Letters to the Editor

A Case Report of Reduction in Alcohol Craving and Protection Against Alcohol Withdrawal by Gabapentin

Sir: Gabapentin is a novel anticonvulsant that has been used in the treatment of epilepsy and, more recently, psychiatric disorders, including bipolar affective disorder,[1,2] behavioral dyscontrol,[3] and anxiety disorders.[4,5] We have had good results in using it to augment selective serotonin reuptake inhibitors in the treatment of obsessive-compulsive disorder (OCD), with few, and generally benign, side effects. We describe here a serendipitous finding: a patient with OCD and comorbid, long-standing severe alcohol dependency lost his craving for alcohol and stopped drinking precipitously without signs of withdrawal approximately 3 weeks after beginning treatment with gabapentin.

Case report. Mr. A is a 38-year-old man with OCD, alcohol dependence, and history of amphetamine dependence. Mr. A's OCD symptoms, predominantly contamination fears of germs and resultant frequent hand washing, began at the age of 13 and have been severe. To avoid contact with "contaminated" objects, he frequently stayed in bed for most of the day. Since age 27, when he first entered treatment, he has been treated with maximum doses of sertraline, sertraline plus buspirone, fluoxetine plus clomipramine, clomipramine plus buspirone, paroxetine, and paroxetine plus olanzapine, with little symptom relief. He began abusing alcohol at age 21 and amphetamines at age 25, and these substances reportedly alleviated his OCD symptoms. Twelve years ago, he completed a 6-month alcohol treatment program, but relapsed soon afterward. He quit using amphetamines $1^1/_2$ years ago, but continued to drink heavily, about a fifth of liquor a day. An attempt to wean him from alcohol by using clonazepam was unsuccessful owing to his continued alcohol craving. His medical history is significant for AIDS and hypertension.

Seven months ago, we added gabapentin to augment the paroxetine OCD treatment. His other medications, taken for years, included hydrochlorothiazide and atenolol for hypertension, quaifenesin for sinus congestion, and anti-HIV medications (indinavir, zidovudine, and lamivudine). He was started on gabapentin, 300 mg b.i.d., for 1 week, then increased to 300 mg t.i.d. for 1 week, then 600 mg b.i.d. One month later, he returned to clinic and reported that, although he had no reduction in his hand-washing frequency, he was less avoidant of "contaminated" objects and also had more energy and motivation. Moreover, he had stopped drinking 10 days previously ($2^1/_2$ weeks after starting gabapentin), had experienced no symptoms of withdrawal, and had no craving for alcohol. He reported the alcohol cessation had not been planned, but rather was a result of a loss of alcohol craving since starting gabapentin treatment. His only gabapentin side effect was transient dizziness. At that time, we increased the gabapentin to 900 mg b.i.d. for 1 week, then 1200 mg b.i.d. One month later, he continued to be abstinent from alcohol and had no craving. He avoided "contaminated" objects even less, but washed his hands more frequently as a result of contact with these objects. He continued to have increased energy and motivation and no longer spent the day in bed. He had no gabapentin side effects. We then increased gabapentin to 1200 mg t.i.d., which he tolerated well with only transient sedation. Now, after 7 months on gabapentin treatment, although his hand-washing frequency remains the same, he continues to have no craving for alcohol.

This case is the first known report of gabapentin reducing alcohol craving in a person with alcohol dependence. Gabapentin was reported to effectively treat alcohol withdrawal in 6 patients,[6] and it also apparently protected our patient against withdrawal. The protective effect of gabapentin against the convulsant and anxiogenic aspects of alcohol withdrawal has been reported in mice,[7] as has its protective effect against alcohol withdrawal excitability in mouse hippocampal slices.[8] In one case report, gabapentin reduced the effects of cocaine withdrawal and craving.[9] The mechanism of gabapentin's anticonvulsant and anxiolytic activity is unknown. It is structurally related to the neurotransmitter gamma-aminobutyric acid (GABA), but does not interact with GABA receptors, metabolically convert to GABA, or inhibit GABA uptake or degradation.

On the basis of this case report, the case report of gabapentin's protection against alcohol withdrawal, and the neurobiological studies of gabapentin's protective effect against alcohol withdrawal in mice, we believe a prospective, placebo-controlled study of gabapentin to investigate its effect on alcohol craving and withdrawal in patients would be worthwhile.

