History of Trauma in People With Schizophrenia Predicts Need for Seclusion and Restraint

Sir: Studies from the United States suggest that the lifetime prevalence of both severe traumatic events and posttraumatic stress disorder (PTSD) is higher in people with schizophrenia than in the general population. It has been suggested that comorbidity with PTSD is characterized by more severe schizophrenic symptoms and could be associated with poorer outcome. Psychiatric inpatient treatment under some circumstances can be experienced as traumatic and can cause PTSD-like symptoms, particularly if compulsory interventions such as involuntary treatment, seclusion, and restraint are necessary. Patients with schizophrenic disorders are the patients most frequently exposed to such interventions.

We have compared treatment outcome and adverse experiences during hospital stay in inpatients with schizophrenic disorders with and without a history of trauma.

Method. The study was conducted from October 1, 2004, to March 31, 2005. We interviewed consecutively admitted patients with schizophrenic disorders (ICD-10 F2) with the Posttraumatic Diagnostic Scale. We inquired also for traumatic experiences during previous psychiatric treatment, but we did not include them as criterion A events (DSM-IV) of life-threatening character and thus did not take them into account in making PTSD diagnoses. Baseline and outcome measures (Positive and Negative Syndrome Scale [PANSS] score, Global Assessment of Functioning [GAF] score, length of stay) and adverse experiences during treatment (suicide attempts, seclusion, restraint) were recorded prospectively. One hundred seventy-three subjects were screened; of these, 118 subjects (56 males and 62 females) gave informed consent and participated in the interview.

Results. Subjects who were and were not included did not differ in age, nationality, length of stay, number of previous admissions, GAF and PANSS score at admission, or frequency of adverse experiences. The percentage of men was lower among included subjects. A lifetime history of criterion A events was reported by 58 subjects (49.2%; 43.3% among females), and a PTSD diagnosis could be established in 33 subjects (28.0%; 32.3% among females). The most frequently reported traumatic experiences were violent assault (28.8% of all subjects), witnessing violent assault (15.2%), and sexual assault by non–family members (10.2%).

In tune with the literature, violent assaults were more frequent among men and sexual assaults were more frequent among women. Subjects with and without lifetime history of trauma did not differ with respect to age, length of stay, number of previous admissions, GAF and PANSS score at admission and discharge, or suicide attempts, nor were these differences found between subjects with and without comorbid diagnosis of PTSD or between genders. However, seclusion and restraint (including the index admission, the mean number of previous admissions was 8.9) were experienced by 16.6% of the individuals without history of trauma but in 56.1% of those with a history of trauma (p < .0001). This difference applied for both females (11.8% vs. 51.9%, p < .01) and males (23.1% vs. 60%, p < .01). During index admission, 10.2% of patients without history of trauma but 22.8% of those with such history underwent seclusion or restraint (p = .06).

The prevalence of PTSD among our sample of patients with schizophrenia was similar to that reported in available U.S. studies, but the prevalence of lifetime traumatic experiences was considerably lower. We suggest that traumatic experiences can be reactualized during inpatient treatment and may lead to an unhappy cycle of adverse experiences of compulsory intervention and retraumatization.

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

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Aripiprazole-Associated Seizure

Sir: Aripiprazole is a novel antipsychotic agent with unique pharmacologic properties. It has both partial agonist and antagonist effects to dopamine receptors and is considered a dopamine stabilizer. Aripiprazole treatment was reported to have low incidence of side effects; its side effect profile includes extrapyramidal side effects, body weight gain, and metabolic disturbances. Both typical and atypical antipsychotics can lower the seizure threshold; the seizure risk of aripiprazole was reported to be 0.1%. In a literature search, I found only 1 case report of aripiprazole-induced seizure in premarketing clinical studies. Here, I report a seizure attack in a male schizophrenic patient treated with aripiprazole.

Case report. Mr. A, a 40-year-old man, has suffered from DSM-IV schizophrenia, paranoid type, for 10 years. His symptoms included delusions of control and auditory hallucinations. He was hospitalized in 2005 owing to relapse of his psychotic symptoms. Mr. A had no history of seizure attack. He was initially treated with risperidone 5 mg daily, which was discontinued due to extrapyramidal side effects 1 week later.
The patient was then treated with aripiprazole 10 mg daily and flunitrazepam 2 mg per night; this treatment was associated with good response for 6 weeks until the seizure attack. He was witnessed to lose consciousness and fall, followed by tonic-clonic generalized convulsion for about 3 minutes, then postictal confusion for about 1 hour. Findings of laboratory tests were within normal limits. However, physical examination revealed that he had a right shoulder fracture. Mr. A was transferred to surgery for an operation. After the episode, his medication was changed to diazepam 10 mg daily and olanzapine 5 mg and flunitrazepam 2 mg every night. No seizure attack has been observed since then.

