Deep and periventricular white matter hyperintensities correlate with persistent memory deficits in depressed elderly in a dose-dependent fashion.

**Background:** Late-life depression is associated with cognitive deficits that often persist despite adequate antidepressant treatment. Potential etiologic factors for this phenomenon include shrinkage of frontal lobe and hippocampal volumes, white matter hyperintensities, and hypercortisolemia. In a previous study, the authors demonstrated that hippocampal volume, but not cortisol concentration, in depressed elderly patients predicted persistence of cognitive impairment 6 months later. In this study, they wanted to extend their observations beyond 6 months and examine the relationship between white matter hyperintensities and cognitive function before and after depression treatment in the elderly.

**Objective:** The authors hypothesized that cognitive impairments persisting 18 months after depression treatment would be predicted by baseline white matter hyperintensities and frontal and hippocampal volumes but not cortisol concentrations.

**Participants/Methods:** The authors recruited 102 adults aged ≥60 years (66 with major depressive disorder and 36 controls). A battery of neuropsychological tests was administered at baseline, 6 months, and 18 months assessing memory, processing speed, and executive function. Depression severity was measured at the same time points. Baseline diurnal salivary cortisol was collected for 3 consecutive days. Baseline brain MRI was used to measure total brain volume, hippocampal and frontal lobe volumes, and white matter hyperintensities.

**Results:** Complete data were available for 35 subjects in the depression group (mean age, 74.1 years; 80% females) and 29 in the control group (mean age, 72.8 years; 76% females). The depressed group had fewer years of education, higher baseline cortisol levels, and worse performance in all cognitive domains at the 18-month follow-up visit than did the control group. Mean illness duration before study referral was over a year, and illness severity was moderate, yet most participants partially remitted by study’s end. Differences in end point cognitive measures in depressed versus nondepressed subjects were not moderated by baseline cortisol or any volumetric measures. However, there was a significant dose-dependent interaction between deep and periventricular white matter hyperintensities and final memory performance in depressed versus control individuals. Severe deep hyperintensities at baseline were also associated with poorer executive function at the end point.

**Conclusions:** White matter hyperintensities in control subjects did not predict poor cognitive performance. However, baseline deep and periventricular white matter intensities in depressed individuals were robustly associated with deficits in memory and executive function 18 months later in a dose-dependent fashion.

**Reviewer’s Comments:** The authors hypothesize that depressed brains may be more vulnerable than nondepressed brains to cognitive damage associated with white matter hyperintensities. Alternatively, the neuropathology or distribution of these signals in depressed patients may increase their vulnerability to cognitive impairment. It is notable that despite improvement in depression and repetition of neuropsychological tests over time, individual performance in the depressed group still worsened over time regardless of processing speed. (Reviewer-Charlotte O. Ladd, MD).

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Keywords: Depression, Cognition, MRI

Print Tag: Refer to original journal article
Antiepileptic mood stabilizers and antipsychotics outperform older antidepressants in a meta-analysis of the treatment of borderline and schizotypal personality disorders.

**Background:** The American Psychiatric Association (APA) Practice Guideline for the Treatment of Borderline Personality Disorder is almost 10 years old. In 2006, two meta-analyses of pharmacotherapeutic options for borderline personality disorder yielded differing results. Current pharmacotherapy recommendations for severe personality disorders are lacking.

**Objective:** To clarify the potential therapeutic benefit of antidepressants, antipsychotics, and mood stabilizers on 3 symptom domains in patients with borderline or schizotypal personality disorder without prominent Axis I pathology.

**Participants/Methods:** 35 placebo-controlled, randomized, controlled trials were found in the literature; 14 were excluded based on study flaws or the use of a drug class other than that specified. Outcome variables were classified by consensus into the 3 main symptom headings: cognitive-perceptual symptoms, impulsive-behavioral dyscontrol, and affective dysregulation, which was further subdivided into depressed mood, anxiety, anger, and mood lability. The authors calculated the standardized mean differences between groups in each study and then pooled the data using either fixed- or random-effects models as appropriate. Global functioning was also measured.

**Results:** Antidepressant treatment with tricyclic antidepressants, monoamine oxidase inhibitors, mianserine, fluoxetine, or fluvoxamine had no effect on cognitive-perceptual symptoms, behavioral dyscontrol, or depressed mood. These medications had a small to moderate effect on anxiety and anger. The mood stabilizers carbamazepine, valproate, topiramate, and lamotrigine, by contrast, had a very large effect on behavioral dyscontrol, anxiety, and anger. These medications had a moderate effect on depressed mood and no effect on cognitive-perceptual symptoms. High- and low-potency typical antipsychotics as well as olanzapine, risperidone, and aripiprazole had a moderate effect on cognitive-perceptual symptoms and anger but no effect on depressed mood, behavioral dyscontrol, or anxiety. Global functioning improved most with mood stabilizers, followed by antipsychotics.

**Conclusions:** Antiepileptic mood stabilizers were more beneficial than antipsychotics or older antidepressants for the treatment of behavioral dyscontrol in patients with borderline or schizotypal personality disorder. Antipsychotics were most beneficial for cognitive-perceptual symptoms, while antidepressants were most helpful for anxiety and anger. The authors use the results to challenge the 2001 APA practice guideline recommendation to use antidepressants as a first-line treatment for borderline personality disorder.

**Reviewer's Comments:** Unfortunately, the authors do not comment on the fact that most of the antidepressants in these studies are not widely used today. To alter treatment recommendations based on these findings would be premature. The authors also fail to discuss the teratogenic risks of the 2 most commonly used mood stabilizers in these studies: carbamazepine and valproate; giving either of these medications to young women is relatively contraindicated. Using older antipsychotics as first-line treatment might also be problematic based on the high likelihood of adverse effects. Thus, more studies are needed to guide treatment of these disorders. (Reviewer: Charlotte O. Ladd, MD).

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**Keywords:** Borderline Personality Disorder, Schizotypal Personality Disorder, Mood Stabilizers, Antipsychotics, Antidepressants

Print Tag: Refer to original journal article
Can Pharmacogenetics Predict Suicidal Events? 

Association of FKBP5 Polymorphisms With Suicidal Events in the Treatment of Resistant Depression in Adolescents (TORDIA) Study.

Brent D, Melhem N, et al:

Am J Psychiatry 2010; 167 (February): 190-197

Polymorphisms modulating glucocorticoid receptor sensitivity are associated with suicidal events in adolescents receiving treatment for depression.

**Background:** Pharmacogenetics aim to personalize pharmacotherapy by tailoring medications to individual genetic variation. Although extensively researched in adults, little is known about individual genetic variations influencing adolescent response to psychiatric medication treatment. The Treatment of Resistant Depression in Adolescents (TORDIA) study is a large multi-site trial investigating treatments for adolescent depression that is refractory to an initial antidepressant trial.

