety disorders, but its effect on learning in healthy adults has not yet been assessed.

Objective: To investigate the hypothesis that DCS also enhances declarative learning in humans by activating hippocampal neurocircuits.

Participants/Methods: The authors recruited 20 men and 20 women aged 18 to 35 years. Patients were randomly assigned to receive either placebo or a single dose of 250 mg DCS immediately before memory testing within an fMRI scanner. Declarative memory was assessed with 2 tasks using a mirror system to view stimuli. The first task involved item category association in which subjects gradually learned to assign 3-digit numbers to 1 of 2 categories based on immediate feedback of right or wrong assignments, initially guessed at random by the subject. Data were collected over 6 cycles. The second task involved object location in which 64 of 96 objects were presented in 1 of 4 quadrants, and subjects were later presented with all 96 objects and asked to identify old versus new ones and to recall the placement of old objects.

Results: 11 of 40 subjects found the item category association task too difficult with the noise of the fMRI scanner, so their data were not included in the analyses. For the remaining 29 individuals, a 2-way analysis of variance with repeated measures on cycle (as within-subject factor) found significant effects for group ($F = 5.45$) and cycle ($F = 8.69$), but no group x cycle interaction effect. Both groups' performance improved with advancing cycles, but the DCS group improved much more quickly than the placebo group, differentiating from baseline by cycle 4 instead of cycle 6. There was no difference in end performance between the 2 groups, nor was there a difference between cycles 4 to 6 in the DCS group. Subjects who had received DCS showed increased fMRI activity in the cornu ammonis (CA) region of the right hippocampus. There was no group difference in performance on the object location task, in which right CA hippocampal activity was associated with encoding information.

Conclusions: A single 250 mg dose of DCS enhanced the speed of learning in a declarative memory task in healthy adults by 50% but did not raise the learning ceiling. The authors propose that DCS recruits silent CA circuitry to accelerate learning by indirectly upregulating glutamatergic signaling.

Reviewer's Comments: DCS is an exciting potential augmentation strategy for hastening the learning process. This study suggests that its usefulness may extend beyond the fear circuit into the declarative learning process in healthy adults. (Reviewer-Charlotte O. Ladd, MD, PhD).

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Keywords: D-Cycloserine, Declarative Memory, Hippocampus, NMDA Receptor

Print Tag: Refer to original journal article
Background: Although it does not take a scientist to point out that soldiers returning from Iraq and Afghanistan have high burdens of morbidity and illness attributable to mental and emotional disorders, a growing number of studies have made important contributions to highlighting the extent and severity of these issues. However, in the face of a high prevalence of conditions, studies have shown that relatively few soldiers with a mental problem seek and follow through with care within 1 year. Presumably, this may be a function of access issues. However, it also may involve stigma and may differ by service category (active duty soldiers or National Guardsmen).

Objective: To evaluate the "rates of utilization of mental health care among active duty and National Guard soldiers with mental health problems 3 and 12 months after they returned from combat in Iraq."

Methods: A survey was administered to soldiers who served in multiple combat teams between December 2003 and October 2007. It contained measures of specific diagnoses, as well as 5-point scales to rate the types of barriers to care. Respondents also provided information about specific services utilization, having received any specific mental health diagnosis, as well as general endorsement of having difficulties with stress, emotional, alcohol-related, or family problems. Respondents also rated the severity of the problems.

Results: Survey results were obtained from 15,918 soldiers. Active duty soldiers with mental disorder risk had significantly lower reported utilization of services, and had significantly higher rates of stigma compared to National Guard soldiers at both 3 and 12 months, a pattern that held true regardless of whether soldiers had a specific diagnosis or reported difficulties in general. Both groups, however, reported similar organizational barriers to care, although these barriers were somewhat different. Active duty soldiers more likely cited scheduling and availability issues, whereas National Guard members scored significantly higher on concerns about cost. National Guard servicemen were more likely to use services at 12 months after deployment (27% vs 13%), even when controlling for stigma, sex, or rank.

Conclusions: Comparing National Guard and active servicemen, the use of mental health services highlights the association between perceived stigma and lower utilization of services—both significantly more common in the active duty group than in the National Guardsmen.

Reviewer's Comments: While the study highlighted how stigma was more prominent in the less-cared for active duty group, differences in the use of services held even when controlling for stigma. The authors also observed that the large gap in the use of services at 12 months could also reflect the 12-month time-limited nature of Veterans Affairs health benefits for National Guardsman at the time of the survey that might also have encouraged this later possible rush for care, as they also cited cost as a concern. These kinds of structural barriers to care, in confluence with perceptions of stigma, are important to understand and need to be better addressed. (Reviewer-Gary S. Belkin, MD, PhD, MPH).

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Keywords: Mental Health Access, National Guard, Active Duty, Afghanistan, Iraq

Print Tag: Refer to original journal article
Mental health courts appear to decrease the number of re-arrests in those individuals who choose the program over traditional criminal courts.