There was no history of seizure attack, head injury, or central nervous system infection in this patient, nor did he have family history of convulsion or neurologic disorders. The patient also has no history of substance abuse disorders. There are 3 records of electroencephalographic findings within normal limits in his past hospitalization stays. Hence, aripiprazole was highly suspected as the offending agent.

Aripiprazole is a new antipsychotic agent (on the market in Taiwan only since 2005); thus, there is limited information about the drug in postmarketing surveillance. The seizure attack in this patient treated with aripiprazole warrants the precaution of the likelihood of seizure attack related to aripiprazole. Risk factors for psychotropic drug–related seizure such as personal and family history of convulsion disorders, head injury, or concomitant medical illnesses are not found in this patient. Hence, individual genetic susceptibility such as slow metabolic rate or idiosyncratic receptor binding of aripiprazole might play an important role in this patient. Further pharmacogenetic study is needed to address this issue.

Dr. Tsai reports no financial or other relationship relevant to the subject of this letter.

The author appreciates the kind writing assistance from Prof. Chia-Hsiang Chen, M.D., Ph.D.

REFERENCES

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Atypical Depression: Category or Specifier?

Sir: The article on atypical depression by Novick et al.1 found that individuals with major depressive disorder (MDD) with atypical features, as compared with MDD without atypical features, were more likely to be female and have a younger onset age—the most replicated findings in atypical depression.2–4 Most atypical depression literature has implied that atypical depression is a subtype of MDD.5,9 Recent studies showed that atypical depression is more common in bipolar II disorder than in MDD.4,6,7,10,11 Similarity between bipolar II disorder and MDD atypical depression would support a categorical atypical depression (vs. a DSM-IV-TR specifier approach).

To test the similarity between bipolar II disorder atypical depression and MDD atypical depression, comparisons should be made between features most commonly reported to distinguish atypical depression and non-atypical depression, such as gender and onset age. If atypical depression were a category, no differences in gender and onset age should be found between bipolar II disorder and MDD atypical depression.

To that end, a database of consecutive non–tertiary care outpatients with bipolar II disorder and an MDD major depressive episode (MDE) seen at the author’s outpatient private practice from June 1999 through December 2005 was scanned. Patients had been interviewed with the Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version,12 by a senior clinical/research psychiatrist (the author) during the first visit; patients had been off treatment with psychoactive drugs for at least 2 weeks when they presented. Full study methods are reported in a previous Journal article.13 Because data were recorded for different goals, bias is unlikely.

For patients with bipolar II disorder (N = 379), the mean (SD) age was 41.3 (13.0) years; 67.2% were female, and atypical features were present in 53.0%. Patients with MDD (N = 271) had a mean (SD) age of 46.6 (14.6) years; 61.6% were female, and atypical features were present in 29.1%. Patients with atypical depression (N = 280), compared with non-atypical depression (N = 370), were significantly more likely to be female (72.5% vs. 59.1%, χ2 = 12.4, df = 1, p = .000) and had a younger mean (SD) age at onset of first MDE (22.7 [10.5] years vs. 29.3 [13.6] years; t = 6.7, df = 648, p = .0000). Mean (SD) onset age for patients with bipolar II disorder atypical depression (N = 201) was 21.5 (9.9) years; in patients with MDD atypical depression (N = 79), it was 25.7 (11.6) years (t = 3.0, df = 278, p = .0026). Females constituted 72.6% of patients with bipolar II disorder atypical depression and 71.1% with MDD atypical depression (χ2 = 0.0, df = 1, p = .9348; N = 278). We tested whether differences in gender and onset age between atypical depression and non-atypical depression were diagnosis-independent. Logistic regression of atypical depression versus gender found an odds ratio (OR) of 1.8 (95% CI = 1.3 to 2.5, p = .000); when bipolar II disorder was controlled for, the OR was 1.7 (95% CI = 1.2 to 2.4, p = .001). No interaction between gender and diagnosis was found (p = .703). Two-way analysis of variance of onset age in atypical depression versus non-atypical depression, by diagnosis, found a significant diagnosis effect (F = 22.7, p = .0000); an interaction was found between atypical depression and diagnosis (F = 9.5, p = .0021).