**Objective:** The authors examined the DNA of a subset of depressed adolescents in the TORDIA trial, genotyping 21 polymorphisms on 12 genes believed to play a role in depression etiology and treatment response. These polymorphisms involved genes encoding serotonin and glutamate receptors; tryptophan hydroxylase and monoamine oxidase A; norepinephrine, dopamine, and serotonin transporters; corticotropin-releasing factor receptor 1; brain-derived neurotrophic factor; and FKBP5, which encodes a protein that reduces the sensitivity of the glucocorticoid receptor.

**Participants/Methods:** Recruitment into the TORDIA study required an initial failed selective serotonin reuptake inhibitor (SSRI) trial. All participants were cross tapered to another SSRI or venlafaxine, each with or without weekly cognitive behavior therapy (CBT), yielding 4 treatment groups. Of 292 patients, 176 participated in the genotyping arm of the study. Outcome measures included adequate treatment response and suicidal events. Suicidal events in the TORDIA study were positively associated with family conflict and the use of trazodone for sleep; therefore, the genotyping data were controlled for these factors, as well as for medication, cognitive behavioral therapy (CBT), and medication-by-CBT interaction.

**Results:** In the overall TORDIA sample, CBT was associated with a greater response rate, a trend that failed to reach significance in this smaller sample. Suicidal events (including ideation and behaviors) were associated with parent-child conflict, more severe depression, less educated parents, and the use of trazodone. Although there was no relationship between clinical response and genotype, suicidal events were associated with the FKBP5 rs1360780 TT and FKBP5 rs3800373 GG genotypes. These associations existed in all treatment groups and in nonresponders. A total of 18 adolescents experienced a suicidal event in this study: 4 subjects attempted suicide, 2 communicated suicidal ideation (SI) with intent, 4 expressed new-onset SI, and 8 experienced worsening of pre-existing SI.

**Conclusions:** 2 polymorphisms in the FKBP5 gene were associated with suicidal events in adolescents receiving antidepressant medication with or without CBT. These FKBP5 alleles result in reduced sensitivity of the glucocorticoid receptor to cortisol, thereby decreasing negative feedback in the hypothalamic-pituitary-adrenal axis.

**Reviewer’s Comments:** As there was no placebo group in this study, it is not known whether or not, or to what extent, suicidal events were related to treatment or depression quality itself. Future studies need to more closely examine the interplay between genetic variation in the HPA axis, stress vulnerability, treatment response, and adverse outcomes. (Reviewer-Charlotte O. Ladd, MD).

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Keywords: Suicidal Events, Glucocorticoid Receptor, Pharmacogenetics

Print Tag: Refer to original journal article
Spousal deployment to Afghanistan or Iraq is associated with an increased rate of depression, anxiety disorders, adjustment disorders, and sleep disorders among U.S. army wives.

Background: Deployment causes significant stress to military spouses, including fear of harm or death to their loved one, having to maintain household needs alone, acting as a single parent, and isolation. Reunion can also cause significant stress, especially if the soldier returns with symptoms of PTSD, traumatic brain injury, substance use disorder, or physical injury, all common ailments among soldiers returning from Iraq and Afghanistan.

Objective: The authors of this study hypothesized that the utilization of mental health care and rates of mental health disorders would be higher among spouses of soldiers who were deployed for at least a month between 2003 and 2006 compared to spouses of nondeployed soldiers.

Methods: Data were gathered from the Defense Manpower Data Center records, electronic medical records from the Standard Ambulatory Data Record, and TRICARE, the insurance covering non-VA health care visits. A total of 250,626 wives were represented in this study. Linear risk regression models were used to estimate differences between spouses of deployed versus nondeployed soldiers.

Results: Two-thirds of spouses were deployed at least once during the study period; 36.6% of wives with deployed husbands received at least one mental health diagnosis during the 4-year time frame, compared to 30.5% of wives whose husbands were not. Compared to wives of nondeployed soldiers, wives of soldiers deployed for 1 to 11 months exhibited an 18% higher rate of depression, 25% higher rate of anxiety disorders, 21% higher rate of sleep disorders, and 23% higher rate of adjustment disorders; each of these factors was substantially increased even more in women whose husbands were deployed for >11 months (24%, 29%, 40%, and 39%, respectively). Mental health care utilization was 19% higher with shorter deployments and 27% higher with deployments >11 months. The rates of bipolar disorder, psychosis, and alcohol use disorders did not change appreciably.

Conclusions: The excess number of cases of depression and anxiety per 1000 wives attributed to spousal deployment was 27.4 and 15.7, respectively, for absences of ≤11 months and 39.3 and 18.7, respectively, for absences >11 months. The total number of excess cases of mental health diagnoses associated with 1 to 11 month deployment was 41.3 per 1000, or 3474 additional mental health diagnoses among 84,105 wives of deployed spouses. The authors did not discern whether mental health utilization was more common before, during, or after the soldier's deployment.

Reviewer's Comments: This study highlights the mental health burden on wives of soldiers deployed to Iraq and Afghanistan. Future studies should delineate the specific burdens of pre-deployment anticipation, absence during deployment, and reunion on soldiers’ spouses and extended families. A large percentage of soldiers return scarred emotionally or physically. Efforts are needed to increase support for both soldiers and their families. (Reviewer-Charlotte O. Ladd, MD).

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Keywords: Mental Health Utilization, Combat, Deployment

Print Tag: Refer to original journal article
Bilateral epidural prefrontal cortical stimulation, delivered in on/off stimulation cycles, shows efficacy in treatment-resistant depression, even to the point of remission for most.

**Background:** Research has suggested that the anterior and midlateral prefrontal cortices play different but complimentary roles in mood regulation. Therefore, both anterior and midlateral prefrontal regions offer a distinct opportunity for targeted antidepressant treatments. Epidural cortical stimulation (ECS) is a unique therapeutic approach. Leads are placed through a burr hole in the skull but above the dura mater and thus remain separated from the underlying cortical region by the arachnoid space. ECS is more direct than transcranial magnetic stimulation or vagus nerve stimulation and potentially safer than deep brain stimulation, which involves passing the electrodes through brain tissue.

**Objective:** To test the potential safety, tolerability, and potential therapeutic effects of bilateral anterior and lateral ECS in treatment-resistant depression.