**Background:** There are now >200 mental health courts in the United States. Mental health courts have separate dockets and participation is voluntary. Once an individual enters the program, he or she agrees to follow a treatment regimen, modify his or her behavior, and be monitored by the court in exchange for dismissal of charges or avoidance of incarceration. Most courts are nonadversarial, using a team approach. The mission of the courts is to address the underlying mental health causes of each defendant's behavior while protecting the public.

**Objective:** To evaluate the effectiveness of a North Carolina mental health court in reducing recidivism 2 years after defendants exited the program and to further evaluate effectiveness by comparing defendants who completed the court process with noncompleters.

**Methods:** Defendants may choose to enter the mental health court if they have a diagnosis of mental illness, which is often accompanied by a diagnosis of substance abuse. The defendants in this court agree to a minimum of 6 months of continuous and consistent compliance with treatment, behavioral change, and court appearances. The research group then compared arrests in the 2 years after court exit (whether they completed the court process or not) with arrests in the 2 years before mental health court entry.

**Results:** In the 2 years before their key arrests, the cohort had a mean of 4 arrests. Approximately 90% of key offenses were misdemeanors. Misdemeanor assault and nuisance offenses, such as panhandling, were most common. While 61% of defendants completed mental health court, the 39% who did not complete mental health court returned to traditional criminal court for adjudication. Overall, defendants had a 48% re-arrest rate in the 2 years after exiting mental health court. The proportion was significantly less than in the 2 years before entry, which was 97%. Only 28% of completers were rearrested in the 2 years after court exit versus 81% of noncompleters.

**Conclusions:** Defendants who completed the mental health court were 88% less likely to be rearrested than those who did not; there still were comparably fewer re-arrests for the noncompleters as well.

**Reviewer's Comments:** The problem is that this study does not answer whether those who choose to enter the mental health court system are higher functioning, and then they self-select further by completing the court process. Nevertheless, this paper strongly supports the efficacy of mental health courts. (Reviewer-John G. Koutras, MD)

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Keywords: Adjudication, Criminal Behavior, Treatment

Print Tag: Refer to original journal article
Driving and Dementia -- When to Give Up the Keys

A Prospective Study of Cognitive Tests to Predict Performance on a Standardised Road Test in People With Dementia.

Lincoln NB, Taylor JL, et al:

Int J Geriatr Psychiatry 2010; 25 (May): 489-496

A cognitive battery, with an evidenced-based formula such as the one in this study, may be a useful office-based assessment to determine which elderly patients with dementia require a driving road test.

**Background:** There is a roughly 8-fold increase in the risk of automobile accidents in Alzheimer's patients relative to age-matched controls. Of course, in the elderly in general and in Alzheimer's patients in particular, there is a higher injury and fatality rate when involved in motor vehicle accidents due to frailty. However, clinicians generally try to allow elderly patients to maintain their mobility for as long as possible by balancing mobility and safety for continued driving. This freedom is important as removal of a driver's license has been found to increase susceptibility to depression. On-road assessments are expensive, so there is a need for standardized tests that clinicians can utilize in determining safety to drive.

**Objective:** The primary goal of this British study was to validate an equation that combines results from neuropsychological instruments to determine safety to drive in persons with dementia.

**Methods:** The neuropsychological assessments included the: mini-mental state examination; Stroke Drivers Screening Assessment; Behavioral Assessment of the Dysexecutive Syndrome; Visual Object and Space Perception Battery; Salford Objective Recognition Test; Stroop Color Word Test; and the D-KEFS trail making. The subjects were also assessed using the Nottingham Neurological Driving Assessment, which was conducted by a single approved driving instructor highly experienced in assessing people with cognitive disabilities, who remained blind to the cognitive test results and the participants' dementia diagnosis. A total of 65 participants were assessed with both the cognitive tests and the road test.

**Results:** The authors modified a formula based on prior research and the cognitive instruments utilized in this battery, and found that the formula correctly classified 76% of participants, based on the results from their cognitive tests and the results of the actual driving assessment. Fifteen participants were incorrectly classified. Ten were predicted to be unsafe but were found to be safe. More concerning were 5 participants who were predicted to be safe but were found to be unsafe.

**Conclusions:** A carefully constructed cognitive battery, particularly utilizing assessments of visuospatial abilities, can be an effective office-based tool for assessing safety to drive in patients with dementia.

**Reviewer's Comments:** Another approach to assess driving safety in the elderly that has been investigated more in the traumatic brain injury population is a computerized driving simulation exercise. For a more extensive, practical review of the concerns addressed in this British paper, I urge you to review an article entitled "The Older Driver" in the April 28, 2010, issue of JAMA. (Reviewer-John G. Koutras, MD).

