Letters to the Editor

Association of Mild Traumatic Brain Injury With Bipolar Disorder

Sir: Traumatic brain injury has an estimated prevalence of 2,500,000.[1] Mild traumatic brain injury (mTBI), with a Glaskow Coma Scale score of 14 to 15, is a common neurologic disorder and a common cause of neurocognitive deficits.[2] Most of the patients recover fully from mTBI, but 15% to 29% of patients have persistent neurocognitive problems.[2] Mania secondary to head injury has been reported to occur at a 15% higher rate than that seen in the healthy population.[3] Mania secondary to specific medical factors, "type-IV bipolar disorder," has been suggested as early as 1978.[3] One case of bipolar disorder secondary to a "mild" traumatic brain injury with periamygdalar hemorrhage in a 15-year-old girl has been reported.[4] mTBI may have a significant association with bipolar disorder.

While collaborating in the National Institute of Mental Health (NIMH)–sponsored Systematic Treatment and Enhancement Program for Bipolar Disorder (STEP-BD) study, I have recognized a high incidence of patients with a history of mTBI in the local site population. After this was communicated to the 17 other sites, preliminary statistics were run to look at any correlation between mTBI (before vs. after bipolar disorder onset) and bipolar illness. Of the first 535 patients with established bipolar disorder, 126 patients (23.6%) reported a history of mTBI. Fifty-four of the patients reported mTBI before the onset of bipolar symptoms, and 72 patients reported bipolar symptoms preceding mTBI. This finding is similar to the 15-fold increase in secondary mania in patients with head injury compared with the frequency in the healthy population reported in 1 study,[3] suggesting an association between mTBI and bipolar disorder.

An association between mTBI and rapid cycling is hypothesized. Rapid cycling is defined by DSM-IV-TR as "at least 4 episodes of mood disturbance in the previous 12 months that meet criteria for a Major Depressive, Manic, Mixed, or Hypomanic episode."[5(p428)] Among the 535 patients in our initial statistical group, a significantly higher rate of cycling was noted in the group of patients reporting head injury after bipolar disorder diagnosis (9 of 72) compared with those reporting head injury before bipolar disorder diagnosis (2 of 54). This finding may suggest increased cycling in bipolar mood disorder after mTBI and may help us identify a unique set of treatment options for this subgroup of bipolar disorder.

The STEP-BD study was funded by NIMH contract #N01MH80001 through Massachusetts General Hospital and the Western Missouri Mental Health Center.

References

1. National Institutes of Health. Consensus Statement on Rehabilitation of Persons With Traumatic Brain Injury. Bethesda, Md: National Institutes of Health; 1998
2. Hofman PA, Stapert SZ, van Kroonenburgh MJ, et al. MR imaging, single-photon emission CT, and neurocognitive performance after mTBI. AJNR Am J Neuroradiol 2001;22:441–449
3. Evans DL, Byerly MJ, Greer RA, et al. Secondary mania: diagnosis and treatment. J Clin Psychiatry 1995;56(suppl 3):31–37
4. Sayal K, Ford T, Pipe R, et al. Case study: bipolar disorder after head injury. J Acad Child Adolesc Psychiatry 2000;39:525–528
5. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision. Washington, DC: American Psychiatric Association; 2000

Kemal Sagduyu, M.D.
School of Medicine, University of Missouri-Kansas City
Western Missouri Mental Health Center
Kansas City, Missouri

Smoking Cessation and Panic Attacks: A Report of 2 Cases

Sir: Several studies report an association between smoking and panic attacks[1–3] and suggest that in panic disorder patients, cigarette smoking precedes the onset of the first panic attack. Although there is evidence that smoking cessation can reduce the incidence of panic attacks, there is little evidence that smoking cessation is a risk factor for new-onset panic attacks.[1] We report 2 cases of anxiety attacks after acute smoking abstinence that met DSM-IV criteria for panic attacks in nicotine-dependent cigarette smokers participating in an 8-week double-blind, placebo-controlled smoking cessation trial with selegiline hydrochloride.