**Methods:** Eligible participants presented with a nonpsychotic, nonatypical major depressive episode (MDE) as part of either bipolar (I or II) disorder or major depressive disorder (MDD), defined by DSM-IV criteria. All participants scored ≥20 on the 24-item Hamilton Rating Scale for Depression (HRSD) before implantation. Participants were on stable medication regimens for at least 4 weeks before and for 5 months following implantation. The participants were then operated on, with successful implantation of 4 bilateral midlateral frontal paddle leads. Patients were then discharged with a chronic and intermittent bilateral stimulation of all 4 paddle leads. These intermittent settings are radically different from other deep brain stimulation or ECS protocols that have employed constant stimulation 24 hours per day.

**Results:** 5 subjects received ECS in this study, and the average duration of their current depressive episode was 3 years, 7 months. After 4 months of active stimulation, the group showed a mean HRSD improvement of 36%, which increased to 55% at 7 months. Three of 5 patients were remitted at 7 months.

**Conclusions:** This open study with a small sample size shows promising results in this difficult-to-treat population with treatment-refractory depression utilizing bilateral epidural prefrontal cortical stimulation.

**Reviewer's Comments:** Of course, one cannot imagine an invasive procedure such as this one as not having some significant element of risk. One patient did develop an infection at the lead implantation site and underwent successful debridement and antibiotic treatment as well as ipsilateral lead removal. (Reviewer-John G. Koutras, MD).

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Keywords: Epidural, Prefrontal Cortical Stimulation, Refractory Depression

Print Tag: Refer to original journal article
The ESDM, which trains parents to provide intensive behavioral methods for toddlers with AUDs, improves outcomes such as IQ, language, and adaptive functioning.

**Background:** With a prevalence of 1 per 150, autism costs the United States $35 billion per year. In 1987, Lovaas and colleagues developed an early behavioral intervention that resulted in 49% of children in their studies being mainstreamed into regular classrooms and showing significant IQ change. Interventions that are based on the Lovaas model have been termed applied behavioral analysis.

**Objective:** This study is the first randomized, controlled trial of intervention for toddlers with autism, with all children <30 months of age at entry.

**Methods:** The Early Start Denver Model (ESDM) is a comprehensive early behavioral intervention for infants to preschool-aged children with autism spectrum disorder (ASD). The intervention is provided in a toddler's home and is delivered by trained therapists and parents. Forty-eight children between 18 and 30 months old and diagnosed with autism or pervasive developmental disorder (PDD) were randomly assigned to 1 of 2 groups; the ESDM group received 20 hours per week of the ESDM intervention, and the control group received intervention recommendations and referrals for intervention from commonly available community providers. The children were evaluated by experienced examiners naïve to intervention at baseline, 1 year after onset of the intervention, and at either 2 years or at 48 months of age. The toddler version of the Autism Diagnosis Interview–Revised, the Autism Diagnostic Observation Schedule (ADOS), the Mullen Scales of Early Learning (MSEL), and the Vineland Adaptive Behavior Scales (VABS) were all utilized.

**Results:** One or both parents were trained and reported spending an average of 16 hours a week using ESDM strategies. At the 1-year reassessment, the ESDM group demonstrated an average IQ increase of 15.4 points compared to 4.4 points in the control group but no clear improvement in adaptive functioning. At 2 years, the ESDM group had MSEL composite scores that increased 17.6 points compared to 7.0 points in the controls; the largest improvement was in expressive and receptive language. On the Vineland, the ESDM group showed a steady rate of development, while the control group showed an 11.2-point average decline, particularly in the domains of socialization, daily living skills, and motor skills.

**Conclusions:** ASD children in the ESDM group showed greater improvements in IQ scores and adaptive functioning and were more likely to have improved diagnostic status than those ASD children who received community care.

**Reviewer's Comments:** As the authors noted, parents' use of these strategies at home during their daily activities was likely an important ingredient in the program's success. (Reviewer-John G. Koutras, MD).

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Keywords: Autism Spectrum Disorders, Applied Behavioral Analysis, Parent Training

Print Tag: Refer to original journal article
Cannabis use does not appear to be independently related to suicide risk.

**Background/Objective:** Worldwide, cannabis remains the most commonly used illicit drug. There have been many concerns about use of this substance in terms of its impact and risk for development of other forms of substance use disorder as well as the onset of other psychiatric conditions such as psychosis and mood symptoms. Evidence does appear compelling with respect to a greater risk for onset of psychotic outcomes, but evidence to date is more mixed with regard to depression, anxiety, and suicidal outcomes attributable specifically to cannabis use. Many of the possible adverse psychological effects of cannabis use have limited or unclear evidence, including suicide risk for which there is little empirical data. One reason it has been difficult to study this question is the numerous co-occurring risk factors for both suicide and cannabis use such as male gender, alcohol use, and antisocial behavior. Also, since suicide is not a frequent event, the study of this as an outcome of cannabis use needs large, prospective study. The study reported here is such an effort.

**Methods:** The data explored here comes from information about 50,087 men conscripted in Sweden in 1969 to 1970 as part of mandatory military training. Entry into service routinely involved the completion of a self-report questionnaire with respect to social background and drug use (including cannabis use), an interview with a psychologist who coded any psychiatric diagnoses, and completed IQ testing. The frequency of cannabis use was specifically graded according to levels of frequency of use. Suicide deaths among this cohort over time were obtained through the National Cause of Death Register up to 2003. Given the extent of background data collection, confounders for suicide and cannabis use were obtained and controlled for, such as other drug use, IQ, child problem behavior, social relations, socioeconomic position, psychiatric comorbidity, etc.

**Results:** Of the 50,087 recruits in the cohort, there were 459 suicides; 10.7% of the cohort (5380) reported varying degrees of cannabis use at outset. Individual adjustment for each confounder found no unique relationship between cannabis use and later suicide. The strongest predictors among the variables gathered here at baseline that did predict later suicide were problematic behavior in childhood (eg, truancy, violence), other drug use, adjustment problems, alcohol or tobacco use, and other psychiatric diagnoses.

**Conclusions:** When controlling for other confounding variables, baseline cannabis use does not predict later suicide over an approximately 30-year observational period.

**Reviewer's Comments:** An obvious problem with this study is that the use of cannabis at one point in time may or may not reflect the pattern of interim or ongoing use and so may not reflect any differential effect of continued or longer duration of use on risk. (Reviewer-Gary S. Belkin, MD, PhD, MPH).

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Keywords: Cannabis Use, Suicide

Print Tag: Refer to original journal article
The diagnostic category of GAD appears to overlap in risk profile and symptom patterns as depression, more so for anxiety disorders, but also patterns unique to GAD itself, suggesting perhaps unique pathways of pathogenesis.

