

Strict Elimination Diet May Be Effective in Treating ADHD Children

A Randomised Controlled Trial Into the Effects of Food on ADHD.

Pelsser LMJ, Frankena K, et al:

Eur Child Adolesc Psychiatry; 18 (January): 12-19

A 5-week "exclusion" diet appears to produce marked reductions in parent and teacher rated ADHD, although results may be subject to bias by non-blind assessments.

Background: Dietary studies using restricted food (elimination diet) have shown some evidence of efficacy in the treatment of attention deficit/hyperactivity disorder (ADHD) in selected subgroups (eg, those with food sensitivity or atopic disorder). While a previous small open trial has previously shown significant symptom reductions in unselected children with ADHD, controlled trials of benefits of dietary interventions are lacking.

Objective: To assess the efficacy of a restricted elimination diet in reducing symptoms in an unselected group of children with DSM-IV ADHD.

Design: Randomized controlled trial.

Interventions: 5 weeks of a restricted foods elimination diet or a wait-list control condition.

Participants: 27 children (aged 3 to 8 years) with DSM-IV ADHD, combined or hyperactive/impulsive type.

Methods: Subjects were assigned randomly to either an intervention group (15) or a waiting-list control group (12). After a 2-week baseline period during which subjects continued their usual diet and parents completed food diary measures, children assigned to the restricted diet ate only rice, turkey, lamb, vegetables, fruits, margarine, vegetable oil, tea, pear juice, and water. Subjects were assessed at baseline and at week 9 using parent and teacher ratings on the Conners Scale and the ADHD Rating Scale (ARS).

Results: The intention-to-treat analysis showed that the proportion of subjects in the intervention group rated as clinical responders (a decrease in the baseline score for both the Conners and ARS 50%) was significantly larger than that in the control group (parent, 73% vs 0%; teacher, 70% vs 0%). There were very large effect sizes for active treatment on both the abbreviated Conners (parent $d=2.8$; teacher $d=2.4$) and the ARS (parent $d=2.1$; teacher $d=2.5$) Eighty percent of the sample had comorbid oppositional defiant disorder at baseline. Dietary restriction also produced a large effect size ($d=1.1$) on comorbid oppositional defiant disorder (ODD) symptoms measured by a parent-report structured interview. At week 9, there were fewer subjects in the intervention group who met criteria for ODD than in the control group (27% vs 83%).

Conclusions: A strictly supervised elimination diet may be effective in treating children with ADHD. Further research on the extent to which dietary factors are important in the etiology and management of the disorder is needed.

Reviewer's Comments: Neither parents nor teachers were blind to group status since they were required to supervise the child's diet throughout the day. This may have resulted in inflated effect sizes due to expectancy bias. Replication should require independent, blind evaluations of outcome, together with more objective measurements of motor behavior and executive functioning. Despite the intensive nature of the diet and supervisory requirements, only one subject in the intervention group dropped out due to burden. It is unclear whether observed benefits are maintained long term and if compliance with a restricted diet is possible for extended periods.

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Deterring Malingered Psychopathology

Deterring Malingered Psychopathology: The Effect of Warning Simulating Malingeringers.

King J, Sullivan KA:
Behav Sci Law; 27 (1): 35-49

In some contexts in Australia, malingering is considered fraud, which is also considered a criminal act.

Background: The majority of research on malingering centers on methods of detection. However, as individuals become savvier about the symptoms of mental illness and the psychological tests involved, it seems unlikely that there will ever be a foolproof malingering test. What may be more likely, and certainly more practical, is focusing more effort on developing ways to minimize or deter the behavior. Warning individuals that a test is designed to "catch fakers" has shown promise in this area, but another method of deterrence—punishment—has not been adequately tested.

Objective: To assess whether warning individuals about sanctions for malingering on personality and psychopathology screening measures would deter that behavior.

Participants/Methods: 67 psychology students at a university in Australia were recruited for the study by offering course credit for participation. Most students were female, in their mid-20s, and had no history of mental illness. The self-report Personality Assessment Inventory (PAI) and Symptom Checklist 90 (SCL-90) tests were administered after participants had been randomly assigned to 1 of 3 groups: those who were told to fake symptoms in order to obtain \$100 (the unwarmed malingeringers); those who were told about the cash incentive, but also told that the tests could detect malingering and course credit would be revoked if anyone was found faking (the warned malingeringers); and those told to perform their best with a chance to win \$100 (the control group).

Results: On the PAI, warned malingeringers produced lower scores on psychopathology and personality scales than unwarmed malingeringers, with the exception of mania and antisocial features. There was little attempt to fake these symptoms. Similar results were found on the SCL-90, with the exception of obsessive-compulsive disorder. In general, the symptoms reported by warned malingeringers were very similar to those in the control group. The reported psychopathology of unwarmed malingeringers was significantly greater than controls.

Conclusions: The implementation of a malingering warning and threat of punishment appeared to deter simulated malingeringers to the point where they resembled individuals who were not trying to malingering.

Reviewer's Comments: This was an elegant study that kept my attention all the way through, even though I am not sure I agree with the potential implications of the research. Even though it was performed on university students without major incentives to lie, it demonstrated that, in a relatively healthy population, the threat of sanctions or punishment can reduce lying. This is a component of deterrence theory for crimes, but I do not know if it should be used in patient care. Even psychological testing for malingering can be an opportunity for therapeutic intervention, and threatening patients seems to ruin that opportunity.

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Link Between Community Violence and Mental Disorder

The Intricate Link Between Violence and Mental Disorder: Results From the National Epidemiologic Survey on Alcohol and Related Conditions.

Elbogen EB, Johnson SC:
Arch Gen Psychiatry; 66 (February): 152-161

While violence is more likely among those with severe mental illness, this appears to be due to other factors that also happen to be related to illness, especially comorbid substance disorder.

Background/Objective: Research into the links between mental illness and violence has a very long history. The authors of this study used the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), which was a longitudinal, nationwide survey with subsequent follow-up interviews, to look at mental illness at baseline and subsequent violence episodes of various types in a large, representative population.

Methods: NESARC was a face-to-face random sample survey of almost 35,000 Americans. It consisted of 2 separate, sequenced structured interviews that included a DSM-IV diagnostic interview to determine lifetime and recent diagnosis of major depression, schizophrenia, bipolar disorder, and/or substance disorder. Subjects were also asked about a range of historic, sociodemographic, and circumstantial factors already known to be associated with violence risk, such as early life exposure to violence, recent unemployment, marital status, and family history of violence. In the second interview, subjects were asked detailed questions about a range of violent behaviors in the intervening period.