Case 1. Ms. A, a 52-year-old white woman with a history of smoking 1.5 packs of cigarettes/day since age 14 but no history of depression or anxiety disorder, was in the fourth week of participation in a smoking cessation study with selegiline hydrochloride. After the blind had been broken, it was determined that Ms. A had been prescribed active selegiline at the start of the study. Within 12 hours of her initial attempt to quit, which she made during the fourth week of the study, she experienced a sudden episode of palpitations, feelings of losing control, tachypnea, and diaphoresis lasting about 2 minutes. Symptoms were relieved by smoking 2 cigarettes. Five days later, during a second attempt to quit, she experienced a similar anxiety episode, which was again alleviated by cigarette smoking. Subsequently, she neither tried to reduce nor quit smoking during the remainder of the 8-week trial. At 6-month follow-up, she continues to smoke and has not reexperienced similar anxiety attacks.

Case 2. Ms. B, a 47-year-old divorced white woman with a past history of major depression but no history of panic attacks, reported smoking 1 pack of cigarettes/day for 31 years prior to her enrolling in the study. After the blind had been broken, it was determined that Ms. B had been prescribed placebo at the start of the study. After 36 hours of smoking abstinence during

the third study week, she experienced an episode of severe and sudden-onset anxiety, dizziness, sweating, light-headedness, tremulousness, palpitations, confusion, and disorientation for about 2 hours. Symptoms were relieved after smoking 2 cigarettes. Subsequently, she did not achieve smoking abstinence and remained free of panic attacks during the remainder of the trial and at 6-month follow-up.

These 2 cases may represent new-onset panic attacks causally related to acute smoking abstinence. It is notable that a previous report suggested that uncontrolled panic attacks developed in 2 patients after smoking cessation.[4] In the present report, both subjects reported no previous history of panic attacks, but 1 subject (Ms. B) reported a past history of major depression. Of note, the panic-like symptoms in both individuals subsided after smoking resumption. The onset of these panic symptoms was most likely not related to study medication (selegiline hydrochloride) since 1 subject was prescribed placebo. While depressive symptom relapse has been observed in some[5,6] but not all smoking cessation studies,[7,8] neither subject reported symptoms after acute abstinence that were consistent with a major depressive episode.

Nicotine is known to activate central serotonin systems in animals, and nicotine withdrawal reduces serotonergic function[9] in a manner similar to that of catecholamines.[10] Acute reduction of central serotonergic function may explain the pathophysiology of smoking abstinence–induced panic attacks.[11]

The following points should be noted in relation to these 2 cases: (1) the symptoms of these attacks were distinct from DSM-IV–defined nicotine withdrawal; (2) the onset of panic attacks during smoking cessation attempts may predict smoking cessation failure; and (3) treatment with selective serotonin reuptake inhibitors might be considered in patients who report panic symptoms during smoking cessation. Further study of smoking cessation and the onset of panic attacks appears warranted.

Supported in part by grants R01-DA-14039, R01-DA-13672, K12-DA-00167, and P50-DA-13334 from the National Institute on Drug Abuse (NIDA) and a Young Investigator Award from the National Alliance for Research on Schizophrenia and Depression (NARSAD) to Dr. George. Ms. Vessicchio and Mr. Termine report no financial affiliation or other relationship relevant to the subject matter of this letter.

