



Antidepressant-Induced Mania (ADM) Among People with COD

A recent study of medical charts at a bipolar specialty clinic gives new support to the idea that antidepressants can induce mania in some bipolar patients. For some time, clinicians have been concerned about the problem of antidepressant-induced mania (ADM), but most research has not supported the connection between antidepressants and manic or hypomanic episodes. This study looked at ADM and examined differences between patients with bipolar disorder and a substance use disorder (SUD) and patients without SUD. The article presents solid evidence for a significantly increased risk of ADM in patients with co-occurring bipolar disorder and SUD. The article also comments about why the increased risk to these clients may not have been identified in prior research.

Manwani and colleagues investigated medical charts from 98 patients who were treated at a bipolar clinic between 2000 and 2004. These patients accounted for 335 antidepressant trials during that period. Of the sample, 55 patients (accounting for 184 of the trials) had a lifetime history of a SUD. For this study, an episode of ADM was defined as hypomanic or manic symptoms within 12 weeks of beginning a new antidepressant medication. There were some substantial differences between patients who did and did not have a SUD history—e.g., clients with SUD were almost twice as likely as those without SUD to be prescribed lithium (48.3% vs. 28.5%), and clients without SUD were twice as likely to receive divalproex as those with SUD (43% vs. 20.1%) and almost three times as likely to be prescribed an antipsychotic (31.8% vs. 11.4%). The univariate analysis of differences in the number of antidepressant trials leading to ADM between patients with and without a SUD history showed little difference in the percentage of ADM episodes they experienced

(20.7% of trials for those with SUD and 21.4% of trials for those without). However, using a multivariate regression model of analysis, the authors found that:

- Patients with a lifetime SUD were five times as likely to experience ADM,
- The incidence of an antidepressant trial leading to an ADM was greater for clients with Type II or with bipolar disorder not otherwise specified than for Type I,
- Females were more likely than males to have an episode of ADM in response to an antidepressant trial, and
- Bupropion was the antidepressant least likely to cause an ADM.

The authors surmise that older research studies excluding people with a SUD might have led to subject pools that underrepresented individuals considerably more likely to experience an ADM than the subjects studied. Additionally, they describe how other confounding factors might have served to hide the effects of having a history of SUD on the likelihood of suffering an ADM. A discussion of the limitations of their study (e.g., it was non-randomized, non-blind; concomitant therapy may have obscured treatment effect; no measures of adherence to medication regimens) is also given.

Manwani, S. G., Pardo, T. B., Albanese, M. J., Zablotsky, B., Goodwin, F. K., & Ghaemi, S. N. (2006). Substance use disorder and other predictors of antidepressant-induced mania: a retrospective chart review. *Journal of Clinical Psychiatry*, 67(9), 1341–1345.

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COD Research

Epidemiology

Bolton, J., Cox, B., Clara, I., & Sareen, J. (2006). Use of alcohol and drugs to self-medicate anxiety disorders in a nationally representative sample. *Journal of Nervous & Mental Disease, 194*(11), 818–825.

This study used a large national sample ($N = 5877$) to determine the extent and repercussions of self-medication with alcohol and other drugs for anxiety disorders. Among individuals with anxiety disorders, rates of self-medication were highest (35.6 percent) for people with generalized anxiety disorder and lowest (7.9 percent) for those with social phobia, speaking subtype. For these individuals, self-medication was associated with co-occurring substance use disorders, mood disorders, and both suicidal ideation and suicide attempts.

Buckner, J. D., Mallott, M. A., Schmidt, N. B., & Taylor, J. (2006). Peer influence and gender differences in problematic cannabis use among individuals with social anxiety. *Journal of Anxiety Disorders, 20*(8), 1087–1102.

Previous research has shown that people who have social anxiety disorder (SAD) have an increased risk for also developing a cannabis use disorder (CUD). The authors looked at how peer influence (a well-known risk factor for cannabis use) affected SAD and CUD. They used a diagnostic interview to assess symptoms of SAD and CUD and found that for women (but not for men) SAD symptoms were significantly correlated with CUD symptoms, and this relationship was moderated by peer use of cannabis as well as alcohol.

Dannon, P. N., Lowengrub, K., Shalgi, B., Sasson, M., Tuson, L., Saphir, Y., & Kotler, M. (2006). Dual psychiatric diagnosis and substance abuse in pathological gamblers: A preliminary gender comparison study. *Journal of Addictive Diseases, 25*(3), 49–54.