Results: 41.68% of the sample had a lifetime diagnosis of a disorder including substance abuse and/or dependence: 21.41% had substance disorders; 10.87% had schizophrenia, bipolar, or major depression only; and 9.4% had one of these comorbid disorders with a substance disorder. Having severe mental illness was associated with greater risk of any violence but only significantly so when accompanied with a substance disorder. A number of factors independently predicted any later violence, including younger age, male gender, lower income, history of violence or watching parental fighting, juvenile detention, perception of threat from others, history of physical abuse by a parent, comorbid disorders, recent victimization, unemployment, divorce or separation in the past year, and reported perception of threat from others. For reported violent acts rated as serious/severe, predictive factors were more limited: younger age, male gender, victimization, unemployment or looking for work in the past year, parental physical abuse, comorbid disorders, substance-only disorders.

Conclusions: Severe mental illness is associated with violence, but mental illness alone does not predict violence. Instead, certain factors that are common among those with illness may predict violence, such as low income, unemployment, comorbid substance use, physical abuse, and juvenile history of violence.

Reviewer's Comments: The study helps narrow some of the key minimum features of an assessment of violence, especially the importance of clinicians to maintain careful assessments of comorbid substance disorders in all patients (particularly those with more severe illness such as major depression, schizophrenia, and/or bipolar disorder).

Additional Keywords: Comorbid Disorder

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Intervention May Reduce Adolescents' Online Display of Sexual Behavior

Reducing At-Risk Adolescents' Display of Risk Behavior on a Social Networking Web Site: A Randomized Controlled Pilot Intervention Trial.

Moreno MA, Vanderstoep A, et al:

Arch Pediatr Adolesc Med; 163 (January): 35-41

A simple email intervention can reduce the display of sexual information (text/photos) on the public MySpace profiles of adolescents (especially females).

Background: Teenagers frequently display information on social networking sites such as FaceBook and MySpace regarding sex, drug use, alcohol use, and other indicators of risk behavior.

Objective: To determine whether an online intervention will reduce references to sex and substance abuse on MySpace by adolescents.

Design: Randomized controlled trial.

Participants: 190 individuals (58.4% male) with a reported age of 18 to 20 years and a public MySpace profile that contained references to drug/alcohol use and/or sexual behavior.

Interventions: A single email was sent from Dr Meg (an adolescent health doctor with a MySpace profile) warning about the public nature of the information within the adolescent's MySpace profile and warning about the dangers of unprotected sex.

Methods: Eligible subjects' profiles needed to contain 1 of at least 3 risk behaviors and a security setting of public. Changes in references to sex, substance use, and security settings were compared between intervention subjects and controls 3 months after the email intervention.

Results: At baseline, 54.2% of the participants' profiles referenced sex and 85.3% referenced substance use. At 3 months, compared with controls, a significantly greater proportion of subjects in the intervention group (13.7% vs 5.3%; $P = 0.05$) removed all references to sex in their profiles. There was no significant difference in the removal of references to substance use (26.0% vs 22%). While the proportion of profiles set to "private" at follow-up was higher in the intervention group (10.5% vs 7.4%), this was not significantly different. The proportion of subjects who made any change was 42.1% in the intervention group and 29.5% in the control group ($P = 0.07$). Logistic regression analysis adjusting for demographics and baseline risk behaviors indicated that the intervention group subjects were 4 times more likely to remove all references to sex than the control group subjects (OR, 4.2). Odds ratios were much larger for females (17.3) than for males (2.9). Subjects who were high reporters of substance use at baseline were much less likely to eliminate all references to substance use (OR, 0.2).

Conclusions: A brief email intervention using social networking sites appears to be able to reduce sexual references in the online profiles of at-risk adolescents.

Reviewer's Comments: This finding is important not only because a simple intervention could reduce displays of sexual information in public profiles (especially for females), but also because such displays have a number of potential adverse consequences in addition to online victimization. Colleges and employers may look unkindly on students with such information posted, and the online broadcasting of this content may normalize risky behavior among peers. The lack of an effect on substance use references may be related to the high baseline prevalence of such information (seen as very normal) or the content of the email (which focused on sexually transmitted diseases/pregnancy risk).

Additional Keywords: Risk Behavior

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How Does Nicotine Improve Memory?

Positive Effects of Nicotine on Cognition: The Deployment of Attention for Prospective Memory.

Rusted JM, Sawyer R, et al:

Psychopharmacology (Berl); 202 (January): 93-102

The mechanism of action of nicotine's improvement in memory and attention remains unclear.

Background: Nicotine has been proven to improve cognition, including attention and memory tasks. Prospective memory is the ability to recall and then do something that you had previously encoded as an intention. An example of this might be thinking you need milk and then remembering to get milk later in the day while at the grocery store. An ongoing debate in the literature is whether it actually takes attentional energy to remember to do something and whether there is a cost of prospective memory on current tasks (ie, does remembering to get milk impair your ability to remember the directions to the grocery store?). Regardless, it is true that nicotine improves prospective memory accuracy.

Objective: To explore how nicotine might improve prospective memory. Two mechanisms were tested: (1) improvement in working attention, and (2) improvement in processing physical attributes of a target (increased salience).

Methods: 2 experiments were conducted on healthy, nonsmoking, adult volunteers in the United Kingdom. In the first experiment, 33 volunteers were randomly and blindly assigned to receive nicotine or placebo nasal spray before performing a memory task involving sorting face cards while trying to remember the prospective memory intention of pressing a button whenever a "7" card appeared. In the second experiment, 60 volunteers underwent the same randomization and then performed a mental math task while trying to remember to push a bar whenever the number "2" appeared. Salience was tested in this experiment by having half of the "2s" in larger font.

Results: In the first experiment, reaction time was unaffected by nicotine, but nicotine did improve the accuracy of detecting a "7" card, the prospective memory target. Also noted in the first experiment was that the accuracy for the card sort was greatly improved without having to remember the prospective memory task. In experiment 2, there was only a small improvement in accuracy with nicotine. Salient targets ("2s" in large font) were detected significantly more frequently, but this was not related to nicotine administration.

Conclusions: Nicotine does not improve prospective memory by enhancing salience of targets or by improving working memory.

Reviewer's Comments: I had to read this article several times before I was able to summarize it accurately. There was a lot of psychological research jargon that made it difficult to read, but if you can get past that and translate it into plain English, it is fairly interesting. It seems important to wonder about nicotine's effects, especially since there is a natural decrease in memory performance with age. Nicotine, delivered safely, may be a relatively inexpensive way to boost that performance.

Additional Keywords: Cognition

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Financial Incentives to Stop Smoking Do They Really Work?