References

1. Breslau N, Klein DF. Smoking and panic attacks: an epidemiologic investigation. Arch Gen Psychiatry 1999;56:1141–1147
2. Amering M, Bankier B, Berger P, et al. Panic disorder and cigarette smoking behavior. Compr Psychiatry 1999;40:35–38
3. Pohl R, Yergani VK, Balon R, et al. Smoking in patients with panic disorder. Psychiatry Res 1992;43:253–262
4. Brodsky L. Can nicotine control panic attacks? [letter] Am J Psychiatry 1985;142:524
5. Glassman AH, Covey LS, Stetner F, et al. Smoking cessation and the course of major depression: a follow-up study. Lancet 2001;357:1929–1932
6. Covey LS, Glassman AH, Stetner F. Major depression following smoking cessation. Am J Psychiatry 1997;154:263–265
7. Tsoh JY, Humfleet GL, Munoz RF, et al. Development of major depression after treatment for smoking cessation. Am J Psychiatry 2000;157:368–374
8. Thorsteinsson HS, Gillin JC, Patten CA, et al. The effects of transdermal nicotine therapy for smoking cessation on depressive symptoms in patients with major depression. Neuropsychopharmacology 2001;24:350–358
9. Koob GF, Le Moal M. Drug addiction, dysregulation of reward, and allostasis. Neuropsychopharmacology 2001;24:97–129
10. Ward KD, Garvey AJ, Bliss RE, et al. Changes in urinary catecholamine excretion after smoking cessation. Pharmacol Biochem Behav 1991;40:937–940
11. Miller HE, Deakin JF, Anderson IM. Effect of acute tryptophan depletion on CO2-induced anxiety in patients with panic disorder and normal volunteers. Br J Psychiatry 2000;176:182–188

Jennifer C. Vessicchio, M.S.W.
Angelo Termine, B.S.
Tony P. George, M.D.
Yale University School of Medicine
Connecticut Mental Health Center
New Haven, Connecticut

Olanzapine for Cocaine Craving and Relapse Prevention in 2 Patients

Sir: A major focus of research in treatment for cocaine and stimulant dependence has been pharmacologic interventions to decrease craving and prevent relapse. Various medications have shown promise in uncontrolled clinical trials, but most fail to show consistent advantage over placebo in double-blind, placebo-controlled trials. Despite this, many practitioners continue to try various medications in an effort to find some means of decreasing cocaine use in dependent patients. Trials of dopamine agonists (bromocriptine, amantadine), dopamine antagonists (typical neuroleptics), antidepressants (bupropion, tricyclic antidepressants, selective serotonin reuptake inhibitors), anticonvulsants, other stimulants, naltrexone, and amino acid supplements have yielded inconsistent results.[1] Use of cocaine appears to generate intense reinforcing effects by promoting flooding of dopamine and serotonergic neurons in mesolimbic pathways, and the intensity of its effects may override the modulatory effects of these medications.[2]

Preclinical research has demonstrated that anticipation of drug use increases mesolimbic dopamine activation, and cocaine-induced neuroadaptations involving the dopamine system may underlie craving and hedonic dysregulation.[2] The atypical antipsychotic agent olanzapine is known to block drug-induced increases in mesolimbic activation; thus, a theoretical biochemical rationale exists for its potential use in the treatment of cocaine craving and subsequently for preventing relapses to drug use.[3] Clinically, the antipsychotic, mood stabilizing, anxiolytic, and sleep-enhancing effects of olanzapine all provide additional rationale to consider it a potentially useful agent for drug abuse treatment.

The very limited preclinical literature that looks specifically at olanzapine and cocaine indicates that pretreatment with olanzapine can attenuate the ability of cocaine to produce a conditioned place preference in rats (this suggests that olanzapine can effectively block the reinforcing effects of cocaine)[4]; however, another report suggests only a partial antagonism without clear-cut dose response.[5] There is 1 preliminary study[6] published in the European literature (in Spanish) of methadone maintenance–treated patients with comorbid cocaine dependence and without a diagnosis of schizophrenia who were administered olanzapine, 5 to 10 mg/day, in an effort to decrease cocaine use. Bano et al.[6] reported that 11 of 21 patients were able to decrease or stop cocaine use without inducting any pharmacokinetic interactions with methadone.