**Background/Objective:** There have been mixed findings as to the degree generalized anxiety disorder (GAD) represents a diagnostically distinct target of treatment rather than an indication of other anxiety or depressive disease-spectrum risks and course. This is a longitudinal study of risk factors for psychiatric disorders and profiles of symptoms and their comparative associations with these disorders as they appear over time in order to further consider the overlap in possible etiological risks and disease course that GAD may have with other conditions.

**Methods:** The Early Developmental Stages of Psychopathology study was a prospective, longitudinal follow-up study of 3021 adolescents who ranged from 14 to 24 years of age at baseline assessment. Assessments included standardized diagnostic interviews with subjects and parents, family psychiatric and family separation history questionnaires, rating interviews for different behavioral domains such as behavioral inhibition, validated rating measure of resilience, interim onset of psychiatric disorder as well as measures of several dimensions of family functioning, recalled child rearing experiences, and structured interviews to assess personality dimensions with respect to novelty seeking, reward dependence, and harm avoidance.

**Results:** Over time, GAD onset was significantly related to onset of depressive and anxiety disorders; each predicted the other. However, relatively speaking, the magnitude of the association was greater between GAD and anxiety disorders (with an HR of 4.14 for having GAD predicting having another anxiety disorder, and an HR of 5.05 for the opposite relation) than GAD and depressive disorders (HRs of 1.88 to 2.54). When risk profiles in terms of family history, personality features, etc were examined in terms of their predictive value for later onset of these disorders, factors associated with GAD overlapped for all of those that were also specific for anxiety disorders (eg, parental GAD, behavioral inhibition, childhood separation events, parental overprotection). However, GAD risk factors more partially overlapped with risk factors uniquely for depression (parental depressive disorders). Unique risk factors for GAD but not the other disorders included reward dependence personality features at baseline and dysfunctionally scored family functioning.

**Conclusions:** GAD has substantial overlap in onset patterns with depression; however, it shows markedly more overlap in terms of shared risk factors with anxiety disorders and has risk factors unique from both that relate to family climate and personality features.

**Reviewer’s Comments:** This study gives pause to thoughts from some investigators to group GAD more with depressive disorders; it reinforces instead pathogenetic links with anxiety disorders, but also underscores certain unique onset pathways of this, sometimes muddled but also in some ways reasonably distinct, condition. (Reviewer-Gary S. Belkin, MD, PhD, MPH).

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Keywords: Anxiety, Depression, GAD

Print Tag: Refer to original journal article
Based on recent trends in population levels of smoking and obesity, it is estimated that by 2020, the negative effects on life expectancy of obesity will outweigh the gains attributable to smoking.

**Objective:** The health of the U.S. population is increasingly reliant upon health conditions that reflect behaviors. For example, obesity and smoking account for a substantial amount of deaths and impact life expectancy. These 2 conditions have experienced opposite trends. What is the net effect of these opposing trends?

**Methods:** This study combined 3 national population survey instruments. It obtained rate-trends in national body mass index (BMI) through physical measures reported as part of the National Health and Nutrition Examination Survey (NHANES), with historical trends obtainable to identify BMI by gender for 1971 through 1975, 1988 through 1994, 1999 through 2002, and 2003 through 2006. The NHANES gathered specific information about trends with respect to smoking frequency during the 1978 through 1979, 1990 through 1991, 1999 through 2001, and 2004 through 2006 periods. The magnitude of the impact of smoking and obesity on health was estimated using the Medical Expenditure Panel Study, which included self-rated health status and function as well as smoking frequency and BMI, and the risks for each on death identified through life tables from the National Center for Health Statistics and the Social Security Administration and NHANES studies. These data were analyzed in a stepwise fashion to first establish and project trend rates for each condition, then to estimate relative risk of death and disability from these conditions, and then to generate life tables extrapolating overall mortality and disability trends tied to the changing rate estimates.

**Results:** During the 15 years before 2005, overall smoking prevalence decreased by 1.4% per year, and obesity increased by 0.5% per year. Forecasted trends, then, for 2005 through 2020 are that the portion of the population smoking will decline by 21%, but that the share of the population with normal weight will decline by 35%, with 45% of the population considered obese by 2020. Therefore, the net effect of these 2 trends is actually an overall decline in life expectancy (0.71 years) and quality-adjusted life expectancy (0.91 years). Eliminating both smoking and obesity would have a remarkable effect of extending life expectancy by 3.76 years and quality-adjusted years by 5.16 years.

**Conclusions:** Increasing trends in obesity will reduce life expectancy and quality-adjusted life-year expectancy in ways that outweigh gains expected from reduction in smoking and those associated health effects.

**Reviewer’s Comments:** The implication of this research is that there lies the potential to actually reverse overall population health gains in life expectancy since the early 20th century due to a sustained increase in obesity to remarkable levels. This challenge affects all aspects of behavioral health sciences—not only individual treatments and the challenges of scaling them up, but also the kinds of population level interventions (commodity regulation, incentives, public education messaging) that have been responsible for declines in smoking. (Reviewer-Gary S. Belkin, MD, PhD, MPH).
A medical care management program implemented in a CMHC appears effective in enhancing the impact of and access to primary medical care for patients with severe mental illness.

**Background:** The problem of premature mortality among individuals with serious mental illness due to a higher risk of medical comorbidities is now well known and receiving widespread attention and concern. With that said, there remain few evidence-based approaches to improve primary medical care in community mental health center (CMHC) settings. Care management (the use of a functional coordination, education, treatment engagement, and brief intervention role to a "mid-level" care manager) has shown increasing effectiveness in managing a range of chronic disease conditions.

**Objective:** To describe a model of using medical care managers in a CMHC setting.

**Methods:** Eligible subjects were among outpatients seen at an urban Atlanta CMHC. Patients were randomized to usual care or the assignment of a care manager. The care manager was one of 2 full-time registered nurses following manualized protocols for the screening, follow-up, and monitoring of target conditions. Managers used motivational interviewing, educational, and action plan materials and techniques to engage individuals in medical care participation, follow-up, and other health-promoting behaviors. Charts and interview content were used to assess the quality of care to the degree primary medical care met 23 indicators established by the U.S. Preventive Services Task Force. In addition, patients with established cardiometabolic conditions had their care evaluated using the RAND Community Quality Index; their severity of illness was rated along the Framingham Cardiovascular Risk Index based on their medical profiles. A standardized measure of quality of life was also administered.

**Results:** 407 subjects were randomly assigned. Over the 12-month period, the average proportion of indicated preventive services doubled among the intervention group to 58.7% but remained almost unchanged (21.8%) in the comparison group. The intervention group experienced twice as many physical examinations (70.5% vs 35.6%) and screening tests (50.4% vs 21.6%), 4 times as many educational interventions, and >6 times as many indicated vaccinations (24.7% vs 3.8%). In just 1 year's observation, these changes resulted in significantly increased rates of sustained use of a provider of primary care, increased quality of life scores, and reduction in the Framingham Risk Index scores.