Recent research has shown an association between pathological gambling (PG) and mood, anxiety, and substance use disorders and found that PG responds to treatment with SSRIs, mood stabilizers, and opioid antagonists. The authors gave a comprehensive psychiatric diagnostic evaluation to 78 people with PG (26 female and 42 male). They found that in males PG was correlated with substance abuse (including alcohol abuse) and that among females it was correlated with major depression, affective disorders, anxiety disorders, and eating disorders. Patterns of psychiatric comorbidity differed according to gender.

Edwards, C., Dunham, D. N., Ries, A., & Barnett, J. (2006). Symptoms of traumatic stress and substance use in a non-clinical sample of young adults. *Addictive Behaviors, 31*(11), 2094–2104.

The authors assessed the relationship between symptoms of trauma and alcohol use in a college student sample. They found that traumatic stress symptoms accounted for 55 percent of the variance in alcohol use among the sample. They also found that dissociative behavior, intrusive thoughts, and low level use of tension reduction behavior all contributed to self-reported use of alcohol.

Johnson, S. D., Striley, C., & Cottler, L. B. (2006). The association of substance use disorders with trauma exposure and PTSD among African American drug users. *Addictive Behaviors, 31*(11), 2063–2073.

The authors investigated trauma exposure, substance use, and PTSD in a sample of 1098 African Americans substance users who were not in treatment. Of this group, over 40 percent had experienced a traumatic event and 44 percent of that group had PTSD. Early onset of various types of substance use was associated with PTSD.

Lyons, M. J., Schultz, M., Neale, M., Brady, K., Eisen, S., Toomey, R., Rhein, A., Faraone, S., & Tsuang, M. (2006). Specificity of familial vulnerability for alcoholism versus major depression in men. *Journal of Nervous & Mental Disease, 194*(11), 809–817.

The authors interviewed 3372 pairs of male twins to assess (using DSM-III-R) alcohol dependence (AD) and major depression (MD). Those men who had coexisting MD and AD experienced greater severity for each disorder than those who had only one of the two disorders. In cases where one twin had MD, the other was more likely to have MD alone and

MD with co-occurring AD but not AD alone (the pattern existed for twins who had AD). Authors believe these data support the conclusion that MD increases risk for AD and AD increases risk of MD.

Services & Service Systems

Screening & Assessment

Kimerling, R., Trafton, J. A., & Nguyen, B. (2006). Validation of a brief screen for Post-Traumatic Stress Disorder with substance use disorder patients. *Addictive Behaviors, 31(11), 2074–2079.*

The authors evaluated 4-item instrument for use in screening for Post-Traumatic Stress Disorder (PTSD) with people who have substance use disorders. The instrument was self-administered by 97 substance use disorder treatment clinic patients, and then patients were interviewed using the Clinician Administered PTSD Scale (CAPS). The screening instrument identified 91 percent of those people who had PTSD according to the Clinician Administered Scale (compared to 25 percent of cases, which were able to be identified from patient medical charts).

Services Integration

Ries, R. K. (2006). Co-occurring alcohol use and mental disorders. Improving outcomes in alcohol dependence treatment. *Journal of Clinical Psychopharmacology, 26(6-Supplement 1), S30–S36.*

The author reviews literature on COD, discussing prevalence, difficulties involved in treatment, and relapse prevention. He also describes a biopsychosocial, integrated treatment model for treating people with COD.

Treatment Planning & Services

Baker, A., Richmond, R., Haile, M., Lewin, T. J., Carr, V. J., Taylor, R. L., Jansons, S., & Wilhelm, K. (2006). A randomized controlled trial of a smoking cessation intervention among people with a psychotic disorder. *American Journal of Psychiatry, 163(11), 1934–1942.*

The authors investigated the efficacy of smoking cessation interventions with regular smokers who had psychotic disorders ($N = 298$), comparing an integrated psychological and nicotine replacement intervention, which included nicotine replacement therapy, motivational interviewing, and cognitive behavior therapy, with a standard smoking cessation treatment. Abstinence rates were no different for the two groups—however a significantly greater percentage of participants who completed all sessions of their treatment had stopped smoking at followup compared to those who missed one or more sessions. Treatment completers were also more likely to have been continuously abstinent (21 percent) at the 3 month followup than non-completers (4 percent). The study showed a strong dose–response relationship between attendance at treatment sessions and smoking reduction.