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The Nosology of Compulsive Skin Picking

Sir: Arnold and colleagues[1] have made an important contribution by providing detailed information about the demographic and clinical characteristics of patients with compulsive skin picking. Despite the apparently high prevalence and associated morbidity of compulsive skin picking,[2,3] there has to date been relatively little empirical research on its phenomenology or treatment.[4,5] Interest in this disorder might be further encouraged if the field were to agree on an appropriate diagnostic category and name for a behavior that has previously been characterized in many different ways (psychogenic excoriation, neurotic excoriation, dermatotillomania, pathological skin picking).

One possibility is that the disorder falls under the DSM-IV diagnosis of stereotypic movement disorder. However, this diagnosis is arguably problematic in a number of ways. First, stereotypic movement disorder is classified as a disorder usually first diagnosed in infancy, childhood, or adolescence and is often associated with mental retardation, whereas psychogenic excoriation often has its onset in intellectually normal adults.[1,2,5] Second, the rather strict criteria for stereotypic movement disorder might exclude many patients who suffer from compulsive picking; the DSM-IV requires that the behavior markedly interfere with normal activities or result in self-inflicted bodily injury requiring medical treatment.

Another possibility is that the behavior should be classified, like trichotillomania, in the DSM section on impulse-control disorders not elsewhere classified, as an impulse-control disorder not otherwise specified. Interestingly, skin picking and hair pulling have a number of clinical features in common.[1,4,5] Nevertheless, the classification of trichotillomania along with disorders like pathological gambling and kleptomania is itself a moot decision. Certainly, a significant portion of patients with hair-pulling[6] or skin-picking[1] behavior do not experience both an increased sense of tension before the behavior and a sense of relief, pleasure, or gratification after the behavior (features that are listed as characteristic of the impulse-control disorders in the DSM system).

A third possibility would be for the DSM system to establish a separate category of diagnoses for various forms of compulsive self-injurious behavior. A number of authors have suggested that obsessive-compulsive disorder (OCD) itself fits poorly into the anxiety disorders[7] or that there should be a separate category of obsessive-compulsive spectrum disorders.[8] Nevertheless, it should be emphasized that compulsive self-injurious behaviors (hair pulling, skin picking) differ in significant ways, both phenomenologically and perhaps also neurobiologically, from classical OCD.[4,9]

Although the term *compulsive skin picking* arguably has the disadvantage of being too redolent of OCD, we are inclined to favor this name over *neurotic excoriation* (a term that has been phased out of the DSM), *psychogenic excoriation* (the etiology of the condition is in fact unknown), and *dermatotillomania* (too unwieldy). In view of the problems with the categories of stereotypic movement disorder and impulse-control disorder, we are also inclined to believe that a change in the DSM system is needed in order to categorize compulsive skin picking, trichotillomania, and other forms of compulsive self-injurious behavior appropriately.

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Drs. Arnold and McElroy Reply

Sir: We appreciate the comments of Drs. Stein and Simeon and agree that there is a need for consensus about the appropriate classification and name for this behavioral disorder characterized by excoriation.

Our group has hypothesized that this disorder may be best conceptualized as an impulse-control disorder. Most of the subjects in our study experienced irresistible impulses, mounting tension with the impulse, and relief or pleasure with enactment of the impulse.[1] As in trichotillomania and other impulse-control disorders, subjects with psychogenic excoriation perform harmful behaviors with occasional automatic enactment of the behaviors.

However, although the majority (N = 27, 79%) of the 34 subjects in our study had features of an impulse-control disorder, 2 subjects had only compulsive symptoms and were given a diagnosis of obsessive-compulsive disorder (OCD). Five subjects had excoriation that was only in response to pruritus and were given a diagnosis of undifferentiated somatoform disorder without a diagnosis of impulse-control disorder.[1] Excoriation may therefore be a symptom of several disorders (including medical disorders) that must be ruled out before a diagnosis of an impulse-control disorder is made.