**Conclusions:** A medical care manager role included in a CMHC significantly improved the likelihood of receiving guideline-indicated primary medical care, compliance with care, reported quality of life, and a reduction of cardiovascular risk.

**Reviewer’s Comments:** This could prove to be a feasible and cost-effective approach to integrating needed primary medical care within the treatment of seriously mentally ill by relying on dedicated "bridges of care" rather than trying to fully integrate specialist providers of care. (Reviewer-Gary S. Belkin, MD, PhD, MPH)

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Keywords: Medical Care Management, Mental Illness, Medical Comorbidity

Print Tag: Refer to original journal article
Use of an 8-question personality inventory helps predict 6-week antidepressant treatment response.

**Background:** The influence of personality on treatment response of depression remains controversial, with multiple reviews and meta-analyses arriving at different conclusions. It also remains poorly understood whether personality traits contribute to or are the result of recurrent depressive episodes.

**Objective:** To address this question utilizing data from a large French outpatient sample (n=9515) originally aimed at investigating the cognitive effects of major depressive disorder as defined by DSM-IV criteria.

**Participants/Methods:** Patients with a primary DSM-IV diagnosis of major depression disorder were included in the study. Personality traits were assessed in a brief screening interview using the Standardized Assessment of Personality – Abbreviated Scale (SAPAS), consisting of 8 yes/no descriptive questions reflecting core attributes of personality disorders, such as "Do you have trouble making and keeping friends?," "Do you have trouble trusting others?," and "Do you depend on others a lot?" The "yes" answers are summed to yield a total score from 0 to 8. An antidepressant was prescribed after initial assessment, and follow-up occurred 6 weeks later. Response was defined as a 50% reduction in the Hospital Anxiety and Depression Scale score. Data were analyzed using the Pearson test, and structured equation modeling with SAPAS score as an ordinal variable (below or above 4).

**Results:** The mean initial SAPAS score was 3.82; 86.5% of the sample completed the follow-up assessment (n=8229). The response rate was 29.5% over the 6-week period. Responders were more likely to be younger, male, single or married versus divorced or widowed, well educated, and have a shorter duration of depression and fewer past episodes. The SAPAS score was inversely associated with treatment response, with higher scores associated with nonresponders. The SAPAS score was also significantly correlated with the number of past episodes and episode severity. In structure equation modeling, the negative effect of past episodes on treatment response appeared to be mediated in large part by the SAPAS score.

**Conclusions:** The authors concluded that personality factors play a central role in initial depression treatment response, but they were unable to determine whether these factors represented a vulnerability to depression or a result of repeated depressive episodes (kindling).

**Reviewer's Comments:** The authors used a cutoff of 4 on the SAPAS scale as an indicator of high/low scores. Somewhat surprisingly, the mean was very close to this cutoff at 3.82, perhaps contributing to the low response rate overall. This study did not include a control group; therefore, it is unknown to what extent the response rate is attributed to a placebo effect. Still, I was interested in this article primarily for its use of a brief personality screen to help predict short-term antidepressant response in outpatient practice, which might be useful in guiding treatment in time-limited settings. (Reviewer-Charlotte O. Ladd, MD, PhD).

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Keywords: Depression, Personality Disorder, Treatment Response

Print Tag: Refer to original journal article
Lack of Fear Response as a Toddler May Lead to Adult Antisocial Behavior

Association of Poor Childhood Fear Conditioning and Adult Crime.
Gao Yu, Raine A, et al:

Am J Psychiatry 2010; 167 (January): 56-60

Poor fear conditioning in 3-year-old children appears to be associated with criminal behavior by young adulthood.

**Background:** Poor autonomic fear conditioning is a well-replicated correlate of adult criminal and psychopathic adult criminal offending. It is hypothesized that individuals learn to avoid antisocial acts by associating stimuli that are associated with antisocial events with later socializing punishments. This associated learning should result in anxiety and anticipatory fear whenever the individual contemplates committing an antisocial act, which in turn motivates the individual to avoid these stimuli and the commission of antisocial, rule-breaking behavior. Within this framework, poor conditionability, as measured by reduced response to the reinforced conditioned stimulus followed by the aversive stimuli compared to a control stimulus not followed by an aversive event, may give rise to criminal acts in some individuals.

**Objective/Participants:** The research team measured classically conditioned emotional responses at age 3 years in a birth cohort of 1,795 children and followed them up after 20 years to assess outcome for criminal convictions at age 23 years. The authors of this article hypothesize that compared to non-criminals, criminal offenders at the age of 23 would show reduced fear conditioning at age 3.

**Methods:** The participants were from Mauritius, a tropical island in the Indian Ocean. The ethnic makeup of the cohort was mostly Indian. The children were then exposed to a conditioning paradigm that involved pleasant and unpleasant sound tones, while electrodermal data were collected via a polygraph machine. When the cohort was 23 years of age, official court records were searched for registration of offenses that included property, drug, violence, and serious driving offenses. A social adversity index was also formed from 9 variables assessed by social workers who visited the children's homes at age 3. The variables included parental education level, employment level, single-parent status, teenage mothers, parental separation, large family size, poor health of mother, and overcrowded home.

**Results:** A significant group-by-stimulus interaction indicated that the criminal offender group failed to show fear conditioning at the age of 3 years old. The criminal offender group and the comparison subjects did not differ significantly on the social adversity index.

**Conclusions:** A lack of fear conditioning in 3-year-old children appears to confer a risk for later criminal behavior by young adulthood, with no evidence pointing toward an association with socioeconomic variables.

**Reviewer's Comments:** This is a fascinating study that points to the possibility that decreased amygdala activity on functional imaging scans in adult psychopathic offenders, when presented with a moral decision, may be, in part, the result of certain genetic/early childhood neurobiological predispositions. Amygdala hyporesponsiveness has also been reported in children with callous-unemotional traits. (Reviewer-John G. Koutras, MD).

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Keywords: Criminal Behavior, Fear, Conditioning, Social Adversity

Print Tag: Refer to original journal article
Discussions about limiting alcohol advertising among TV time slots with high adolescent viewership may underestimate the impact such advertising also has when shown in markets with supposedly less adolescent viewership.