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Keywords: Driving Safety, Dementia, Neuropsychological Testing

Print Tag: Refer to original journal article
Spanking May Be the Spark for Childhood Aggression

Mothers’ Spanking of 3-Year Old Children and Subsequent Risk of Children’s Aggressive Behavior.
Taylor CA, Manganello JA, et al:

Pediatrics 2010; 125 (May): e1057-e1065

This study reinforces that mental health professionals should recommend against corporal punishment due to a risk of increasing a child’s subsequent aggressive behaviors.

Background: In a 2005 U.S. poll, 72% of adults reported that it was “OK to spank a child.” A 2003 meta-analysis showed linkages between corporal punishment (CP) of children and risks for poor outcomes in childhood, including aggressive and/or antisocial behavior, mental health problems, and physical maltreatment. However, most of the studies conducted are not longitudinal and did not control for the child’s initial level of aggression and key potential confounders.

Objective: This study was designed to answer the question of whether a mother’s use of CP on a 3-year-old child is linked to risk for that child being more aggressive at 5 years of age, while controlling for baseline child aggression and other potential confounders.

Participants/Methods: The sample was obtained from the Fragile Families and Child Well-Being Study (FFCWS), a population-based cohort of families from 20 large U.S. cities. The index child’s aggression at age 3 years was assessed using the Child Behavior Checklist for age 3. The mother was interviewed for how frequently she spanked the 3-year-old child. Also assessed when the child was age 3 were child neglect, mother’s experience of intimate partner aggression and violence, maternal parental stress, maternal mental health issues, and substance abuse in an attempt to determine potential confounders. At 5 years of age, the child was administered the Child Behavioral Checklist for age 5, with particular attention to aggressive behaviors. Familial demographic variables were also analyzed.

Results: A mother’s more-frequent use of CP (>2 times in the previous month) when the child was age 3 was a statistically significant predictor of higher levels of aggression when the child was age 5 years. Less frequent CP use, when adjusted for maternal parenting risks and the child’s baseline level of aggression at age 3, was not associated with higher levels of aggression at age 5.

Conclusions: The final statistical model, which included all assessed demographic features, suggests that the odds of the child having a higher level of aggression at age 5 were increased by approximately 50% with more frequent use of CP at age 3.

Reviewer’s Comments: The findings of this study seem to support a social learning approach to understanding the cycle of violence, whereby the child learns to be aggressive by being treated directly with aggression. The problem with CP is that it is not necessary, as there are alternatives, and it is probably best to generally recommend against its use. (Reviewer-John G. Koutras, MD).

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Keywords: Corporal Punishment, Childhood Aggression

Print Tag: Refer to original journal article
Intensive internet use may reflect a distinct condition, but scaled endorsement of use is highly correlated with depression and suicidality making consideration of internet addiction as a unique disorder likely to remain an area of controversy.

**Background:** Problematic, intense, compulsive use of the internet, or internet addiction, has been getting attention for consideration as a distinct disorder as the content for DSM-V evolves. Areas of high internet use, such as South Korea and China, with China having the largest volume of broadband use in the world, have identified this emerging syndrome as a public health problem, especially among adolescents. Efforts to operationalize and explore the validity of such a label have found wide-ranging prevalence rates (0.9% to 38%), which raise questions as to the reliability and consistency in definitions as well as probably a wide variation of such behaviors among different subgroups.

**Objective:** In the face of still evolving criteria and understanding of what such criteria might mean in terms of a distinct condition, the study here used serial surveys of adolescents in Hong Kong to look at both the stability of a criteria set to uniquely and independently discriminate, as well as the correlation of such symptoms with others, such as scale-measured depression and anxiety.

**Methods:** A 2-wave household survey of adolescents aged 15 to 19 years included questions regarding suicidality, depression and anxiety (Center for Epidemiologic Studies Depression Scale and Depression Anxiety Stress Scales, respectively), and endorsement of statements as to the frequency, need, and social-occupational impact of use of the internet. It was administered to 511 subjects who were then followed-up 1 year later with a 62% follow-up response rate.

**Results:** Of 8 items of queried internet use, 71.6% endorsed 0 to 2 symptoms, 21.6% endorsed 3 to 4 symptoms, and 6.7% endorsed ≥5 symptoms. While scores on internet use items and thresholds were sufficiently able to be statistically discriminated from other measured psychological dimensions, such scoring was highly correlated to comorbid psychiatric conditions, especially suicidality and depression. The square root of the average variance of internet addiction items, a common metric for establishing the discriminating value of a collection of items, was 0.51, which was larger than correlation coefficients of these symptoms with other correlates.

**Conclusions:** While showing marginally discriminant characteristics, internet use symptoms and scaled intensity also significantly varied along measures of suicidality and depression.

**Reviewer's Comments:** The apparent unique behavior of internet use items further supports this as a robustly coherent behavior, but still one that may be primarily driven and sustained when excessive and intrusive by other psychological conditions. Likely, more work to be done to settle what excess surfing, means. (Reviewer-Gary S. Belkin, MD, PhD, MPH).