The difference in onset age between bipolar II disorder and MDD atypical depression does not seem to support a categorical atypical depression. However, the similar gender frequency between bipolar II disorder and MDD atypical depression does seem to support a categorical atypical depression. If onset age were a more important diagnostic validator than gender,14 a categorical atypical depression would not be supported. The logistic regression finding suggests that the greater number of females is a diagnosis-independent feature of atypical depression, whereas the 2-way analysis of variance finding suggests that atypical depression onset age is diagnosis-dependent (diagnosis was an effect modifier), not supporting a categorical atypical depression. Results would support atypical depression as a specifier if onset age were more important than gender for diagnostic validity. A broad view of atypical depression presenting in several mood disorders should be followed, as such a view could increase insight into the now much-debated issue of its diagnostic validity.3,4,5,15–17

Dr. Benazzi reports no financial or other affiliation relevant to the subject of this letter.
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Dr. Novick Replies

Sir: This brief report touches on several interesting issues. In general, it stimulates one’s curiosity about how diagnostic categories (or descriptions) achieve validity, and it raises the question of whether age at onset is a more important diagnostic validator than gender. More specifically, it highlights the question of whether one should continue to approach the “atypical” descriptor as a specifier and not as a separate category. While having the answer to the latter question may clarify our use of different terms, it may be more interesting to know whether making the distinction would inform alternative treatment approaches or yield different clinical outcomes. In addition, the author bases the conclusions on an initial premise that suggests that “similarity between bipolar II and MDD [major depressive disorder] atypical depression would support a categorical atypical depression.” However, it is not clear whether this premise holds true; therefore, the conclusions may be unwarranted. Further elucidation would be welcome.

Dr. Novick reports no financial or other affiliation relevant to the subject of this letter.

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Psychotic Episode Possibly Induced by Light Therapy in a Nondemented Patient

Sir: Light therapy is a well-established therapeutic method to treat affective disorders, particularly seasonal depression. It has also been reported to be effective in schizoaffective disorder. Furthermore, light therapy has been used to treat advanced sleep phase syndrome. Known side effects of light therapy include mild hypomania and paranoid delusions in patients with Alzheimer’s disease. We report a case of a psychotic episode after light therapy in a nondemented patient suffering from schizoaffective disorder.

Case report. Ms. A, a 38-year-old woman with schizoaffective disorder according to ICD-10, was suffering from advanced sleep phases after complete remission of a prior psychotic episode. To treat the advanced sleep phases, we started evening light therapy in an outpatient setting in May 2002. The patient had not been treated previously with light therapy. We applied light therapy daily at 6:00 p.m. for 30 minutes using standard bright light (full spectrum, 10,000 lux).

Under this procedure, the sleep phases normalized during the first weeks of treatment. Furthermore, the general state of the patient improved. However, after 6 weeks of light therapy, the patient had to be admitted to our hospital again because of a new psychotic episode with anxiety, pressured thinking, and acoustic hallucinations of dialoguing voices, which was a typical pattern of a psychotic episode in this patient. We stopped light therapy immediately after the psychotic symptoms occurred, and Ms. A was admitted to the hospital 2 days later. Because the psychotic symptoms included sleep disturbance, it was impossible to evaluate the effect of the light therapy on the sleep phases after the beginning of the psychotic episode.

Both before and after the psychotic episode, Ms. A’s medication regimen of flupenthixol depot injections was continued without modification. The psychotic symptoms regressed rapidly after light therapy was stopped, and Ms. A was discharged with no psychotic symptoms after 3 weeks of hospitalization. During hospitalization, no other treatment apart from discontinuing light therapy and continuing the flupenthixol medication (without changing the dosage or the frequency of injection) was applied.

Light therapy is considered an effective therapeutic method with considerably few side effects. However, the risk of inducing psychotic symptoms, at least if used in patients with schizoaffective disorder, must be taken into account. To our knowledge, this is the first report of a psychotic episode prob-
ably induced by light therapy in a nondemented patient. Of course, an accidental coincidence in this single observation cannot be ruled out and must be considered when evaluating the presented case.

The reported case should lead to further studies, including, preferably, an A-B-A design, to clarify the causality between light therapy and psychotic episodes. However, clinicians should be aware of this possible side effect and need to screen their patients carefully when using light therapy in schizoaffective disorder.