A Randomized, Controlled Trial of Financial Incentives for Smoking Cessation.

Volpp KG, Troxel AB, et al:

N Engl J Med; 360 (February 12): 699-709

Financial incentives enhance the likelihood of enrolling in and completing a smoking cessation program, and in maintaining abstinence from tobacco use.

Background/Objective: Smoking is the deadliest of addictions. Despite reduced smoking and wide acceptance of banning smoking from most areas of public life, smoking is still the leading preventable cause of premature death in the United States. Given that the estimated benefit in terms of health and productivity savings to businesses for each smoker who quits is \$3400, a strategy of large employers providing outreach and financial incentives to adhere to a smoking cessation program makes sense.

Methods: Recruitment at a large firm in the United States involved company intranet and on-site recruiting and information distribution on the opportunity for participation for current smokers in a cessation program. Interested subjects were randomly assigned to receive general information counseling about community-based programs and services in their area only, or to also receive \$100 for completion of such a program, an additional \$250 for confirmed cessation of tobacco use by a cotinine test within 6 months of enrollment, and an additional \$400 for continued verified cessation. Subjects who did not stop smoking at the first post-enrollment contact at 3 months had a chance to do so at a second 6-month follow-up. Thus, outcomes of continued cessation were identified at 9 or 12 months, and then again at 15 or 18 months after enrollment. Such outcomes were compared with those in the same intervals in the counseling-only comparison group.

Results: 878 subjects underwent randomization to counseling only and incentive-added groups. The incentive group experienced significantly higher quit rates than the information-only group at 9 or 12 months (14.7% vs 5.0% cessation rate) and at 15 or 18 months (9.4% vs 3.6%) after enrollment. The incentives also worked, in part, due to the fact that they were significantly more successful in retaining individuals for treatment; 15.4% of incentive members versus 5.4% of information-only members successfully enrolled in a cessation program completed the program (10.8% vs 2.5%) and stopped smoking at 6 months (20.9% vs 11.8%).

Conclusions: A strategy of workplace-based recruitment and financial incentives was significantly more successful than recruitment and information counseling only in getting smokers to participate and complete a cessation program, and to be smoke-free well over a year after enrollment.

Reviewer's Comments: While overall data find that such programs are cost-effective and exceed quit rates for people left to their own devices, the study remains sobering in terms of the continued drop-off during the observation period in sustained cessation, as well as the overall limited rates of cessation by the end of observation (<10%).

Additional Keywords: Financial Incentives

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How Often Is Deliberate Self-Harm Occur Related to Suicide?

How Often Does Deliberate Self-Harm Occur Relative to Each Suicide? A Study of Variations by Gender and Age.

Hawton K, Harriss L:

Suicide Life Threat Behav; 38 (December): 650-660

The reported ratio of attempted to completed suicide in the United States, regardless of age or gender, is 8:20.

Background: Deliberate self-harm (DSH) means intentional self-injury or self-poisoning regardless of any intent to die. This type of behavior is far more common than actual suicide, but can be just as alarming as it can end in suicide or increase one's risk of serious harm. Ratios of DSH to suicide are useful in determining suicide-risk assessments, but the ratios that are currently reported do not factor in differences in age or gender.

Objective: To examine the rate of DSH to suicide in a town in the United Kingdom. The authors' hypothesis was that there would be higher ratios in females than males, but that this difference would decrease with age.

Methods: All patients aged 10 years who presented to an Oxford hospital for DSH between 1995 and 2004 were included in the study. A database called the Oxford Monitoring System for Attempted Suicide was used. The rate of DSH was compared to the annual suicide rate (as determined from national statistics and death certificates) across different age groups. In addition, ratios were calculated using only 1 episode of DSH per individual in order to control for multiple episodes. Suicidal intent with each presentation to the hospital was measured using the Suicidal Intent Scale.

Results: 4705 individuals presented to the hospital with DSH in 10 years. Overall, the ratio of DSH to suicide was 36:1. It was much higher in females (87.9:1) than males (18.7:1). The ratio for teenagers of both sexes was >200:1 compared to 10:1 for those aged 60 years. The ratio for teenage females was 10 times higher than that for teenage males; however, the ratio for females aged 60 years was only double that of males of the same age.

Conclusions: The ratio of DSH to suicide decreased as individuals aged. The higher ratio in females than in males also decreased with age.

Reviewer's Comments: I did not find the results particularly surprising, but I was impressed with the amount of data collected over so many years. It was nice to see actual numbers associated with self-harm and suicide rates rather than just trends. The biggest issue is probably the generalizability to patients you might see in your private practice; these patients all presented to the hospital for their injuries. This almost assuredly underestimates the rates of self-injury. Also, the patients were all from Oxford. I do not know if there are any real differences between British and American citizens in terms of self-injury and suicide, but the ratios reported in this study were much higher than those in the United States.

Additional Keywords: Risk Assessment

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Correlates of Treatment-Emergent Mania

Correlates of Treatment-Emergent Mania Associated With Antidepressant Treatment in Bipolar Depression.

Frye MA, Helleman G, et al:

Am J Psychiatry; 166 (February): 164-172

Minimal manic symptoms in terms of motor activation, pressured speech, and language-thought disorder (ie, racing thoughts) predict treatment-emergent mania.

Background/Objective: The common challenge of depression and the use of antidepressants in bipolar patients in outpatient practice carry with it the risk of antidepressant-precipitated mania or, as it is often referred to, treatment-emergent mania. The study was an attempt to prospectively follow up patients and to assess a range of characteristics that might help clinicians predict those who do, versus those who do not, go on to develop mania.

Methods: Patients in the Stanley Foundation Bipolar Network were prospectively followed up for 10 weeks. All patients had DSM-IV bipolar I or II depression confirmed by structured interview, were being treated with a mood stabilizer or antipsychotic prior to the antidepressant trial, and had depression of at least moderate severity as identified through cut-off ratings on validated symptom scale measures. A range of clinical history and features and sociodemographic information were obtained for each patient. Patients were followed up and underwent repeat symptom severity assessments for changes in the degree of both depressive and manic symptom severity twice at a 1-week interval and then bi-weekly for an additional 8 weeks. Potential predictive characteristics of 3 groups were compared: those who developed treat-emergent mania or hypomania; those who did not respond to antidepressant treatment at all; and those who responded to treatment but did not have treatment-emergent mania or hypomania.