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**Keywords:** Adolescents, Internet Addiction, Prevalence

**Print Tag:** Refer to original journal article
How to Treat Co-Occurring Depression and Alcohol Dependence

A Double-Blind, Placebo-Controlled Trial Combining Sertraline and Naltrexone for Treating Co-Occurring Depression and Alcohol Dependence.

Pettinati HM, Oslin DW, et al:

Am J Psychiatry 2010; 167 (June): 668-675

Combined treatment with naltrexone, sertraline, and weekly cognitive behavioral therapy improves abstinence in alcohol dependence with concurrent depression.

Background: Alcohol dependence frequently presents with comorbid depression that is either independent of alcohol use or secondary to it. Whether to treat major depression with antidepressants in the context of active alcohol dependence remains controversial.

Objective: This study explores the efficacy of sertraline and naltrexone combined with weekly cognitive behavioral therapy (CBT) on alcohol relapse and depression. The authors hypothesized that simultaneous pharmacotherapy of both alcohol dependence and depression would lead to reduced relapse and depression compared to monotherapy or CBT alone.

Participants/Methods: 170 participants with both major depressive disorder and active alcohol dependence were randomized to 1 of 4 groups: (1) CBT alone with 2 placebo medications; (2) CBT with sertraline and placebo, (3) CBT with naltrexone and placebo, and (4) CBT with sertraline and naltrexone. Sertraline was titrated to 200 mg within 10 days and naltrexone to 100 mg within 1 week. High doses were used based on previous studies. Participants were required to be sober for 3 days prior to study entry, and treatment lasted 14 weeks. Depression was measured with pre- and post-Hamilton Depression Rate Scale (HAM-D) scores, and abstinence was measured with breathalyzer readings and self report using the Alcohol Timeline Feedback method.

Results: The majority of participants were single, Caucasian men with a high school education and a mean age of 43 years. Half had a family history of depression. Subjects drank heavily prior to study entry (12 drinks per day) and had moderate depression (mean HAM-D, 23). Side effects were common in those treated with sertraline. Serious adverse events, including inpatient detoxification and rehabilitation, were also common, but less so in the combined naltrexone and sertraline group (P<0.02). This group was also more abstinent from alcohol (P=0.001), with greater time to relapse and fewer heavy drinking days. Ironically, there was no effect of naltrexone monotherapy in time to relapse. There was also no treatment effect of sertraline, with or without naltrexone, on HAM-D scores.

Conclusions: In this study of alcohol-dependent middle-aged depressed adults, combined treatment with naltrexone and sertraline was more effective in assisting abstinence when combined with CBT than was either medication alone. This difference occurred regardless of the fact that sertraline treatment did not improve depression compared to placebo plus CBT. The mean post-treatment HAM-D scores ranged from 7 to 10.

Reviewer's Comments: It is hard to reconcile the robust effects of combined treatment in this study when both medications were ineffective when used alone. The data suggest that it may not be fruitful to prescribe sertraline in the absence of naltrexone in early treatment for alcohol dependence with comorbid depression. Alternatively, the 2 drugs prescribed concomitantly may improve outcomes when used in outpatient substance abuse programs with CBT. (Reviewer Charlotte O. Ladd, MD, PhD).

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Keywords: Alcohol Dependence, Depression, Naltrexone, Sertraline

Print Tag: Refer to original journal article
Consider switching medication or cognitive behavioral therapy treatment if there is a lack of treatment response in the first month of treatment for bulimia nervosa.

**Background:** Multiple studies have demonstrated that antidepressant medications, including both tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs), are consistently superior to placebo in reducing bulimic symptoms. Although TCAs and SSRIs seem to have roughly equal efficacy, SSRI antidepressants have fewer side effects and are better tolerated. Fluoxetine is the only antidepressant approved by the Food and Drug Administration for the treatment of bulimia nervosa (BN). An increasing number of studies have examined early or rapid response to treatment as an indicator of eventual response.

**Objective:** To examine the response to antidepressant medication in the largest treatment trials conducted for BN to determine whether clinically useful guidelines can be developed to predict likelihood of nonresponse to fluoxetine on the basis of symptomatic response during the first several weeks of treatment.

**Methods:** Data for this study were provided by Eli Lilly from 2 previously published studies of fluoxetine for treatment of BN. A total of 785 patients were included, with 231 receiving placebo and 554 receiving fluoxetine. Receiver operating characteristic (ROC) curves were constructed to evaluate whether symptom change during the first several weeks of treatment predicted eventual nonresponse to fluoxetine at the end of the trial.

**Results:** At week 3, if fluoxetine was discontinued for patients who demonstrated a <60% reduction in binge eating, approximately 73% of patients would be correctly classified as eventually not responding to fluoxetine and 23% of patients who would eventually respond to fluoxetine would be classified as nonresponders.