Many patients who are in the early stages of recovery from cocaine dependence experience cue-induced cravings, especially when they are exposed to people, places, or things associated with their previous drug use. This phenomenon might

include driving past the house of a dealer, socializing with other drug-using peers, the anticipation of usual weekend social events and drug-use routines, or emotional triggers such as anger, irritability, anxiety, depression, or insomnia. Patients may also experience visceral somatic sensations or autonomic hyperactivity as part of the experience of drug craving.

My colleagues and I have had relatively good experience treating such individuals with low-dose p.r.n. olanzapine. A number of our patients have reported that olanzapine effectively helps to put time and distance between the thought and action of returning to drug use and may serve as a key relapse prevention tool. The following cases illustrate what we believe to be the first report in English of olanzapine use in this regard.

Case 1. Ms. A is a 41-year-old divorced white woman with no prior psychiatric history who entered our treatment facility reporting an escalating pattern of cocaine use over the preceding 9 months. She stated that she began using cocaine recreationally following her divorce 3 years ago when she began to date a man who occasionally used cocaine intranasally on a "social" basis. She enjoyed the cocaine-induced euphoria, and her social life began to focus more and more on cocaine use. Her initial sporadic use pattern became a routine part of her weekend plans, and she noted that by Thursday or Friday of each week, her cravings became quite profound and included a number of somatic effects including "butterflies" in her stomach, increased heart rate and anxiety, and intense preoccupation with the ritualistic process of buying and using cocaine on Friday afternoons after work. She eventually began smoking crack cocaine, and this led to significant life dysfunction including financial stress, family problems, and job jeopardy. She also began selling personal belongings to afford the cocaine, and her personal hygiene and cognitive capacities gradually deteriorated. She sought treatment after an intervention by family members and significant others.

Ms. A was hospitalized for 3 days on an inpatient unit and subsequently followed up in a day hospital program for 2 weeks before transitioning to weekly outpatient care. During initial visits, she reported that the intensity of her cravings for cocaine made her very fearful of relapse, and she was prescribed olanzapine, 2.5 mg b.i.d. p.r.n., for these cravings. She also worked hard to learn other relapse prevention strategies and attended 12-step recovery meetings. Nevertheless, she still experienced cravings, especially on Friday afternoons, before Sunday football games (another ritualistic drug use event), and sometimes when she had difficulty sleeping and found herself reminiscing about previous cocaine use experiences. She utilized the 2.5-mg olanzapine doses approximately every other day during her 2-week stay in the day hospital program, and as her cravings dissipated with prolonged abstinence, her use of olanzapine gradually decreased. Ms. A reported that the subjective effect of the p.r.n. olanzapine was to "take the edge off"—to decrease anxiety and preoccupations and to provide a generalized calming effect. Subsequently, the cravings dissipated and she was able to utilize her coping skills without adjunctive pharmacologic intervention. At 6-month follow-up, however, she still finds that having a small supply of olanzapine in her glove compartment provides a "security blanket" just in case she is confronted with an urge or is feeling vulnerable to resuming drug use.

Case 2. Mr. B is a 36-year-old married African American man who entered treatment after a crack cocaine binge during which he smoked approximately $800 worth of crack cocaine over a 5-day period. He had a 5-year history of cocaine abuse interspersed with several periods of prolonged abstinence but stated that his neighborhood environment and the frequency of drug use among peers made it difficult for him to remain in recovery. He had recently lost a job with a trucking company due to a positive urine drug screen. His wife had issued him an ultimatum regarding their relationship because he had been spending all of their money on drugs rather than basic life necessities such as rent, food, and child support.