**Background:** Underage drinking is common and starts early. Data from 2005 estimate that 36% of ninth graders reported drinking in the prior 30 days, 33% of twelfth graders reporting binge drinking (≥5 drinks in 2 hours). Around 17.5% of all alcohol expenditures are apparently for underage drinkers. Advertising also seems strongly linked to these trends. A longitudinal study of seventh graders found exposure to alcohol advertising was associated with a markedly higher risk of heavy use. With kids aged 8 to 18 years, watching an average of 3 hours of TV per day, and increasingly on cable television, the marked increase as well in recent years of cable-based alcohol advertising, raises concerns, and resulted in voluntary industry restrictions on placing such advertising in programming or time slots especially represented by adolescent viewership, with a threshold of 30% of viewers being underage as the adopted cutoff for limiting such ads.

**Objective:** However, the authors here argue that such policies and preference for restrictions on those markets might underestimate the impact of exposure to advertising in "adult" time or programming slots that adolescents see.

**Methods:** The authors obtained viewership data from Nielsen Media Research. This database, which details programming and viewer characteristics for a representative sample of the population, allowed identification of every alcohol industry advertisement on cable television between 2001 and 2006, when they aired, which programming, and to relate that to the viewership characteristics at the time, such as, in this case, percentage of audience age 12 to 20 years, as well as a wealth of other sociodemographic information about viewers.

**Results:** During this time, alcohol industries placed 608,591 ads. In time slots when underage viewership was ≤30%, every 1% increase in adolescent viewership was associated with an increase of 7% in the incidence of alcohol advertising. The association was even greater for female viewers. Programming where the adolescent viewership was predominantly female (55%), had around 50% more alcohol advertising than where the audience was <45% female.

**Conclusions:** Alcohol advertising increased as adolescent viewership increased from 0% to 30%, especially when the viewers were women. Underage viewers were thus exposed to more advertising than would be expected through incidental exposure to ads aimed only at an older audience.

**Reviewer's Comments:** The authors draw from this work the policy point that trying to limit advertising to programs exceeding a 30% threshold of underage viewers does not adequately limit the exposure to or apparently, the implied effort to target placement of (implied by association though not proven) such ads to those viewers. (Reviewer-Gary S. Belkin, MD, PhD, MPH).

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Keywords: Alcohol Advertising, Adolescents

Print Tag: Refer to original journal article
Adolescents who self-identify as GLB are more likely to have higher rates of sexual activity and substance abuse, depressed mood, and have at least a 2 to 3 times higher rate of suicidal ideation than their heterosexual peers.

**Background:** For gay, lesbian, and bisexual (GLB) adolescents, the lifetime risk of suicide attempt is between 20% and 40%, approximately 2 to 6 times that of non-GLB adolescents. GLB adolescents report higher rates of risk factors for suicidal behavior, including depression, anxiety, and alcohol/substance abuse. Even after controlling for these typical risk factors, GLB sexual status is independently associated with suicidal ideation and attempt. Some have proposed that adolescents with same-sex attraction/fantasy or behavior, but heterosexual identity, differ in important ways from both heterosexual-identified youth without same-sex attraction/fantasy or behavior and GLB-identified youth and that they may not be at risk for poor mental health outcomes. However, no studies have specifically examined risk for suicide behavior for these different groups.

**Objective:** To compare the risk of suicidal ideation and attempts separately in 4 groups of adolescents, controlling for traditional risk factors: (1) adolescents who reported heterosexual identity without same-sex attraction/fantasy or behavior; (2) adolescents with GLB sexual identity; (3) adolescents with unsure sexual identity; and (4) adolescents with heterosexual identity and same-sex attraction/fantasy or behavior.

**Methods:** 1856 Canadian adolescents completed the Quebec Youth Risk Behavior Survey (QYRBS), with additional items related to sexual orientation and same-sex attraction/fantasy and behavior.

**Results:** 1624 of the students (87.5%) reported heterosexual identity without same-sex attraction; 3.1% identified as GLB, 3.2% identified as unsure, and 6.2% reported heterosexual identity but same-sex attraction/fantasy or behavior, including 1.8% who reported same-sex behavior). Students with a GLB identity were significantly more likely to report a depressed mood. In multivariate analysis, after adjusting for depressed mood, abuse histories, etc, students with a GLB identity and students with unsure identity were almost 2 to 3 times more likely to report suicidal ideation compared to students with heterosexual identity without same-sex attraction/fantasy or behavior. Students with heterosexual identity and same-sex attraction/fantasy or behavior were not at significant risk.

**Conclusions:** Dichotomizing sexual orientation into GLB versus heterosexual may not accurately capture the nature of risk related to GLB status.

**Reviewer's Comments:** Although multivariate analyses, such as that employed in this study, help to "sterilize the field" of other confounding associations, they also do not accurately represent patients we may encounter. For example, in this study, the GLB group had higher rates of substance abuse, physical and sexual abuse history, and depression, which, when taken together, place them at an almost 5 times greater risk of suicidal ideation. (Reviewer-John G. Koutras, MD.)
**Measuring Outcomes for Depression -- What Is Useful?**

**Advantages of Using Estimated Depression-Free Days for Evaluating Treatment Efficacy.**

Vannoy SD, Arean P, Unützer J:

Psychiatric Serv 2010; 61 (February): 160-163

DFD measures can be derived from symptom scale scores in depression outcomes studies and might provide a more real-world feedback value to clinicians and patients as to the effectiveness of treatment.

**Background:** Symptom rating scales, used for tracking outcomes of treatment, have been developed and are often used primarily within the context of research on the efficacy of treatments. Measures such as the relative statistical magnitude of decline in a Hamilton depression score, for example, might provide a construct-based measure of comparative efficacy, but may not be so clearly related to the lived experience of patients from which to draw practical conclusions as to their improvement in every day clinical care decisions. Also, such measures do not translate well into describing impacts related to cost-effectiveness, what the "improvement" reflects about a patient's capabilities, impact on life, etc. The measure of "depression-free days" (DFDs) has emerged as a possible measure that might help to capture a more practical window on patient benefit and experience and allow cost-benefit information. Roughly, this means what it says—the number of days over a given period that were spent "free" of threshold depression. Such estimates are based on mathematical estimates of days based on interval score changes. Therefore, the more frequent symptom scores are available and the smaller the interval of symptom level and change that is available, the more accurate these estimate-averages can be.

**Objective:** To determine the feasibility and accuracy of making such DFD estimates by using a commonly used scale in both research and practice, the Patient Health Questionnaire (PHQ-9), and a common research outcome tool, the Hopkins Symptom Checklist (HSCL-20).

**Methods:** Data from a large study of collaborative care for depression gathered regular interval outcome scores for patients in treatment for major depressive disorder using both the PHQ-9 and the SCL-20. DFDs were calculated using these scores at different intervals.