We agree that the current DSM-IV definition of an impulse-control disorder does not take into account the heterogeneity of the behavior associated with psychogenic excoriation or trichotillomania, as well as other impulse-control disorders such as kleptomania and pathological gambling. Indeed, like other impulse-control disorders, psychogenic excoriation appears to span a compulsivity-impulsivity spectrum.[2–5]

Our group has proposed a bidimensional model to account for the heterogeneity of the behaviors found in disorders like psychogenic excoriation.[2] In this model, both compulsivity and impulsivity are characterized by the presence of irresistible or compelling images or impulses associated with anxiety or tension and/or by repetitive behavior aimed at reducing the discomfort associated with the original image or impulse. Purely compulsive states are further characterized by "harm-avoidant" behaviors, insight into the senselessness of the behavior, resis-

tance to performing the behavior, and the absence of pleasure when the behavior is performed. Purely impulsive states, in contrast, would be characterized by harmful but potentially exciting behaviors, little insight, little resistance, and pleasure when the behavior is performed. Various combinations of these 2 pure states could account for the similarities sometimes seen in these disorders and also for "mixed" compulsive-impulsive conditions. This model fits our findings of co-occurrence of OCD and impulse-control disorder and the mixture of compulsive and impulsive features in many subjects with psychogenic excoriation.[1] We and others have further hypothesized that the OCD spectrum disorders are related by sharing a core disturbance in compulsivity and/or impulsivity and may constitute a family of conditions more accurately termed compulsive-impulsive spectrum disorders.[3]

Finally, we chose to call this disorder *psychogenic excoriation* for several reasons. *Excoriation* is the term used in the dermatological literature and is broader than the term *skin picking*. We used *psychogenic* because it implied a psychiatric cause for the excoriation. We avoided using *compulsive* because it was too suggestive of obsessive-compulsive disorder and *neurotic* because of negative connotations of this term. We may also support the use of the term *dermatotillomania*. It is no more unwieldy than "trichotillomania" and may underscore the similarities of the 2 disorders. In addition, other dermatological problems that are related, have similar names, and should also be included with other impulse-control disorders are onychotillomania (nail excoriation) and onychophagia (nail biting).

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Transient Syncope and ECG Changes Associated With the Concurrent Administration of Clozapine and Diazepam

Sir: Syncopal attacks have been reported in patients who were treated with a combination of clozapine and benzodiazepines.[1,2] These patients had a sudden loss of consciousness and no visible respiration or measurable blood pressure followed by recovery within 5 minutes to a few hours. Also, a lethal case[3] and severe orthostatic hypotension[4] have been reported for this combination of drugs. We describe a patient who developed a brief syncopal attack with significant electrocardiogram (ECG) changes after clozapine dosage was increased to 300 mg/day while he was receiving diazepam (30 mg/day).

Case report. Mr. A, a 50-year-old man, had symptoms of chronic paranoid schizophrenia resistant to typical neuroleptics. Previously, a reduction in his aggression, anxiety, and hallucinations was achieved through the concurrent administration of haloperidol (90 mg/day), diazepam (40 mg/day), chlorprothixene (700 mg/day), citalopram (40 mg/day), and biperiden (4 mg/day). Despite this heavy medication regimen, Mr. A was regularly isolated because of his aggravated symptoms.

Initially, chlorprothixene was gradually removed from Mr. A's daily medication regimen. Clozapine administration was then begun at 12.5 mg/day; the dosage was increased daily by 12.5 mg to a final daily dosage of 300 mg. Simultaneously, haloperidol treatment was gradually terminated, and Mr. A had received a final dose of 15 mg 2 weeks before the syncopal attack. The diazepam dosage was lowered to 30 mg/day at the time clozapine treatment was initiated. Thirty days after clozapine treatment was started, when the clozapine dose was 300 mg/day and diazepam 30 mg/day, Mr. A collapsed while walking on the ward to receive his morning medication. He regained consciousness, but was soporose and could not move without assistance. He had no chest pains, his blood pressure was 98/70 mm Hg, and his respiratory frequency was 20 breaths/min. An ECG obtained immediately showed signs of sinus bradycardia (40/min) with deep anteroseptal inverted T waves and minor ST segment changes in other leads. Mr. A was moved to an emergency care unit, and no abnormalities in auscultation or laboratory examination results were found (i.e., C-reactive protein and hemoglobin levels, blood leukocyte count, electrolyte level, arterial blood gas analyses, cardiac enzyme level, creatine kinase and its MB subfraction). After an observation period of a few hours, Mr. A was transferred back to his own ward. He recovered, uneventfully, and haloperidol and diazepam treatment resumed. The results of a postrecovery ECG matched those of an ECG obtained 4 years before the incident, which had shown no irregularities. Mr. A's condition remained stable at 1-year follow-up. The decision was made at follow-up to discontinue clozapine instead of diazepam to avoid the possibility of convulsive seizure.