He identified a number of emotional triggers to relapse and stated that in general he had a short fuse and low frustration tolerance and that when he felt angry or overwhelmed, his response was to impulsively go buy some crack cocaine. Mr. B spent 3 days on our inpatient detoxification unit and then followed up with twice-weekly outpatient relapse prevention therapy groups for 1 month. He was given olanzapine, 2.5 to 5 mg b.i.d. p.r.n., for cocaine cravings and insomnia. He utilized the medication only a couple of times per week but reported that it effectively relieved irritability, anxiety, and/or drug cravings that might ordinarily have precipitated a relapse. At 6-month follow-up, Mr. B has had only 1 slip (1 occasion on which he used cocaine) and immediately contacted treatment providers and resumed taking olanzapine to prevent full-blown relapse.

Although neither of the above patients met diagnostic criteria for other major Axis I psychiatric disorders, my colleagues and I have had other patients with affective disorders, schizophrenia, and anxiety disorders who have also responded well to olanzapine as a relapse prevention agent in the management of comorbid substance use disorders. It is our impression, however, that the effects of olanzapine are independent of its mood-stabilizing or sedative effects, as we have had less success with agents with these properties (i.e., anticonvulsants, sedating antidepressants).

Given the significant substance abuse comorbidity in psychiatric patients (and psychiatric comorbidity in substance abuse patients),[7] any additional agents that may improve treatment outcomes and positively impact families and psychosocial functioning should warrant further interest. We hope that our clinical experience with olanzapine for cocaine craving and relapse prevention stimulates additional controlled trials.

Dr. Longo has been on the speakers bureau for Eli Lilly, Abbott, Bristol-Myers Squibb, and Pfizer.

References

1. Welsh CJ, Liberto J. The use of medication for relapse prevention in substance dependence disorders. J Psychiatr Pract 2001;7:15–31
2. Dackis CA, O'Brien CP. Cocaine dependence: a disease of the brain's reward centers. J Subst Abuse Treat 2001;21:114–117
3. Hutchison KE, Swift R, Attias E, et al. Effects of olanzapine on cue-elicited craving in moderate to heavy social drinkers: preliminary results [abstract]. Alcohol Clin Exp Res 1998;22(suppl 3):114A
4. Meil WM, Scheichter MD. Olanzapine attenuates the reinforcing effects of cocaine. Eur J Pharmacol 1997;340:17–26
5. Van Campenhout N, Dettaes P, Meert TF. Inability of antipsychotics to antagonize the cueing properties of cocaine in rats. Pharmacol Biochem Behav 1999;64:435–438
6. Bano MD, Mico JA, Aqujetas M, et al. Olanzapine efficacy in the treatment of cocaine abuse in methadone maintenance patients: interaction with plasma levels [in Spanish]. Actas Esp Psiquiatr 2001;29:215–220
7. Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse: results from the Epidemiologic Catchment Area (ECA) study. JAMA 1990;254:2511–2518

Lance P. Longo, M.D.
Aurora Behavioral Health Services
Milwaukee, Wisconsin

Sleep-Related Eating Disorder Induced by Olanzapine

Sir: Sleep-related eating disorder (SRED) is a recently described syndrome combining features of sleep disorders and eating disorders. This disorder consists of partial arousal from sleep followed by rapid ingestion of food, commonly with at least partial amnesia for the episode the following day.[1,2] As reviewed by Schenck and Mahowald,[3] the most frequent disorders responsible for SRED are sleepwalking, sleepwalking combined states (e.g., combined with amitriptyline treatment or periodic limb movement), restless legs syndrome, obstructive sleep apnea, eating disorders, and triazolam abuse. As far as we know, SRED has never been described in association with an atypical antipsychotic drug.

We present here 1 case of SRED induced by addition of olanzapine to the treatment of bipolar I disorder in a patient with a family history of sleepwalking.