**Conclusions:** A majority of patients with BN who will not respond to fluoxetine can be identified early in treatment, even by the third week.

**Reviewer's Comments:** The authors point out that these results are consistent with studies of cognitive behavioral therapy (CBT) in randomized controlled trials of adults with BN. The question remains, what treatment options should be turned to for the nonresponders to either medication or CBT? Does this group represent a refractory group, regardless of treatment type? At least the findings from this study help to reaffirm that it is probably wise to change treatment strategies earlier, rather than waiting for some response later in the course of treatment. (Reviewer-John G. Koutras, MD).

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Keywords: Bulimia Nervosa, Antidepressants, Fluoxetine

Print Tag: Refer to original journal article
A care-manager–based model in which a mid-level provider can coordinate management and provide basic psychological interventions to anxiety disorders among primary care attendees appears effective among a range of such disorders.

**Background:** "Collaborative care" for depression uses mid-level health extenders to promote adherence to treatment by patients and to alert clinicians as to options and milestones (eg, failure to improve symptom score over a certain period of time) that might prompt changes in medication. Such mid-level providers also deliver simple, often behavioral-activation–based counseling interventions to enhance depression outcomes.

**Objective:** This study took all that a step further and substantially added to such a role a set of psychotherapeutic skills and tracking/screening tools to enable Anxiety Clinical Specialists to both track progress and response and to intervene to treat a range of common anxiety conditions in collaboration with a psychiatric consultant and primary care provider.

**Methods:** The Coordinated Anxiety and Learning Management (CALM) intervention involved a web-based outcomes tracking system based on serial use of the Overall Anxiety and Impairment Scale (OASIS) and computer-assisted guides to assist (mostly social worker sand nurse-level care managers) to guide the sequencing and re-assessment of effectiveness of interventions to address 4 disorders (panic disorder, generalized anxiety disorder, social anxiety disorder, and posttraumatic stress disorder). After a baseline interview, individuals were randomized to usual care (UC) or the CALM intervention. Care managers were trained to use a 10- to 12-week cognitive behavioral therapy (CBT) module based on evidence of the generalization of several components to several disorders (eg, self monitoring, relaxation training, hierarchy development, etc) along with several sessions tailored to a given disorder (eg, exposure, cognitive restructuring). Patients on entry could receive a selective serotonin reuptake inhibitors and/or CBT depending on preference and were reconsidered for changes or augmentation based on response to treatment at given intervals.

**Results:** Compared to UC patients, CALM patients showed greater response and remission rates as measured by Brief Symptom Inventory Scale scores (12-month response rates, 63.66% vs 44.68% and 12-month remission rates, 51.49% vs 33.28%, respectively). Improvement in depression, functioning, and quality-of-care ratings were also greater in the CALM group at the end of the study.

**Conclusions:** The "extender-care" model for providing and managing care for patients with mental health conditions in primary care settings appears effective for a range of anxiety conditions.

**Reviewer's Comments:** The study is important in that it takes a model that has been studied for single conditions and really pushed the concept to manage and sort a broader range of roles and illness, supporting its utility as an overall way to organize care. This could prove a very influential approach for the development of primary care system approaches, especially in the context of a growing interest in "medical homes" and their inclusion of behavioral health care, and in accountable and integrated care outcomes of health systems as an expectation of reimbursement and health reform. (Reviewer-Gary S. Belkin, MD, PhD, MPH).

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Gender May Affect Symptomatology in Bipolar Disorder

Gender and Depressive Symptoms in 711 Patients With Bipolar Disorder Evaluated Prospectively in the Stanley Foundation Bipolar Treatment Outcome Network.

Altshuler LL, Kupka RW, et al:

Am J Psychiatry 2010; 167 (June): 708-715

In bipolar disorder, women are more likely to experience depressive symptoms than men that are related to a higher incidence of rapid cycling and anxiety disorders.

**Background:** It is well known that patients with bipolar disorder spend much of their time ill, but it is unclear whether there are gender differences in the percentage of time spent depressed versus manic versus euthymic.

**Objective:** Based on previous studies, Altshuler and colleagues hypothesized that women spend more time depressed than men in the context of bipolar disorder.

**Methods:** The authors tested this hypothesis using a 7-year prospective study at 7 sites in the U.S. and Europe as part of the Stanley Foundation Bipolar Treatment Outcome Network. A total of 711 patients with bipolar I or II disorder were followed naturalistically by study psychiatrists at a frequency of approximately once per month. Symptoms of depression and mania were monitored at each visit with the Inventory of Depressive-Symptomatology (IDS) and the Young Mania Rating Scale (YMRS), respectively. Significant depressive symptoms were defined as an IDS ≥14 and YMRS <8 to exclude mixed episodes. Significant manic symptoms were defined as YMRS ≥8; euthymia was defined as IDS <14 and YMRS <8. Both depression and manic symptoms were further subdivided into mild, moderate, and severe. Data were analyzed using repeated-measures mixed-effects regression.