The authors report no financial or personal conflict of interest relative to this letter.

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SPECT Imaging and Treatment of Pyromania

Sir: Although described in the medical literature for 200 years, pyromania is poorly understood.1 A recent study of psychiatric inpatients revealed that 3.4% endorsed current symptoms and 5.9% had lifetime symptoms consistent with pyromania.2 Understanding the neurobiology and treatment of pyromania may have public health consequences.

Case report. Mr. A, an 18-year-old man, reported a chief complaint of “feeling addicted to setting fires.” He described an 8-month history of setting multiple fires. After setting his first fire, Mr. A described a sense of calm, as it reduced his daily preoccupation with fires. His urges, however, returned within 2 weeks. Over the course of 8 months, Mr. A reported that the fires needed to be more intense to reduce his urges and that the urge-free periods between fires gradually grew shorter. Unable to control his behavior and wanting treatment, Mr. A voluntarily surrendered himself to authorities. Mr. A spent 14 months in prison, and upon release, requested treatment for daily urges to set fires.

Mr. A underwent a structured psychiatric assessment that included examination of DSM-IV impulse-control disorders. Mr. A met DSM-IV criteria for pyromania based on a module compatible with the Structured Clinical Interview for DSM-IV Disorders.2 There was no sexual component to the fire setting.

He denied symptoms consistent with other current or lifetime Axis I disorders. There was no history of conduct disorder, and structured examination of DSM-IV personality disorders found no personality pathology. Mr. A, his parents, and teachers all reported that he had been an ideal student, well-liked, friendly, and involved in community and school activities. IQ testing revealed above-average intelligence, consistent with prior school performance. Single photon emission computed tomography (SPECT) imaging revealed a left inferior frontal perfusion deficit.

Mr. A underwent 3 weeks of daily cognitive-behavioral therapy (CBT). Sessions lasted approximately 90 minutes each day. Therapy focused on imaginal exposure and response prevention, cognitive restructuring of responding to urges, and relaxation training. Concomitantly, Mr. A began a course of topiramate, starting at 25 mg/day. After 3 weeks of CBT and 1 week of topiramate 75 mg/day, Mr. A denied urges to set fires. Mr. A continued on topiramate treatment for the next 12 months without urges to set fires. After 12 months, follow-up SPECT imaging demonstrated no perfusion deficits. Mr. A has continued, symptom-free, on medication for 20 months.

This case represents the first examination of the possible neurobiology and treatment of DSM-IV pyromania. Topiramate, in combination with CBT, may be beneficial in treating behavioral addictions such as pyromania because of its hypothesized mechanism of modulating cortico-mesolimbic dopamine function.3 Controlled studies are needed to substantiate this observation. Because this is a single case report, these results may not generalize to the larger population of people with pyromania.

Dr. Grant reports no financial or other relationship relevant to the subject of this letter.

REFERENCES

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Use of a TENS Unit to Treat Self-Cutting in a Patient With Borderline Personality Disorder

Sir: Self-cutting and self-mutilation are common manifestations of borderline personality disorder.1 As the self-destructive behavior is relieving to the patient, it can be difficult to extinguish. In the past, behavioral approaches have used aversive stimulation, such as strong electric shocks, to reduce self-mutilation. Other successful approaches have involved relaxation, thought stopping, desensitization, withdrawal of reinforcements, and covert sensitization.2 However, these methods have required intensive inpatient work and may be difficult to apply to the outpatient setting. Ineffective treatment is of great
concern, as self-cutting can lead to lifelong scarring, emergency department visits, hospitalizations, wound infections, and accidental death.

Herein I describe a case of a novel treatment for self-cutting using a self-administered transcutaneous electro-nerve stimulator (TENS) unit, a device used to deliver a nonharmful electric current to the skin and underlying musculature and nerves. The device can be adjusted to vary from being painless to painful.

**Case report.** Ms. A, a 47-year-old white woman, was diagnosed with severe bipolar disorder, borderline personality disorder (both using DSM-IV-TR criteria), and fibromyalgia. At the time of this report, she is receiving maintenance electroconvulsive therapy, gabapentin, risperidone, and clonazepam to good effect to control her bipolar component. She is a complex patient who has been in treatment with me for about 2 years.