Because the patient received the last dose of haloperidol 2 weeks before the incident, it seems unlikely that haloperidol was responsible for this attack, and no serious adverse side effects have been reported for the concurrent administration of biperiden or citalopram with either clozapine or benzodiazepines.[2]

The pathophysiology of possible clozapine-benzodiazepine interactions, however, is not well researched. Blood clozapine levels were not monitored, as the medication regimen had just been initiated and the dosage had not stabilized. Diazepam and other benzodiazepines may increase blood clozapine levels,[5] although an earlier study reported no such influence.[6] This is probably not of primary consideration in the present case, however, since clozapine monotherapy has not been reported to induce ECG changes. Moreover, diazepam is metabolized by CYP2C19, a cytochrome P450 isoenzyme not directly involved in the metabolism of clozapine.[7]

Unfortunately, ECG results were not reported in former syncopal cases.[1,2] ECG results in the present case simulated myocardial ischemia, but no cardiac enzymatic leakage was found. The bradycardia and hypotension justify a classification of neurocardiogenic syncope.[8] However, this condition is more common in younger patients, and some identifiable trigger is usually involved, e.g., an emotionally upsetting event. Postural hypotension also may have contributed to the syncope in the present case, since the patient was prescribed biperiden, a potent anticholinergic agent.

This case report adds support to the opinion that beginning clozapine therapy in the context of established benzodiazepine treatment may pose a risk for serious adverse drug interaction. Further, such a combination may modify ECG findings and mimic myocardial ischemia. In clinical practice, we recommend ECG monitoring if syncope occurs in the context of a clozapine-diazepam combination. Also, our report suggests that patients taking these 2 medications together should be monitored more closely, even though a clozapine-diazepam interaction is rare and cannot be conclusively determined to be the definitive cause for this attack. Further studies are indicated to establish the relevance of this interaction.

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Treatment of Inhalant Abuse With Risperidone

Sir: Because inhalants are inexpensive, readily available, and easily concealed, they are frequently the first mood-altering substances used by children.[1] Surveys reveal inhalant use as early as 6 years of age, increasing to a rate of 21.6% in 8th grade.[2] Acute effects of inhalants include euphoria, spatial and visual distortions, and impulsivity. Chronic use leads to neurologic and psychiatric symptoms including incoordination, irritability, paranoia, aggression, and cognitive impairments.[3] Poor school and job performance and delinquency follow.[3,4] Treatment of inhalant use disorders is difficult. This report describes the effects of risperidone in one patient with inhalant-induced psychosis and dependence.

Case report. Mr. A, a 25-year-old white man, first inhaled rubber cement at 12 years of age. At age 20, he began inhaling gasoline and carburetor cleaning fluid almost daily, producing psychosis with visual and auditory hallucinations and paranoia. After 2 hospitalizations, his psychosis and mood lability responded only partially to thioridazine, 50 mg q.i.d., and divalproex, 500 mg t.i.d. Despite 3 inpatient chemical dependency treatments, inhalant use continued, causing separation from his wife and loss of job. Recurrent gasoline inhalation produced further psychosis and threats to and aggressive shoving of family members, requiring a third hospitalization. Risperidone (0.5 mg b.i.d.) effectively reduced the hallucinations and paranoia and eliminated aggressive behavior. At 4-week follow-up, Mr. A reported significant reductions in paranoia and craving for inhalants. He started a new job. With an increase in risperidone to 1 mg b.i.d., paranoid thoughts ceased and craving for inhalants was markedly reduced. At 12 week follow-up, he had not relapsed. The 12 weeks without inhalant abuse was the longest time he had maintained since age 20. His abstinence from inhalants was confirmed by his parents and probation officer.

Since there was no concomitant psychosocial intervention, his unprecedented abstinence from inhalants associated with reduced inhalant craving may be attributed to risperidone. This report suggests that additional study of the effectiveness of risperidone in relieving both psychosis and craving may be of value.

This report complements the finding of Hernandez-Avila et al.[4] that antipsychotics are useful in treating inhalant use disorders. Since Hernandez-Avila et al.[4] and Byrne et al.[3] emphasize the need for long-term treatment, risperidone may be preferable to typical antipsychotics. It may be more effective and less likely to produce acute extrapyramidal symptoms or tardive neurologic dysfunction. Because of the limitations of this uncontrolled single case report, these suggestions need further investigation in appropriately designed clinical studies.

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