**Results:** Men reported euthymia at a greater percentage of visits than women (56.9% vs 50.4%). Women reported significant depression at a greater percentage of visits than men (35.6% vs 28.7%), a difference accounted for by a higher incidence of rapid cycling and anxiety disorders (posttraumatic stress disorder, obsessive-compulsive disorder, and specific phobias) in women. Among bipolar II but not bipolar I patients, there was a gender difference in the percentage of visits spent hypomanic, with men reporting hypomanic symptoms more frequently than women (13.7% of visits vs 8.1% of visits). Both men and women were less likely to report depressive or manic symptoms as time passed in the study, indicating improvement with treatment.

**Conclusions:** In this large, prospective, multisite study, both men and women reported euthymia at a majority of visits, although women were ill more often than men, with more frequent depressive symptoms that were associated with rapid cycling and anxiety disorders. Hypomanic and manic symptoms tended to occur more commonly in men than women.

**Reviewer’s Comments:** The authors did not include mixed states in their analysis, and it is unclear how these states were accounted for. Although not emphasized in the study, the observation that patients reported euthymia at a majority of visits is reassuring as is the fact that they were less ill over time. (Reviewer-Charlotte O. Ladd, MD, PhD).

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Keywords: Gender, Depressive Symptoms

Print Tag: Refer to original journal article
What Might Herald Conversion to Psychosis?

Neuropsychology of the Prodrome to Psychosis in the NAPLS Consortium: Relationship to Family History and Conversion to Psychosis.

Seidman LJ, Giuliano AJ, et al:

Arch Gen Psychiatry 2010; 67 (June): 578-588

While distinct neuropsychological features characterize individuals who are clinically high risk for conversion to a psychotic disorder, such a neuropsychological profile does not as yet appear a specific predictor of who might convert.

**Background:** Many domains of neuropsychological functioning have been shown to be important features of schizophrenia, especially with respect to verbal memory and processing speed. Neuropsychological deficits also appear in the premorbid stage among individuals who later develop the disease, and thus have been under study as potential markers to predict who will actually convert among individuals at risk for developing schizophrenia. Any effort to provide earlier treatment or develop preventive intervention for vulnerable individuals will require a reliable way to identify those most at risk to convert. Individuals at high risk for conversion have tended to be divided among those with strong familial-historical high-risk factors (FHR) and those with clinical high-risk factors (CHR) (ie, those having specific subsyndromal symptoms, such as isolated thought disorder, paranoia, unusual thinking, or unusual behaviors, etc).

**Objective:** To look for the predictive value of profiles of neuropsychological deficits among both FHR and CHR individuals and assess whether such profiles differed across these groups.

**Methods:** 8 centers specializing in these issues collaborated to recruit patients into this prospective study. Criteria for CHR and FHR were determined through standardized structured interviews and scoring for those purposes. Cognitive performance was assessed in CHR and FHR subjects, as well as comparison controls, through a comprehensive battery of neuropsychological testing performed at baseline. Individuals were then prospectively followed for 2.5 years and assessed for development of full DSM-IV psychotic disorder.

**Results:** The FHR and CHR groups had comparable overall scored neuropsychological impairment, although the pattern of deficits differed. Verbal learning and memory and processing speed were more uniquely impaired in the CHR group compared to controls. Nonetheless, the pattern or severity of deficits did not independently predict greater likelihood of conversion in either group, although worse verbal memory did predict a more rapid time to conversion.

**Conclusions:** While neuropsychological burdens are clearly present among CHR and FHR groups and show, in some ways, distinct patterns between them, such features predicted time to conversion but could not independently predict likelihood of conversion to a full disorder.

**Reviewer’s Comments:** This study is one of those rarities; it is the publishing of negative results. However, continuing efforts to refine understanding of the features that contribute to and herald the onset of psychotic illness will nonetheless benefit by this further filling in specific ways neuropsychological features evolve across risk groups over time. The details of the domains of impairment and their distribution across risk groups are worth reading in some detail in the accompanying article. (Reviewer-Gary S. Belkin, MD, PhD, MPH).

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Keywords: Schizophrenia Conversion Prediction, Neuropsychology, CHR, FHR

Print Tag: Refer to original journal article
Clozapine No Better as First Choice for Tx of Schizophrenia

A Randomized Trial Comparing Clozapine and Typical Neuroleptic Drugs in Non-Treatment-Resistant Schizophrenia.
Meltzer HY, Bobo WV, et al:
Psychiatry Res 2010; 177 (May 30): 286-293

Clozapine lacks superior efficacy to first-generation antipsychotics in non–treatment-refractory patients with schizophrenia.