Barrowclough, C., Haddock, G., Fitzsimmons, M., & Johnson, R. (2006). Treatment development for psychosis and co-occurring substance misuse: A descriptive review. *Journal of Mental Health, 15(6), 619–632.*

The authors prepared a descriptive review of the treatment literature concerning people who have psychosis and misuse substances. They also describe a randomized, controlled treatment trial currently underway in the United Kingdom. The literature they review generally emphasizes the use of integrated treatment strategies that are matched to the client's level of motivation for change. Literature also supports the use of motivational strategies but suggests that brief therapies are not very effective with this population.

Berlin, I., & Covey, L. S. (2006). Pre-cessation depressive mood predicts failure to quit smoking: The role of coping and personality traits. *Addiction, 101(120), 1814–1821.*

The study looked at 600 individuals who smoked more than 15 cigarettes per day who were not currently diagnosed with depression. The Beck Depression Inventory (BDI) was used to determine symptoms of depressed mood; The Revised NEO Personality Inventory (NEO-PI-R) was used to assess personality; and the Revised Ways of Coping Checklist (RWCC) was used to assess coping. Authors were able to use BDI score to independently predict smoking cessation, and

smokers who scored greater than 10 on the Inventory were less likely to quit than those with lower scores. Higher BDI scores were also correlated with significantly higher scores for neuroticism and lower scores for extraversion and conscientiousness on the NEO-PI-R and higher scores for blaming self, wishful thinking, and problem avoidance and lower scores for problem focus on the RWCC. The NEO-PI-R and RWCC scores, however, did not directly predict smoking cessation.

Brown, E. S., Beard, L., Dobbs, L., & Rush, A. J. (2006). Naltrexone in patients with bipolar disorder and alcohol dependence. *Depression and Anxiety*, 23(8), 492–495.

The authors conducted a 16-week, open-label study of naltrexone treatment for 34 patients with bipolar and alcohol dependence disorders who were entered in an out-patient treatment program. Patients receiving Naltrexone showed significant improvement on the Hamilton Rating Scale for Depression (HRSD-17) and Young Mania Rating Scale (YMRS) and had fewer days of alcohol use and less alcohol craving.

Buydens-Branchey, L., & Branchey, M. (2006). n-3 polyunsaturated fatty acids decrease anxiety feelings in a population of substance abusers. *Journal of Clinical Psychopharmacology*, 26(6), 661–665.

Previous studies have demonstrated that n-3 polyunsaturated fatty acids (PUFAs) can decrease behaviors related to anxiety. The authors tested the efficacy of a PUFA supplement for reducing feelings of anxiety in substance abuse treatment patients. The study lasted 3 months and was a double-blind, randomized trial. Those who received the PUFA supplement had significantly lower anxiety symptom scores that persisted 3 months after treatment concluded.

Castellanos, N., & Conrod, P. J. (2006). Brief interventions targeting personality risk factors for adolescent substance misuse reduce depression, panic and risk-taking behaviours. *Journal of Mental Health*, 15(6), 645–658.

The authors investigated the effectiveness at interventions targeted toward particular personality traits (i.e., negative thinking, anxiety sensitivity, impulsivity, and sensation seeking) associated with substance abuse in adolescents; 423 participants, ages 13 to 16, were randomly assigned to receive a personality-matched, cognitive-behavioral intervention or a no intervention control group. Youth who received the negative thinking intervention had a moderate reduction in depression scores, and those who received the anxiety sensitivity intervention had a moderate reduction in panic attack scores and truancy. There was a small but significant reduction in shoplifting among all youth who received a targeted intervention.

Dermatis, H., Galanter, M., Trujillo, M., Rahman-Dujarric, C., Ramaglia, K., & LaGres, D. (2006). Evaluation of a model for the treatment of combined mental illness and substance abuse: The Bellevue Model for peer-led treatment in systems change. *Journal of Addictive Diseases*, 25(3), 69–78.

The authors evaluated the use of a peer-led self-help (PLSH) model program for clients with co-occurring disorders (COD). Inpatient admissions ($N = 461$) were assigned to either the PLSH unit or one of two standard psychiatric units. Among patients with no prior psychiatric hospitalizations ($N = 111$), those in PLSH were more likely to accept aftercare referral (with 93 percent accepting compared to 74 percent of other patients) and more likely to attend aftercare (52 percent compared to 30 percent). Chronically impaired patients with COD ($N = 350$) also experienced a (smaller) improvement from participation in the PLSH program as they were also more likely to accept a referral to aftercare than those in other units (96 percent compared to 81 percent).

Gossop, M., Marsden, J., & Stewart, D. (2006). Remission of psychiatric symptoms among drug misusers after drug dependence treatment. *Journal of Nervous & Mental Disease*, 194(11), 826–832.