Results: 172 adults completed the trial; 44 had treatment-emergent mania, 84 responded well to the antidepressant, and 44 had no response. Age, gender, age at first symptom of bipolar illness, number of prior episodes, rate of rapid cycling or family history, comorbid substance or anxiety disorder, and use of concomitant mood stabilizer (neither dose nor number of agents) did not predict treatment-emergent mania. Data analysis, however, did find significant predictors in the pattern of symptom types as found on structured symptom severity assessment. Factor analysis of these data found that a subset of Young Mania Rating Scale scores (those indicating increased motor activity and speech, and thought disorder [eg, distractibility, racing thoughts]) predicted treatment-emergent mania.

Conclusions: Among a range of clinical, treatment, and sociodemographic features, predictors of treatment-emergent mania among a prospectively followed cohort of bipolar depressed patients treated with antidepressants were scored on dimensions of motor and speech activity and pressured thought (ie, distractibility, racing thoughts).

Reviewer's Comments: The study suggests that a good practice with depressed bipolar patients is to carefully assess certain dimensions of potential manic syndrome, specifically motor activation, pressured speech, and racing thoughts.

Additional Keywords: Correlates

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Trauma Treatment Must Be Individualized

Systematic Review and Meta-Analysis of Multiple-Session Early Interventions Following Traumatic Events.

Roberts NP, Kitchiner NJ, et al:

Am J Psychiatry Adv; (February 2): epub ahead of print

Approximately one-third of patients with acute PTSD go on to develop chronic symptoms.

Background: There is no strong consensus on the best treatment to prevent the development of chronic posttraumatic stress disorder (PTSD) following a traumatic event. Acute stress disorder and acute PTSD have been reported in roughly 20% of the population after various traumas, depending on the nature of that trauma. The standard of care used to be immediate debriefing following trauma, but that is now considered counter-therapeutic.

Trauma-focused psychotherapy has been used as an alternative for chronic PTSD and may offer a better outcome.

Objective: To better understand the efficacy and utility of multiple-session trauma-focused psychotherapy for the treatment and possible prevention of PTSD within 3 months of a traumatic event.

Design/Methods: A meta-analysis of randomized, controlled trials conducted through September 2007 was performed. Multiple databases and journals were searched using 40 keywords. Important researchers were contacted for any other studies. Articles included considered a single multiple-session intervention aimed at reducing or preventing symptoms in adults with PTSD or acute stress disorder. Two reviewers independently read the abstracts, and a third reviewer was used to settle any disagreements. The data from the studies were analyzed to look for any summary effects.

Results: 25 of a possible 250 studies were included: 8 studies evaluated brief psychosocial interventions within a month of a trauma; 15 studies evaluated varying interventions within 3 months of a trauma, including structured writing, trauma-focused cognitive behavioral therapy (CBT), and supportive counseling; and 11 studies examined treatments for people already diagnosed with acute stress disorder or PTSD. There was statistically significant support for trauma-focused CBT over counseling or being on a waiting list. However, this treatment was less effective for those who did not have full-blown PTSD or acute stress disorder.

Conclusions: There was no clear evidence that any single intervention is more effective over others for patients in the 3 months after a traumatic event.

Reviewer's Comments: The take-home point here is that we still do not know how to prevent or treat PTSD. The benefit of trauma-focused CBT was primarily for those who had actually been diagnosed with acute stress disorder or PTSD. Even though the Institute of Medicine advocates exposure therapy as the best treatment, this meta-analysis did not support that recommendation. I remember a lot of debriefing that took place in New York City after September 11, and we found out later that this was perhaps not the most useful intervention.

Additional Keywords: Early Intervention

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Does HIV Increase Incidence of Depression?

Characteristics of HIV-Positive Patients Treated in a Psychiatric Emergency Department.

Bennett WRM, Joesch JM, et al:
Psychiatr Serv; 60 (March): 398-401

Depression is twice as common in HIV-positive patients as in those without HIV.

Background: Patients with HIV often require expert psychiatric and medical care in emergency situations due to the complications of their disease. Given that there are >1 million persons with HIV in the United States, it is important to consider how best to provide appropriate emergency psychiatric services. While information has been published about HIV patients in inpatient, outpatient, and general emergency department settings, no one has described the population of HIV-positive patients presenting to a psychiatric emergency department.

Objective: To calculate the prevalence of HIV among patients treated in a psychiatric emergency department, and to describe the clinical and demographic characteristics associated with that population.

Methods: Data were collected from a quality assurance database, initiated in 1998, at a psychiatric emergency service in Seattle. Data on 58,301 visits and 28,817 unique patients were analyzed for this study. Demographic and clinical information was collected, including symptom severity, diagnosis, substance abuse issues, and housing status. HIV status was calculated at the visit level instead of the patient level in order to capture the information from repeat presenters. The primary outcomes were differences in demographic and clinical variables based on HIV status.

Results: 1.9% of the patients were HIV positive; 2% of the visits were by HIV-positive patients. HIV-positive patients were more often male, African-American, and/or homeless. Those with HIV were more likely to present with suicidal ideation or to have dementia, a borderline personality disorder, or a substance abuse disorder.

Conclusions: HIV-positive patients in a psychiatric emergency setting were more likely to have borderline personality disorder, present with suicidal thinking, or have a substance abuse disorder than those without HIV.

Reviewer's Comments: The HIV prevalence rate quoted in this study of 2% is similar to that of outpatient psychiatric departments and general emergency settings. It is much lower than the rate on inpatient units, roughly 5%. There may be an association with HIV and severe mental illness that would explain this finding. However, the bottom line here seems to be that HIV-positive patients may have more specific needs than other populations, such as those struggling with dementia or suicidality. For example, it would make sense that emergency psychiatrists might want to make sure to conduct mini-mental status examinations on all HIV patients.

Additional Keywords: Emergency Department

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Aripiprazole as Effective as Haloperidol in Tx of Acute Mania

Aripiprazole Monotherapy in Acute Mania: 12-Week Randomised Placebo- and Haloperidol-Controlled Study.

Young AH, Oren DA, et al:

Br J Psychiatry; 194 (January): 40-48

Aripiprazole and haloperidol are similarly effective as monotherapy for the treatment of mania in patients with bipolar I disorder.

Background: Aripiprazole is a widely used second-generation antipsychotic (SGA) with partial D2, D3, and 5-HT1A agonism, and 5-HT2A antagonism. It has shown efficacy as an adjunctive treatment for depression, and has also (as with other SGAs) shown effectiveness in bipolar disorder with placebo studies of its use in acute mania and maintenance/relapse prevention from a manic episode.

Objective: To assess aripiprazole's effectiveness in acute mania when compared not to placebo alone, but to haloperidol.