**Results:** DFD measures were similar across these measures, but increased with the increased number of assessment points (as expected). DFDs went from 153, with 2 SCL-20 assessments, to 197 with 3, and 204 with 4. For the PHQ-9, the days estimated increased from 200 to 265. Thus, while increased data points gathered across the 12 months of observed treatment led to increased estimates and presumably improved accuracy, the rate of increase started to level off after 4 measures. So, 16 PHQ-9 assessment points yielded 273 DFDs, only 3% different from that estimated with 4 points.

**Conclusions:** DFDs appear to be a practicable and perhaps more compelling way to frame clinical scale outcomes data using a modest frequency of scoring.

**Reviewer's Comments:** While a purpose of this exercise was to see the feasibility of generating a more "relatable" scored outcome that spoke more practically to clinicians and patients, the actual impact (use and added value of this measure as reported by clinicians and patients) was not assessed. (Reviewer-Gary S. Belkin, MD, PhD, MPH).

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Keywords: Treatment Efficacy, Depression-Free Days

Print Tag: Refer to original journal article
Exercise, Neurogenesis, and Schizophrenia

Hippocampal Plasticity in Response to Exercise in Schizophrenia.

Pajonk F-G, Wobrock T, et al:
Arch Gen Psychiatry 2010; 67 (February): 133-143

Exercise may enhance hippocampal volumes in a way that translates into cognitive benefits for patients with schizophrenia.

**Background:** Compared to other illnesses with psychotic features, such as bipolar disorder, schizophrenia is marked by the incomplete degree to which any such episodes resolve and by an associated persistent degree of disability. These features appear related to impaired neural plasticity or the ability for brain function to reorganize and "bounce back" from a challenge. Well-known hippocampal cell neuron and neurogenesis abnormalities in schizophrenic adults likely contribute to this impaired plasticity. However, hippocampal neurogenesis in healthy adults has been shown to be enhanced by exercise. Might it have not only the same effect, but also a broader cognitive and functional impact, on patients with schizophrenia?

**Objective:** To determine if increased exercise in humans is a stimulus to hippocampal plasticity.

**Methods:** Patients on stable antipsychotic medication, with a diagnosis of schizophrenia, were randomized to a program of exercise or to a control group. The exercise involved 30-minute sessions with careful measurement of parameters of lactate production, oxygen use, watt production, etc, so as to meet and measure exercise-level physiological performance. A healthy control group matched to demographics, IQ, body mass index, weight, and peak oxygen uptake, was also followed. Baseline and follow-up measures included psychotic symptom scale scores, MRI measures of hippocampal volume, and neuropsychological testing.

**Results:** Relative hippocampal volume increased significantly in patients (12%) and controls (16%) after exercise. There was no change in the control patient group. The hippocampal changes were directly related to improved aerobic consumption and to improved scores on short-term memory.

**Conclusions:** Hippocampal volume appears responsive to exercise in ways that may impact some features of cognitive function among patients with schizophrenia.

**Reviewer's Comments:** These very specific and proximate effects to exercise may or may not translate into changes in illness course or overall functional capabilities, but the links made, between exercise and plasticity and plasticity and some measurable cognitive change, are intriguing, and in some ways return us to very old advice about mental hygiene. (Reviewer-Gary S. Belkin, MD, PhD, MPH).

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Keywords: Hippocampus, Plasticity, Exercise, Schizophrenia

Print Tag: Refer to original journal article
Computer-assisted cognitive remediation may improve targeted outcomes tested in research, but less clearly the functional capabilities of patients.

**Background:** While a previous paper (“Hippocampal Plasticity in Response to Exercise in Schizophrenia”) looks at the possible value of literally exercising the brain so as to bolster cognitive function in schizophrenia, for some time, there has been interest in and dissemination of the practice of cognitive remediation (ie, "exercising" the brain through problem skills, drills, memory and other tasks primarily through computer-assisted programs, puzzles and tasks) much of which originated in work with patients recovering from traumatic brain injury. And while significant literature has emerged that assesses these interventions, uncertainty as to the value of these methods remains.

**Objective:** The authors argue here that some problems with earlier research especially include the varying degree that studies test outcomes specific to the tasks themselves or narrowly defined cognitive domains as opposed to functional capabilities or broader neuropsychological functioning.

**Methods:** Eligible patients had verified diagnoses with schizoaffective disorder or schizophrenia and were randomly assigned to computer-assisted cognitive remediation programs that targeted daily performance skills through staged difficulty tasks emphasizing choosing, executing, and self-monitoring cognitive, problem-solving tasks. The main outcomes were success in remediation tasks, standardized broader “composite” measures of neuropsychological testing apparently better reflecting broader functional capabilities (memory, processing, executive functioning), and proxy reports of community functioning.

**Results:** While subjects improved on 8 out of 10 of the exercise-specific tasks as measures of performance, there was no significant advantage of the intervention versus control condition in terms of any of the composite neuropsychological or functional outcome measures.

**Conclusions:** In this study, subjects improved on exercise tasks, but that did not appear to generalize to broader neuropsychological or functional outcomes.

**Reviewer's Comments:** If cognitive remediation exercises only improve performance on cognitive remediation exercises, then their use is thrown into question. The issue of only measuring practice effects of techniques has long plagued work in using such techniques to enhance performance. The jury is probably still out, but perhaps a focus on a more broad and practical impact could in turn develop different interventions and weed out more effective interventions from a proliferating menu of possibilities. (Reviewer-Gary S. Belkin, MD, PhD, MPH).

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Keywords: Cognitive Remediation, Outcomes

Print Tag: Refer to original journal article
Low VLPFC activity response to partner conflict appears to place an individual at higher risk for a depressed mood and substance use.

**Background:** Self-regulation of emotion and behavior occurs through the use of cognitive skills, such as interpretation, attention, and inhibition. It is well established that these cognitive skills are mediated by a network of neural regions in which the ventrolateral prefrontal cortex (VLPFC) is a major component. Dysfunction in the VLPFC has been observed in multiple psychiatric disorders, such as unipolar and bipolar mood disorders, borderline personality disorder, and substance abuse.

**Objective:** To investigate the proposed model that VLPFC dysfunction may be a biological vulnerability, or diathesis, that interacts with a stressor, such as an interpersonal conflict, to produce problematic mood and behavioral symptoms.

**Methods:** The 27 participants were comprised of 11 couples in dating relationships for at least 3 months and 5 other individuals who were in similar relationships. The participants reported no neurological or psychiatric illness. Subjects viewed pictures of their partner, themselves, and an opposite-sex stranger in 3 facial expression conditions (negative, positive, and neutral). During a functional magnetic resonance imaging (fMRI) scan, participants rated on a scale how each picture made them feel. Neural activity in response to partner-negative versus partner-neutral expressions was expected to be the strongest predictor of self-regulation after conflict. The participants maintained a diary where they recorded whether or not they had a conflict with their partner, and rated (on a scale) the extent to which the conflict was resolved and the extent to which they felt positive and negative mood and engaged in rumination and substance use. The hypothesis was that on days preceded by conflict, low VLPFC activity (or "hypofunctioning" in conflict/mood resolution) would be related to higher levels of overall negative mood, rumination, and substance abuse.