The authors investigated the extent to which the psychiatric symptoms of people who abused drugs were reduced after drug abuse treatment in a residential program or a methadone treatment program. They collected data using structured interviews at intake and at 1 and 6 months after intake. In individuals in residential treatment, the percentage of clients meeting criteria for having a psychiatric case fell from 39 percent at intake to 3 percent at both followup evaluations. In the methadone group, the percentage fell from 15 percent at intake to 5 percent at 1 month and 3 percent at 6 months.

Herbeck, D. M., Hser, Y. -I., Lu, A. T. H., Stark, M. E., & Paredes, A. (2006). A 12-year follow-up study of psychiatric symptomatology among cocaine-dependent men. *Addictive Behaviors, 31*(11), 1974–1987.

The authors carried out a longitudinal study to investigate patterns of psychiatric symptoms among men ($N = 266$) in treatment for cocaine dependence between the years 1988 and 1989. Participants were evaluated 1 year, 2 years, and 12 years after completing treatment. Twelve years after treatment, 52 percent of participants had been abstinent from cocaine for 5 or more years. Clients who had achieved long-term abstinence as well as those who had not both scored high on the Hopkins Symptom Checklist-58 (SCL) at intake and 1 year after treatment, but at 12 years after treatment the group that had long-term abstinence scored significantly lower than others on 4 out of 5 symptom measures. The abstinent group also reported lower rates of depression and psychotic disorders and less use of psychopharmacologic and inpatient treatment.

Miguel-Hidalgo, J. J., Overholser, J. C., Meltzer, H. Y., Stockmeier, C. A., & Rajkowska, G. (2006). Reduced glial and neuronal packing density in the orbitofrontal cortex in alcohol dependence and its relationship with suicide and duration of alcohol dependence. *Alcoholism: Clinical and Experimental Research, 30*(11), 1845–1855.

The authors performed a postmortem analysis of brain tissue to determine the density of neurons and glial cells in the orbitofrontal cortex of 15 alcohol-dependent subjects (8 of which were suicides) and 8 normal controls. They found that those individuals who were alcohol-dependent had significantly lower density of neurons and glial cells than those who were in the control group. Among the alcohol-dependent group there was no significant difference in packing density between suicides and non-suicides. They did find that duration of alcohol dependence and the ratio of duration of dependence to length of life were negatively correlated with neuron density.

Sher, L., Oquendo, M. A., Grunebaum, M. F., Burke, A. K., Huang, Y., & Mann, J. J. (2007). CSF monoamine metabolites and lethality of suicide attempts in depressed patients with alcohol dependence. *European Neuropsychopharmacology, 17*(1), 12–15.

Previous research has shown that lower levels of cerebrospinal fluid 5-hydroxyindolacetic acid (CSF 5-HIAA) are associated with a higher level of lethality for suicides among individuals with major depression and also predict a greater chance of future suicide. The authors compared CSF 5-HIAA levels from 16 high- and 16 low-lethality depressed individuals with alcohol use disorders (but no other substance abuse) who had attempted suicide. They found that CSF 5-HIAA levels were lower in the group whose suicide attempts had higher lethality and concluded that more lethal suicide attempts in people with co-occurring depression and alcohol use disorder are connected to lower serotonergic activity.

Tommasello, A. C., Gillis, L. M., Lawler, J. T., & Bujak, G. J. (2006). Characteristics of homeless HIV-positive outreach responders in urban US and their success in primary care treatment. *AIDS Care, 18*(8), 911–917.

The authors discuss homeless, HIV+ persons who abuse substances and responded to an outreach program and subsequently entered treatment. Their outreach program contacted 3059 people, of whom 1446 entered clinic treatment and 110 participated in the study. Study participants showed significant improvement in mental and physical health at a 12-month followup.

Watt, M., Stewart, S., Birch, C., & Bernier, D. (2006). Brief CBT for high anxiety sensitivity decreases drinking problems, relief alcohol outcome expectancies, and conformity drinking motives: Evidence from a randomized controlled trial. *Journal of Mental Health, 15*(6), 683–695.

The authors screened participants (all women) into high- and low-anxiety sensitivity groups using the Anxiety Sensitivity Index (Peterson & Reiss, 1992) and then randomly assigned participants to attend three 1-hour sessions of brief cognitive behavioral therapy (CBT) to reduce anxiety sensitivity or a control seminar group that discussed ethics. They found that participants with high-anxiety sensitivity who received the CBT intervention also had significant reductions in conformity motivated drinking and emotional relief expectancies; they also had a greater proportional reduction in hazardous alcohol use than participants in the other group.