Participants/Methods: Subjects included patients 18 years of age with DSM-IV defined bipolar I manic or mixed type disorder who were hospitalized with an acute relapse and met certain symptom scale cut offs to establish adequate severity (Young Mania Rating Scale [YMRS] 20, with no more than a 25% decrease between 2 visits and Montgomery-Asburg Depression Rating Scale [MADRS] 17 with no more than a 4-point increase between assessments). Recruited and followed-up in 59 centers around the world, patients were randomized, after a washout phase, to aripiprazole monotherapy (15 or 30 mg/day), placebo monotherapy, or haloperidol monotherapy (5 to 15 mg/day) for 3 weeks, and continued on blinded aripiprazole or haloperidol for an additional 9 weeks. Treatment efficacy was measured at weeks 2, 3, 4, 5, 6, 7, 8, 10, and 12 and included serial follow-up of MADRS and YMRS scores, Positive and Negative Syndrome Scale (PANSS) score, measures of functional impairment, and side effects.

Results: At week 3, the reduction in YMRS was significantly greater in the haloperidol and aripiprazole group relative to the placebo group. At 12 weeks, these improvements were maintained in the haloperidol and aripiprazole groups, and were not significantly different between them (a reduction of 17.2 points for aripiprazole and 17.8 points for haloperidol). MADRS scores did not worsen. Of the adverse events reported, approximately 50% in the haloperidol and 25% in the aripiprazole group were due to extrapyramidal symptoms. However, ratings for these were generally mild and resolved in the majority of subjects, with rates of use of concomitant medication for akathisia, for example, nearly identical in the groups. Weight gain or metabolic parameters also showed no significant changes between or within treatment groups.

Conclusions: Aripiprazole appears as effective as haloperidol and more effective than placebo in the treatment of acute mania, with somewhat greater impact of extrapyramidal symptoms in the haloperidol group effectively managed and not resulting in comparative disadvantage.

Reviewer's Comments: This study lends still further support for use of SGAs in the treatment of mania, but also adds to the rising questions as to whether at least the profile of these drugs with respect to less acute extrapyramidal symptoms is substantial enough to warrant their cost.

Additional Keywords: Aripiprazole

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Acute EPS and IM Antipsychotics

A Meta-Analysis of the Risk of Acute Extrapyramidal Symptoms With Intramuscular Antipsychotics for the Treatment of Agitation.

Satterthwaite TD, Wolf DH, et al:
J Clin Psychiatry; 69 (December): 1869-1879

Intramuscular SGAs are predictably less likely than haloperidol to cause acute EPS, but haloperidol plus promethazine reduces the risk of acute dystonia than that found with the newer agents.

Background: Antipsychotic medications play a key role in the management of acute violence and aggression in patients. Intramuscular (IM) administered preparations of these medications are commonly used, and primarily include first-generation agents (mostly high-potency haloperidol). Haloperidol has a high risk course for acute extrapyramidal symptoms (EPS), including dystonia. Three second-generation antipsychotic (SGA) IM preparations are available (ziprasidone, olanzapine, and aripiprazole). These presumably would avoid the extrapyramidal risks of haloperidol, but studies have not clearly shown the superiority of SGAs on target behaviors, and many trials have not included anticholinergic medications with haloperidol, which would be expected to modify any extrapyramidal risk.

Objectives: To use pooled data and an analysis of experience with IM haloperidol and anticholinergic agents versus SGAs or haloperidol alone in agitation.

Methods: Since there is only 1 reported randomized controlled trial directly comparing short-acting IM SGA with IM haloperidol plus an anticholinergic, the literature search sought to use existing studies that assessed any of the 3 issues of interest: risk ratio (RR) for SGAs, and/or haloperidol alone, and/or haloperidol with anticholinergics with respect to outcomes of dystonia and other EPSs. While a given study may have looked only at the haloperidol alone risk, the grouping of studies by which these 3 kinds of RR were captured, the authors could accumulate more refined risk estimates of each to compare one with each other, despite them not reflecting pooled data of the same head-to-head comparison.

Results: Among RCTs that spoke to any of the 3 risk comparisons (n=2032), SGAs had a significantly lower risk of dystonia (RR, 0.19) or akathisia (RR, 0.25) than haloperidol alone. When all trials were considered (n=3425), the acute dystonia rates for haloperidol alone were 4.7%, 0.6% for SGAs, and 0.0% for haloperidol plus promethazine. Of all patients captured in the available studies who were observed on haloperidol and promethazine (560 patients), none had dystonia reported, while 12 of an accumulated observation pooled from studies on SGAs of 2021 patients, did.

Conclusions: IM use of SGAs for agitation is more likely to cause dystonia than haloperidol alone, but IM use of haloperidol with promethazine is no more likely to do so than are SGAs.

Reviewer's Comments: Since SGAs are much more costly than haloperidol, the option to effectively avoid more concerning reasons to not choose haloperidol will probably look attractive in many institutional settings. One remaining argument for use of SGAs may be the expected and facilitated transition to stable oral use of the same drug as part of ongoing care and treatment, although the relative impact of that strategy with respect to later compliance or ease of upwards titration and length of an acute period of care remain to be established.

Additional Keywords: Extrapyramidal Symptoms

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Substance Use Increases Physical Health Tx Costs

Impact of Substance Disorders on Medical Expenditures for Medicaid Beneficiaries With Behavioral Health Disorders.

Clark RE, Samnaliev M, McGovern MP:
Psychiatric Services; 60 (January): 35-42

Medicaid patients with substance disorders have much higher expenditures for care than other mentally ill patients, due to associated physical disorders.

Background: 1 out of every 8 Medicaid beneficiaries has a substance abuse disorder. While treatment for addictions accounts for only 2% of Medicaid expenditures, the burden on the system of patients with such disorders has been suspected to be much higher. For one thing, medical illness is much more prevalent in this group. With that said, the authors here report that there has been no assessment of the association between substance use disorders and general medical care expenditures. Evidence for the impact of addictions on medical expenditures has been inconsistent.

Objectives: This study examined Medicaid expenditures associated with substance disorders among those beneficiaries with behavioral health diagnosis in representative states (Arkansas, Colorado, Georgia, Indiana, New Jersey, and Washington).

Methods: Data on beneficiaries (age range, 21 through 61 years) in the mentioned states were included. Those with behavioral health diagnoses were grouped as to whether they had severe mental illness (psychoses, bipolar, major depression), other mental illness, or alcohol and drug use diagnosis only. The first 2 groups were divided into those with and without co-occurring substance use. All were assessed with respect to overall expenditures. A validated scoring system to estimate a relative score of overall disease burden for each patient was used so as to control for other illness burden per se as the cause of differences in expenditures.