**Background:** Clozapine demonstrated superiority to olanzapine, risperidone, and quetiapine in the CATIE Phase 2E study, which mostly included patients who had failed the initial phase of the CATIE study due to lack of efficacy of typical or atypical antipsychotic drugs (APDs). In other research, clozapine has also been found to be superior to typical APDs for improving cognition, and superior (at least to olanzapine) for reducing the risk of suicide in both treatment-resistant (TR) and non–TR schizophrenia. In studies with TR patients, clozapine has been found to decrease relapse and rehospitalization rates and to have a longer time to discontinuation compared with typical APDs. There is an ongoing debate about the comparative efficacy of typical and atypical APDs in non-TR patients, a group that includes approximately 70% of patients with schizophrenia.

**Objective:** To describe the effects of typical neuroleptics and clozapine on psychopathology, quality of life, and global functioning over a 2-year period in patients with recent onset of schizophrenia who were not TR.

**Participants/Methods:** 57 patients with schizophrenia completed the 24-month study. Patients were randomized to treatment with clozapine or typical antipsychotics, which included haloperidol, perphenazine, fluphenazine, loxapine, thioridazine and thiothixene. Baseline, 6-week, and 6-, 12-, and 24-month assessments were conducted. The following instruments were used: the Brief Psychiatric Rating Scale (BPRS); the Scale for the Assessment of Negative Symptoms (SANS); and the Quality of Life Scale (QLS). The patients were assessed for extra pyramidal side effects and akathesia. The patients were also weighed, and metabolic laboratory panels were conducted.

**Results:** Clozapine and typical antipsychotics were equally effective in improving psychopathology and quality of life. However, clozapine-treated patients were less likely to relapse, and there were fewer dropouts for any reason in the clozapine-treated group.

**Conclusions:** Clozapine and typical neuroleptics may not differ in their ability to improve psychosis in recent onset non-TR schizophrenia patients, but clozapine may be more effective in encouraging adherence and preventing relapse during long-term treatment.

**Reviewer’s Comments:** This study reinforces the current guidelines of using clozapine in only patients who are TR to first-generation antipsychotics, and, when taken together with the CATIE findings, those who are refractory to the second-generation antipsychotics as well. As would be expected, the clozapine patients gained approximately 30 pounds over the 2-year period compared with 10 pounds for the typical antipsychotic group. (Reviewer-John G. Koutras, MD).

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Keywords: Clozapine, Schizophrenia, Treatment-Resistant, Weight Gain

Print Tag: Refer to original journal article
Having posttraumatic stress disorder confers a substantially increased risk of subsequent development of dementia among affected U.S. veterans.

**Background:** Posttraumatic stress disorder (PTSD) is a common risk among returning soldiers, but it is also a chronic condition. Among Vietnam veterans, apparently 10% to 15% had PTSD ≥15 years after their return from combat, and among WW II and Korean War veterans, combat-related PTSD prevalence was as high as 12% some 45 years later. Those chronic effects included greater health care use and the risk of a range of health conditions. There is reason to believe that among those long-term risks might be heightened occurrence of dementia given the possible effects of such a chronic condition on brain aging and neurophysiological integrity.

**Objective:** The authors used the medical databases of the Veterans Affairs health system to construct a cohort within which to compare onset of dementia rates among those with and those without PTSD at baseline.

**Methods:** The VA National Patient Care Database was used to extract records on veterans who were ≥55 years of age between 1997 and 2000 without a baseline diagnosis of dementia and who had ongoing records for follow-up through 2007. The dataset allowed capture of all diagnoses and forms of care received by these individuals within the VA system during that time period as well as various sociodemographic characteristics, laboratory parameters, and other features, including key medical comorbidities (head injury, stroke, diabetes, substance use, hypertension, depression, etc), which are often associated as confounding risks for dementia.

**Results:** A total of 181,093 veterans were followed; 53,155 had PTSD at baseline (mean age, 68.8 years). Veterans with PTSD had a 7-year cumulative incident rate of dementia of 10.6%. Those without PTSD had a cumulative incident rate of 6.6%, a statistically significant difference ($P < 0.001$). After adjusting for confounding features including head injury history, substance use and depression, those with PTSD remained significantly more likely to develop dementia (risk ratio, 1.77).

**Conclusions:** Having PTSD confers a substantially increased risk of subsequent development of dementia among affected U.S. veterans.

**Reviewer’s Comments:** This study supports a link between these conditions that if replicated, but particularly if confirmed through work that establishes compelling mechanisms that explain such a link, could provide a model for opening up new insights into the unfolding nature of environmental and biological interactions that lead to and connect a range of serious psychiatric conditions. (Reviewer-Gary S. Belkin, MD, PhD, MPH).

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Keywords: PTSD, Dementia, Veterans

Print Tag: Refer to original journal article
Habit reversal training, which includes relaxation training, is very effective in children with chronic tic disorders, such as Tourette.