Case report. Mr. A is a 52-year-old man suffering from DSM-IV bipolar I disorder. Due to a major depressive episode (DSM-IV criteria), he was hospitalized and successfully treated with fluoxetine (20 mg/day), nortriptyline (75 mg/day), and lithium (750 mg/day). After a 9-month follow-up, fluoxetine and nortriptyline were withdrawn. Eight months later, he presented with a hypomanic episode and psychomotor agitation. His lithium level was 0.6 mEq/L. Olanzapine (10 mg/day) was added to his treatment, resulting in a rapid resolution of the hypomanic symptoms. During the next visit, Mr. A reported sleep disturbances that occurred most nights and had begun several days after the initiation of olanzapine. When asleep, he walked through his apartment, went to the kitchen, and ate large amounts of sweet food (jam, chocolate). These episodes were witnessed by his wife who, when trying to awaken him, was met with an aggressive response. In the morning, he had no memory of these episodes. After olanzapine withdrawal, these episodes disappeared rapidly and definitively. The patient had no previous history of parasomnia, but his son had sleepwalking episodes as a child.

Regarding the chronology of the symptoms, the occurrence of SRED in this case appears clearly related to the addition of olanzapine to the treatment of our patient. The predominant disorder responsible for SRED is sleepwalking,[3] and nearly half of the patients with a SRED in a recent case series[2] were given a polysomnographic diagnosis of sleepwalking. Sleepwalking arises during slow-wave sleep and reflects impairment in the normal mechanisms of arousal from sleep, resulting in partial arousal during which motor behaviors are activated without full consciousness.[4] On the one hand, our clinical observation of SRED is compatible with the 2 cases of olanzapine-induced sleepwalking that were recently described and were postulated to be related to an increase of slow-wave sleep by olanzapine.[4] On the other hand, some other adverse events either related to olanzapine—that is, akathisia, increase of appetite,[5] restless legs syndrome, and periodic leg movements[6]—or related to lithium—in particular, nocturia—could be partially responsible for the occurrence of SRED by initiating partial arousal.

Moreover, lithium alone or in combination with antipsychotic drugs may induce somnambulistic-like behavior.[7,8] Olanzapine was recently approved by U.S. Food and Drug Administration for the indication of acute mania and is proposed as adjunctive long-term treatment with standard mood stabilizers.[9] Therefore, clinicians need to be aware of a potential occurrence of a SRED among bipolar patients treated with a combination of olanzapine and lithium.

The authors report no financial affiliation or other relationship relevant to the subject matter of this letter.

References

1. Winkelman JW, Herzog DB, Fava M. The prevalence of sleep-related eating disorder in psychiatric and non-psychiatric populations. Psychol Med 1999;29:1461–1466
2. Winkelman JW. Clinical and polysomnographic features of sleep-related eating disorder. J Clin Psychiatry 1998;59:14–19
3. Schenck CH, Mahowald MW. Review of nocturnal sleep-related eating disorders. Int J Eat Disord 1994;15:343–356
4. Kolivakis TT, Margolese HC, Beauclair L, et al. Olanzapine-induced somnambulism [letter]. Am J Psychiatry 2001;158:1158
5. Conley RR, Meltzer HY. Adverse events related to olanzapine. J Clin Psychiatry 2000;61(suppl 8):26–30
6. Kraus T, Schuld A, Pollmacher T. Periodic leg movements in sleep and restless legs syndrome probably caused by olanzapine [letter]. J Clin Psychopharmacol 1999;19:478–479
7. Landry P, Warnes H, Nielsen T, et al. Somnambulistic-like behavior in patients attending a lithium clinic. Int Clin Psychopharmacol 1999;14:173–175
8. Charney DS, Kales A, Soldatos CR, et al. Somnambulistic-like episodes secondary to combined lithium-neuroleptic treatment. Br J Psychiatry 1979;135:418–424
9. Sanger TM, Grundy SL, Gibson PJ, et al. Long-term olanzapine therapy in the treatment of bipolar I disorder: an open-label continuation phase study. J Clin Psychiatry 2001;62:273–281

Vincent Paquet, M.D.
John Strul, M.D.
Laurent Servais, M.D.
Isidore Pelc, M.D., Ph.D.
Pierre Fossion, M.D.
CHU Brugmann, Free University of Brussels
Brussels, Belgium