Results: 148,457 beneficiaries and records were included in the analysis; 29.3% had a substance use diagnosis. Individuals with substance use disorders, as opposed to other beneficiaries with behavioral health diagnoses, had significantly higher expenditures for physical health treatment costs in 5 of the 6 states explored. Almost 50% of these additional cost burdens were due to treatment for physical conditions. These differences remained statistically significant even after adjusting for overall disease burden experienced by patients with addictions.

Conclusions: The cost impact of addictions is substantial and exceeds the direct cost of mental health and addiction treatment.

Reviewer's Comments: Clinicians treating patients with single or co-occurring substance use disorders to expect and specifically inquire and be familiar with substantially greater overall health care problems and treatments than with other mentally ill patients.

Additional Keywords: Medicaid Expenditure

print tag: () Refer to original journal article.

Effects of Amygdala Activity in Schizophrenia

Evidence That Altered Amygdala Activity in Schizophrenia Is Related to Clinical State and Not Genetic Risk.

Rasetti R, Mattay VS, et al:

Am J Psychiatry; 166 (February): 216-225

Unique findings among schizophrenic patients in terms of difficulty engaging amygdala function in the face of seeing fearful and angry faces appears due to the disease state as opposed to reflecting a genetic vulnerability for the disease.

Background: Individuals with schizophrenia have been noted to have reduced responsiveness of the amygdala in imaging studies of exposure to pictures of fearful faces; but, is that a feature of the disease or of the genetic risks for the disease? The study of face-response processing among family members of patients with schizophrenia, and thus ostensibly at greater genetic risk for the disease, has been a technique to try to get at the degree to which findings, with respect to facial responses, reflect features of the disease versus features of being at risk for the disease, (ie, a shared genetic vulnerability or trait).

Methods: Patients and unaffected siblings were located using the National Institutes of Health (NIH) Clinical Brain Disorders Branch Sibling Study. Healthy subject controls were identified among those within the NIH Clinical Research Volunteer Program. Patients had to be on a stable antipsychotic regimen, and siblings and controls needed to evidence no symptoms of mental disorder or be under treatment for one. All subjects participated in an established, standardized, face-matching task that involved exposure to upper and lower panel images of facial expressions. Subjects were asked to indicate (by pressing a button) when the emotion and face types matched. A separate working memory task was also performed to elicit an expected similarity in inefficient prefrontal cortex among siblings and patients in order to confirm the robustness of the comparison to capture shared, presumably genetically driven, functional neurological characteristics.

Results: 34 schizophrenic patients, 29 unaffected siblings, and 20 health controls participated in the study. As expected, the working memory task demonstrated that siblings and patients shared a pattern of inefficient prefrontal engagement on imaging. However, patients and unaffected siblings did not share similar responses to face exposure, with significantly lower amygdala reactivity for patients relative to siblings and unaffected controls. Patients also showed an inverse significant relationship between their antipsychotic dose and the measure of amygdala coupling.

Conclusions: This study supports the hypothesis that the diminished ability for schizophrenia patients to functionally engage the amygdala in a normal fashion with exposure to fearful and angry faces is related to having the disease, and perhaps, as an effect as well of treatment of the disease, rather than as a function of genetic liability associated with risk for the disease.

Reviewer's Comments: This paper, compared with the paper on responses to similar facial expressions among patients with depression in this edition of *Practical Reviews in Psychiatry*, come to opposite findings, albeit in different disorders, as to the genetic or risk significance as opposed to disease effect of unique brain responses to exposures to this kind of effect in others. Taken together, they may provide potentially interesting perspectives on the ways intersubjective and interpersonal responses are managed by the brain and the clues they hold for the features and onset of mental illness.

Additional Keywords: Clinical State/Genetic Risk

print tag: () Refer to original journal article.

Aripiprazole Improves Symptom Domains in Short-Term Tx

The Acute Efficacy of Aripiprazole Across the Symptom Spectrum of Schizophrenia: A Pooled Post Hoc Analysis From 5 Short-Term Studies.

Janicak PG, Glick ID, et al:

J Clin Psychiatry; 70 (January): 25-35

Aripiprazole shows efficacy across the full set of symptom domains captured by the PANSS that is comparable to that shown by haloperidol and risperidone.

Background: A range of symptom domains are at play in the long-term outcomes and functional capacities of people with schizophrenia. While positive and negative symptoms often get primary attention, these categories varyingly capture the complexity of symptom types in the disorder. The authors argue that the 5-factor model derived from the Positive and Negative Syndrome Scale (PANSS), where symptoms are divided into positive, negative, depression/anxiety, hostility, and disorganization, may better represent the symptom range of interest with respect to meaningful functional outcomes. Aripiprazole has a unique combination of partial D2 agonist activity, potent partial-agonist activity at 5-HT1A receptors at 5-HT2A receptor, which together should benefit mood, anxiety, and disorganized thought. Moderate affinity for H1 and no significant affinity for cholinergic muscarinic receptors should minimize sedation as well as cognitive impairment. It therefore appears to be a compound with some breadth of coverage of the spectrum of symptoms captured by the PANSS.

Objective: To re-analyze pooled data from prior studies of aripiprazole using the PANSS in which placebo, but also haloperidol or risperidone, were used for comparison.

Methods: A factor analysis of PANSS data was performed on pooled results from five 4- to 6-week trials of aripiprazole among in-patients with acute exacerbation of their disease.

Results: The pooled data resulted in observations on 875 patients assigned to aripiprazole, 193 assigned to haloperidol, 95 to risperidone, and 406 to placebo. Aripiprazole was significantly better in terms of score improvements on all 5 factors of the PANSS compared to placebo. However, improvement in all factors with aripiprazole was statistically comparable to improvement also seen with haloperidol and risperidone.

Conclusions: Aripiprazole shows a wide spectrum of effectiveness across a multi-dimensional range of symptom domains captured by the PANSS scoring system, but this impact appears comparable to that seen with haloperidol and risperidone.

Reviewer's Comments: By studying hospitalized patients in acute relapse for relatively short periods of time, any sustained impact across such a range of symptom domains, either absolutely compared to placebo or relatively compared to other active agents (haloperidol, risperidone in this case), is not that well addressed by this study.

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Perceived Coercion Plays Important Role

The Impact of Coercion on Services From the Perspective of Mental Health Care Consumers With Co-Occurring Disorders.

Stanhope V, Marcus S, Solomon P:
Psychiatr Serv; 60 (February): 183-188

This study agrees with earlier findings that low-end coercion does not seem to affect treatment alliance.