**Background:** Prevalence estimates for Tourette disorder in school-aged children suggest a rate of 6 per 1000. Tics begin in childhood, with severity peaking in early adolescence and then declining in young adulthood. The most promising behavioral intervention for reducing tic severity is habit reversal training. The primary components of habit reversal training are tic awareness and competitive response training. Habit reversal teaches competitive response training, which involves engagement in a voluntary behavior physically incompatible with the tic. Rather than simply attempting to suppress the tic, the individual learns to tense certain muscle groups involved in the tic and do an alternative, barely perceptible, motion instead.

**Objective:** To evaluate the efficacy of a comprehensive behavioral intervention for tics (CBIT) based on habit reversal training for reducing tics and tic-related impairment in a large sample of children and adolescents with Tourette disorder.

**Participants/Methods:** 126 patients with Tourette or chronic tic disorder were randomized to either CBIT or control treatment in a 1:1 ratio. The control treatment consisted of supportive psychotherapy and education regarding tic disorders. Patients were permitted to continue medication treatment for tics as long as they were on a stable regimen, and the randomization took medication status into account. Overall, 36.5% of the participants were on anti-tic medication. Outcome assessments were repeated at weeks 5 and 10. The primary outcome measures were the Yale Global Tic Severity Scale and the Clinical Global Impressions-Improvement Scale.

**Results:** The Yale Global Tic Severity Scale Total Tic score was significantly reduced in the behavioral intervention group compared with the control group, with an effect size of 0.68. For behavior therapy, this difference reflects a number needed to treat of 3. Children randomized to behavioral intervention showed a 51% decrease on the Yale Global Tic Severity Scale-Impairment compared to a 30% decrease for the control treatment.

**Conclusions:** According to the authors, “A comprehensive behavioral intervention, compared with supportive therapy and education, resulted in greater improvement in symptom severity among children with Tourette and chronic tic disorder.”

**Reviewer’s Comments:** Interestingly, at the 6-month follow-up point, 50% to 75% of the control group and 60% to 90% of the treatment group exhibited continued benefit. This lack of a large relapse rate in the control group suggests that even supportive therapy and psychoeducation can be beneficial to some patients with chronic tics. The improvement in actual tic severity, however, lies in the behavioral intervention group. (Reviewer-John G. Koutras, MD).

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Keywords: Tourette Disorder, Children, Behavior Therapy, Habit Reversal Training

Print Tag: Refer to original journal article
Organophosphate pesticide exposure appears to be associated with the diagnosis of attention-deficit/hyperactivity disorder.

**Background/Objective:** The developing brain is more susceptible to neurotoxins, therefore placing children at greater risk from pesticide organophosphates. Also, the dose of pesticides per body weight is typically larger for children. Epidemiologic studies linking exposure to organophosphates and neurodevelopment have focused on populations with high levels of exposure, relative to the U.S. population. No studies have addressed possible risks among children with typical levels of exposure. By using data for a representative sample prevalence of U.S. children, this study examines the cross-sectional association between urinary dialkyl phosphate (DAP) metabolite concentrations and attention-deficit/hyperactivity disorder (ADHD) in children 8 to 15 years of age.

**Methods:** The National Health and Nutrition Examination Survey (NHANES) is a population-based health survey that includes questions about demographics, health history and also involves collecting blood and urine samples during physical examinations. In those children who carried a diagnosis of ADHD, the diagnosis was confirmed by administration of the Diagnostic Interview Schedule for Children IV (DISC-IV). Six urinary DAP metabolites were measured.

**Results:** The study sample included 1139 children aged 8 to 15 years; 119 children meeting criteria for any ADHD subtype. Of the total sample, 93.8% of the children had at least 1 detectable DAP metabolite. The odds of meeting DISC-IV criteria for ADHD increased with the total DAP metabolites detected in the urine samples. This association was not explained by gender, age, socioeconomic status, race/ethnicity, fasting duration, or creatinine concentration.

**Conclusions:** Children with levels higher than the median of detectable dimethyl thiophosphate concentrations were twice as likely to be diagnosed with ADHD as were those with undetectable concentrations.

**Reviewer's Comments:** As the authors pointed out, the most important limitation of the present study is the assessment of organophosphate exposure through measurement of DAP metabolites in only 1 spot urine sample. Serial measurements over a longer time would have provided a better assessment of average organophosphate exposure. Also, the authors found a significant association between a specific metabolite and ADHD-hyperactive subtype only (not inattentive or combined types). Since the authors conducted a DISC-IV only on children who were identified as having ADHD prior to the survey, it could be that be that organophosphate exposure actually increases hyperactive behaviors (similar to certain food dyes) and that these children are then more likely to be identified as having ADHD by teachers and primary care providers. This would result in an underestimation of ADHD in the remainder of the sample. (Reviewer-John G. Koutras, MD).

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**Keywords:** ADHD, Organophosphates Pesticides, Risks, DAP, Urinary Metabolites

**Print Tag:** Refer to original journal article