**Results:** The investigators examined VLPFC activity and mood and behavior for days in which no conflict occurred the previous day and then separately for days in which a conflict had occurred the previous day. On days when no interpersonal conflict was reported the previous day, there was no association between VLPFC activity and the participant's mood or substance abuse. However, on days following interpersonal conflicts, participants with lower VLPFC had higher overall negative mood, more rumination, and more substance use.

**Conclusions:** VLPFC activity in response to a laboratory-based affective challenge (negative facial expressions from a partner) predicts the ability to regulate mood and behavior after a real-life affective challenge (an interpersonal conflict with that partner).

**Reviewer's Comments:** This novel imaging study has very promising findings. It is not clear, however, whether those findings translate into actual mental health disorders. (Reviewer-John G. Koutras, MD).

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Keywords: Interpersonal Conflict, Prefrontal Cortex, Depressed Mood

Print Tag: Refer to original journal article
Little Evidence for “Baby Brain” in Young Moms

Cognition in Pregnancy and Motherhood: Prospective Cohort Study.

Christensen H, Leach LS, Mackinnon A:

Br J Psychiatry 2010; 196 (February): 126-132

Pregnancy does not generally worsen cognitive function in young, primiparous women, but it may reduce processing speed after 20 weeks.

**Background:** The lore that pregnancy impairs cognitive function in humans stems from cross-sectional studies and systematic reviews. In contrast, cognitive function in lower mammals appears to improve during pregnancy. For example, pregnant or parous rats outperform their nulliparous counterparts in various memory tasks.

**Objective:** To examine cognitive function in humans prospectively in order to address this issue at an individual level, hypothesizing that both pregnancy and motherhood would worsen cognitive performance.

**Participants/Methods:** The authors utilized a young cohort (age range, 20 to 24 years) recruited from the electoral roll in Australia for the Personality and Total Health Through Life Project in 1999. A total of 1241 women were included in this sample and were followed for 8 years (85% retention). Four domains of cognitive function (cognitive speed, working memory, immediate recall, and delayed recall) were tested at baseline, in 2003, and in 2007. Seventy-six women were tested while pregnant at the second or third time point; 188 were tested as mothers, ranging from days to years’ postpartum from their first child. Only first-time mothers were included in the analyses. Results were analyzed using repeated measures of one-way analyses of variance (ANOVA) with group and time point as factors. Effects of pregnancy were further subdivided into early and late pregnancy.

**Results:** In general, cognitive performance improved over time in most groups, likely from learning with repeated testing. There were 2 exceptions to this trend: (1) women who were pregnant at time 3 exhibited poorer working memory than those who remained nulliparous; and (2) women in the second half of pregnancy at time 2 or 3 exhibited a decline in cognitive speed from previous testing, whereas women who remained nulliparous showed an improvement in processing speed.

**Conclusions:** In young, primiparous women, pregnancy and new motherhood does not generally worsen cognitive function, although decreased processing speed was observed in the second half of pregnancy as was poorer working memory in older pregnant women (aged 28 to 32 years).

**Reviewer's Comments:** Although this is a large cohort study, the results are limited by the relative youth of the cohort, the small number of women actually tested while pregnant (n=76), and the fact that the data analysis was limited to primiparous women. Repeated testing also added an element of learning evidenced by the fact that most groups improved over time on each cognitive measure. Furthermore, the authors had no information on participants’ medication use, stress, or sleep during testing, which may have confounded results. In contrast to rat studies, pregnant women did not outperform nonpregnant women. Although this study may provide reassurance to young expecting mothers, it does not end the debate about "baby brain" given that it excluded those most likely to suffer cognitive deficits (ie, older multiparous moms). (Reviewer-Charlotte O. Ladd, MD, PhD).

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Keywords: Pregnancy, Cognitive Function

Print Tag: Refer to original journal article
Pathological gamblers with bankruptcy histories are distinct from those without bankruptcy in the early and rapid progression of their gambling and their higher rate of mental health comorbidity.

**Background:** Research studies estimate that 0.4% to 1.6% of the U.S. population suffers from pathologic gambling (PG). There is little research, however, on the relationship between PG and personal bankruptcy. One study demonstrated that 19% of pathologic gamblers have filed bankruptcy, whereas only 5.5% of low-risk and 4.7% of at-risk gamblers have done so. Bankruptcy may be an important symptom in PG as it may be a behavioral marker of a more severe variant.

**Objective:** The authors of this study from the University of Minnesota examined the clinical characteristics of individuals with PG who have and have not declared bankruptcy because of their gambling.

**Participants/Methods:** 517 subjects >18 years of age and meeting DSM-IV criteria for PG were included in the sample. PG severity was measured using the Yale-Brown Obsessive-Compulsive Scale Modified for Pathological Gambling (YBOCS) and the Gambling Symptom Assessment Scale. Psychosocial functioning was assessed using the Sheehan Disability Scale. A semi-structured interview was utilized to obtain each subject’s history of first-degree relatives’ gambling and alcohol use.

**Results:** 93 subjects (18%) from the sample had declared bankruptcy because of gambling. Of those who declared bankruptcy, the mean amount of debt at the time of bankruptcy was $33,086. Individuals with PG and a bankruptcy history were significantly more likely to be single (41% vs 27%). No other significant demographic differences were found, including gender. Interestingly, in the measures of gambling severity, such as in the YBOCS for PG, gambling severity was not significantly different in the PG with bankruptcy group compared to those without bankruptcy. However, the PG subjects with bankruptcy reported an earlier age at which gambling became problematic and progressed from first gambling to problematic gambling significantly faster. They also gambled significantly fewer hours per week. The PG with bankruptcy group had significantly greater rates of depressive and substance use disorders, as well as having a first-degree relative with an alcohol use disorder.

**Conclusions:** Problem gamblers who had declared bankruptcy have an earlier age of problem gambling onset, more problems associated with their gambling (financial, marital and occupational), and a greater likelihood of a family history of alcohol use disorders.

**Reviewer's Comments:** Interestingly, PGs who had declared bankruptcy did not lose a greater percentage of their income gambling, did not spend more time gambling, or have a greater severity level of gambling. However, the bankruptcy group had a higher rate of mental health and substance abuse comorbidity. (Reviewer-John G. Koutras, MD).

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Keywords: Pathological Gambling, Alcohol Use

Print Tag: Refer to original journal article