Background: Assertive community treatment (ACT) is an outpatient intervention program for homeless individuals with serious mental illness who have not been successfully engaged by other services. This kind of care involves a team of professionals who meet the patient in the community and work with them on a host of issues, from housing to treatment. ACT has been called the "velvet bulldozer" because it involves supporting clients while also applying pressure to engage in services. There have been concerns that clients may perceive this coercion as overpowering and may be discouraged from participation.

Objectives: To explore the factors related to perceived coercion by ACT clients and understand how this may impact those clients' evaluation of their encounters with ACT team members.

Methods: This was an exploratory study that examined homeless, seriously mentally ill, substance-abusing clients in Philadelphia who were part of an ACT team and a Housing First program (harm reduction model designed to provide immediate housing regardless of sobriety or treatment compliance). From February 2006 to June 2006, a researcher attended the program on a random day of each week and followed a randomly selected case manager to all of his/her visits with clients. After the visit, the researcher conducted an interview with the client that included questions related to coercion, evaluation of the program, satisfaction with treatment, and therapeutic alliance. Eighty individuals were available, and 70 agreed to participate. The data were then analyzed for any relationships between coercion and client satisfaction.

Results: The majority of the clients were African American and male, and most reported a positive experience with their ACT team. Whites and Latinos experienced more coercion than African Americans, and those who were in the program longer experienced significantly more coercion. Higher levels of coercion were experienced in shorter visit contacts. There was a small, although significant, relationship between perceived coercion and a client's dissatisfaction with the service relationship. In the final regression analysis, perceived coercion was the only variable associated with a negative evaluation of an ACT team encounter.

Conclusions: Perceived coercion is an important factor in an ACT team client's perception of the quality of their service contact.

Reviewer's Comments: ACT teams target the most challenging mentally ill population in the community, often including those who have high levels of mistrust, those who wish to remain homeless, and those who do not think that they need treatment for mental illness. This study highlights that subtle factors, such as how coerced a client feels, can significantly impact the efficacy of community outreach. It seems a fine line to balance between allowing clients the freedom to make their own choices and protecting both their own safety and the safety of others.

Additional Keywords: Coercion

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Changing Range of Normal TSH Levels May Impact Clinical Care

Basal Thyrotropin and Major Depression: Relation to Clinical Variables and Treatment Outcome.

Joffe RT, Levitt AJ:

Can J Psychiatry; 53 (December): 833-838

Scores of 7 to 17 on the HDRS indicate mild depression, scores of 18 to 24 indicate moderate depression, and scores >24 indicate severe depression.

Background: Up to 10% of patients with major depression may have subclinical hypothyroidism, elevated basal thyrotropin (TSH), but normal T4 and T3. This is clinically important because there is some literature that indicates that subclinical hypothyroidism converts to hypothyroidism at a rate of 5% per year and that it affects the efficacy of antidepressants. The normal range of TSH is usually between 0.5 and 5.0 mIU/L, but some have suggested that this may miss identifying those with early thyroid failure. In response, a proposal has been made to decrease the upper limit of normal to 2.5 mIU/L.

Objectives: To compare basal TSH values with clinical symptoms and treatment response in subjects with major depression, paying particular attention to definitions of normal TSH ranges.

Participants/Methods: 166 adult outpatients with unipolar depression, enrolled in a mood disorders program in Toronto from 1991 onwards, were enrolled in this study. They were all medication-free at baseline and had a minimum score of 16 on the Hamilton Depression Rating Scale (HDRS). Blood was drawn for thyroid function tests at the outset of the study. Participants were treated with tricyclic or selective serotonin reuptake inhibitor (SSRI) antidepressants for the first 5 weeks, administered another HDRS, and were then treated by psychiatrist preference with the possibility of other medications. Another HDRS was administered at 3 months. For the statistical analysis, the subjects were divided into those with low-normal TSH (0.5 to 2.5) and those with high-normal TSH (2.6 to 5.0).

Results: The subjects in the low-normal TSH group had a significantly higher initial HDRS (19) than those in the high-normal TSH group, along with more insomnia, anxiety, and slightly more suicidal thoughts. There was no significant difference in treatment response rates at 5 weeks or 3 months based on TSH level.

Conclusions: There was no difference in treatment response rates between subjects who had low-normal and those with high-normal basal TSH measurements.

Reviewer's Comments: Although the HDRS in the low-normal TSH group was statistically higher than in the high-TSH group, the actual difference was 1.5 points, which is probably not clinically significant. Despite the relatively weak results of this study, the authors mention the possible relation between depression severity and a blunted thyrotropin releasing hormone (TRH) response. A blunted pituitary response of TRH may be involved with increased levels of cortisol and metabolic changes that could impact mood states. Finally, it seems unlikely (based on this study) that changing the range of normal for TSH levels will have any meaningful impact on clinical care.

Additional Keywords: Depression

print tag: () Refer to original journal article.

Is Self-Medication With Drugs and Alcohol in Anxious Individuals Common?

Self-Medication of Anxiety Disorders With Alcohol and Drugs: Results From a Nationally Representative Sample.

Robinson J, Sareen J, et al:

J Anxiety Disord; 23 (January): 38-45

Use of both drugs and alcohol to self-medicate for anxiety is seen in those with panic disorder plus agoraphobia and in those with comorbid mood and/or personality disorders.

Background: The high rates of comorbidity seen between anxiety and substance use disorders may reflect self-medication, which is the use of alcohol or drugs in an attempt to reduce anxiety. This association has largely been studied in clinical populations, but previous research has focused mainly on self-medication with alcohol.

Objective: To examine the prevalence and comorbidity of self-medication with drugs and/or alcohol for anxiety disorders (panic disorder, social phobia, specific phobia, and generalized anxiety disorder) using a nationally representative sample.

Participants: 43,093 adults from the National Epidemiologic Survey on Alcohol and Related Conditions.

Design: Cross- sectional survey.

Participants/Methods: Subjects were interviewed using the NIAAA Alcohol Use Disorders and Associated Disabilities Interview Schedule IV (AUDADIS-IV) to assess DSM-IV Axis I and II diagnoses. They were also asked if at any time in the past they had used alcohol or drugs for the purpose of reducing their fear, anxiety, or to avoid a feared object or situation.

Results: Overall 10% of those with any anxiety disorder reported self-medicating with alcohol. A smaller proportion (3.1%) reported self-medicating with both alcohol and drugs. Comparing the individual anxiety disorders, 18.3% of those with generalized anxiety disorder self-medicated with alcohol. Similarly high rates were seen for individuals with social phobia (16.9%) and panic disorder with agoraphobia (15.0%). Panic disorder with agoraphobia also had the highest rate of self-medication with both drugs and alcohol (14.9%), twice that seen in generalized anxiety disorder (7.4%). Self-medication with alcohol was significantly associated with increased odds of any lifetime mood disorder diagnosis (OR, 1.8), as was self-medication with both drugs and alcohol (OR, 3.4). A similar association was found with any lifetime personality disorder diagnosis (self-medication with alcohol only, OR, 1.9 and self-medication with both drugs and alcohol, OR, 3.7). In all analyses, self-medication with both drugs and alcohol consistently produced higher ORs than self-medication with alcohol alone.

Conclusions: Self-medication is a relatively common behavior among individuals in the general population with anxiety disorders. Self-medication with both drugs and alcohol may be viewed as a marker of greater severity.

Reviewer's Comments: Generalized anxiety disorder was the most likely to be associated with self-medication with alcohol, suggesting that the inability to be able to use other strategies available to deal with phobia (eg, avoidance) may predispose to self-medication. Using both drug and alcohol to self-medicate was more common in anxious individual with panic disorder plus agoraphobia and in those with comorbid mood and personality disorders, and may reflect inadequate coping mechanisms or an inability to tolerate negative effect. This study was limited by its cross-sectional nature, and precludes the determination of whether comorbidity leads to self-medication or self-medication leads to comorbidity. Future studies should be prospective, and should also measure the quantity of drug/alcohol use, as well as the type of drugs used.

Additional Keywords: Alcohol & Drugs

print tag: () Refer to original journal article.

No Differences in Neural Activity Among SAD Subjects and Controls

Neural Bases of Social Anxiety Disorder: Emotional Reactivity and Cognitive Regulation During Social and Physical Threat.

Goldin PR, Manber T, et al:

Arch Gen Psychiatry; 66 (February): 170-180

Social anxiety disorder is associated with reduced neural activation associated with cognitive regulation for social threat, but not physical threat stimuli.

Background: Social anxiety disorder (SAD) includes information processing deficits regarding threat appraisal and heightened emotional reactivity together with ineffective emotion regulation. The neural bases and specificity of emotional reactivity and cognitive regulation are not well known.

Objective: To investigate behavioral and neural correlates of emotional reactivity and cognitive regulation during processing of social and physical threat stimuli.

Design: Case-control functional magnetic resonance imaging (fMRI) study.

Participants: 15 adult subjects with SAD and 17 healthy controls.

Methods: Subjects watched pictures depicting social (harsh facial expressions) and physical (violent scenes) threatening or neutral images. While in the fMRI scanner, subjects rated the negative emotion experience while "just looking" and then attempted to regulate their emotional reactions using cognitive-linguistic techniques.

Results: Subjects with SAD reported greater negative emotion than controls in response to pictures depicting social and physical threat, but both groups showed a similar reduction in ratings of negative emotion with attempts to regulate. Greater emotion-related neural responses were seen in patients than controls when viewing social threats in regions implicated in cognitive control (dorsolateral prefrontal cortex [PFC], dorsal anterior cingulate cortex [ACC]), visual attention (medial cuneus, posterior cingulate), attention areas (bilateral dorsal parietal), and visual feature detection (bilateral fusiform, superior temporal gyrus). In SAD subjects only, the level of social anxiety symptoms was significantly associated with neural activity in the dorsal/extended amygdala and right middle occipital gyrus. There were no differences in neural activity between SAD subjects and controls when viewing violent pictures. In both cases and healthy controls, greater activity in dorsomedial PFC during cognitive regulation was associated with a significant reduction in ratings of negative emotion. Subjects with SAD showed less cognitive and attention regulation-related brain activation during attempted regulation of social threat than controls.

Conclusions: Compared with controls, subjects with social anxiety disorder showed exaggerated negative emotion reactivity and reduced neural activation associated with cognitive regulation, specifically for social threat stimuli. These findings help to elucidate potential neural mechanisms of emotion regulation that might serve as biomarkers for interventions for SAD.

Reviewer's Comments: These results converge with prior findings of recognition bias and negative emotion reactivity to harsh faces in participants with SAD. Understanding the mechanisms by which social anxiety is associated with this emotional hyper-reactivity of brain behavioral systems may help guide novel treatments. It suggests that individuals with SAD could specifically train in (PFC-mediated) emotion regulation skills, such as inhibition of cognitive elaboration, reallocation of attentional focus, and cognitive diffusion.

Additional Keywords: Information Processing/Cognitive Control

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How Common Are Manic Symptoms in Bipolar Depressive Episodes?

Manic Symptoms During Depressive Episodes in 1,380 Patients With Bipolar Disorder: Findings From the STEP-BD.

Goldberg JF, Perlis RH, et al:

Am J Psychiatry; 166 (February): 173-181

Manic symptoms are seen in two-thirds of those with bipolar depression and are associated with a more severe and complex clinical state.

Background: Mixed affective states are associated with increased relapse rates and increased suicidality. Bipolar depressive episodes are frequently accompanied by subsyndromal manic symptoms, but their frequency and associated features are not well studied.

Objective: To determine the frequency and clinical correlates of manic symptoms during episodes of bipolar depression.

Design: Case-control study.

Participants: 1,380 subjects with bipolar I (n=401) or II (n=979) depression from the National Institute of Mental Health's Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD).

Methods: Illness characteristics were compared in patients with pure bipolar depressed episodes and those with a full mixed episode or subsyndromal mania (1 to 3 DSM-IV manic symptoms).

Results: Two-thirds of the subjects had concomitant manic symptoms (54% subsyndromal, 14.8% full mixed episode), most often distractibility, flight of ideas or racing thoughts, and psychomotor agitation. Only 31% of bipolar depressed subjects had no manic symptoms. Patients with either subsyndromal or full mixed features were significantly more likely to be male, have an earlier age of onset, rapid cycling in the past year, bipolar I subtype, history of suicide attempts, and more likely to have a history of substance abuse or dependence than those with pure bipolar depressed episodes. Although the 3 groups did not differ in their mean number of days spent with depression in the past year, those with any concomitant mania features had more days with irritability or mood elevation.

Conclusions: Subsyndromal manic symptoms frequently occur during bipolar I or II depression, represent a more severe and complex clinical state, and may merit recognition within DSM-V as a distinct subtype.

Reviewer's Comments: It was interesting to note that the specific manic symptoms most frequently seen did not include elation or grandiosity, so that DSM-IV B criteria for mania may serve to reduce recognition of subsyndromal mixed affective states. The high prevalence of manic symptoms in this sample could not be explained by iatrogenic induction of manic symptoms in bipolar depression since the number of manic symptoms was actually lower in those taking an antidepressant.

Additional Keywords: Manic Symptoms

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