Although she attends supportive and insight-oriented therapy twice weekly, her borderline pathology has been difficult to treat. While she has exhibited the full spectrum of borderline symptoms, her self-cutting was the most troubling issue within her treatment. The patient would have once- or twice-weekly episodes of extreme despair, leading to dissociative episodes. These events would typically occur late at night or in the early morning. Self-cutting would bring relief by ending both the dissociation and the despair.

In one such event, the patient took an insulin needle and cut herself approximately 100 times across her forearms, bilaterally, requiring an emergency department visit and multiple stitches. Self-cutting resulted in 2 other emergency department visits in the year prior to this report. It also contributed to my decision to hospitalize her once for self-destructiveness when the self-mutilation escalated in severity and began occurring daily. Her cutting was unaffected by a full course of Dialectical Behavioral Therapy and the hospitalization—she was found cutting as an inpatient.

Four months prior to this report, the patient was prescribed a TENS unit (EpiX VT, Empti, St. Paul, Minn.) for dual purposes. Primarily, it was given to her for the treatment of her fibromyalgia, an indicated use for the device. However, the patient was also given the TENS unit to allow her to self-administer nerve and muscle stimulation with minimal medical risk. She was told of the rationale and gave her informed consent. She obtained the TENS unit for $720 through insurance. I instructed the patient to apply the electrode as if treating sciatica, using 2 leads placed bilaterally on the lower back or buttocks.

Since receiving the device, the patient has had no further episodes of self-mutilation. She reports using the device during the day and the night. She states she still wants to cut when she begins to feel “stress” or “depressed” but, instead, uses the TENS device and it makes her feel “alive again.” She now wears it most of the day, often powered down. When she feels unpleasant emotions or begins to dissociate, she turns on the TENS unit. If the unit is on but seems ineffective, she changes the “pattern” of the stimulating current and/or increases the amount of current and degree of sensation or pain. The patient habitually wears the TENS unit on her back, and others are unaware that she is using it. Because it is hidden, she reports that she often surreptitiously turns the unit on or modifies its settings, usually resulting in immediate relief.

TENS units are in common use for the treatment of chronic pain as well as in rehabilitation and physical therapy. The units work by applying a known current and voltage to the skin, usually arcing between 2 to 4 self-adhesive electrodes that the patients apply to themselves. The electrodes are either single-use or multiple-use. The multiple-use variety often last through several weeks of daily use. The treatment is believed to help reduce the perception of pain by flooding the thalamus with a benign stimulus that also closes the neuronal gates to other, more noxious stimuli. Also, the nerve stimulation may cause an increase in endorphins.

TENS units vary in their size and programming. Most units are quite small and appear to be a pager. They are unobtrusive and can easily be slipped into a pocket. The wires that attach the unit to the electrodes can be threaded through a small hole in a pocket, thereby making the treatment completely invisible.

In addition to size variations, units also vary according to their programming. Most units have the ability to vary the current over time. Thus, for example, one might choose a ramping-up effect over several seconds, or choose a random “pinging” or twinge-like program. Depending on the model, TENS units can have a few programs to more than a dozen. Patients often seem to find 2 or 3 different voltage/current/time programs that they prefer and switch between them for variety.

TENS units cost between $50 to $750. The electrodes cost around $20 for several weeks of treatment. If electrodes are overused to the point that they no longer evenly apply to the skin, there is a small risk of a resulting burn. There are also small risks associated with allergic reactions to the electrode adhesive. As a result, patients should examine the electrode sites daily when using the device. For the same reason, it is not advisable to wear a TENS unit while sleeping.

Electrodes should not be applied to the head. One should avoid placing the electrodes on the neck over the carotid arteries. TENS units are contraindicated in patients wearing a pacemaker or defibrillator, as the 2 devices may interact. Presumably, patients who have had a vagus nerve stimulation device implanted are also excluded. The safety of the TENS unit during pregnancy has not been established, and if a TENS unit is nonetheless used, the leads should not be placed on the lower back, abdominal, or pelvic areas.

While I believe that this case is encouraging, one should be cautious about overinterpreting its significance. The patient’s very dramatic improvement might be related to her becoming a “special patient” rather than the intervention. Also, the significance of just 1 case is questionable. Finally, one might question the ethics of giving a masochistic patient a device that could, conceivably, be used to self-punish. Nevertheless, if these findings are replicated in additional cases, a formal clinical trial testing whether TENS units can be used to safely reduce self-mutilation might be justified. Such a study could have a placebo treatment arm, using the TENS unit with minimal or infrequent output. Thus, participants might serve as their own controls.

Dr. Block reports no financial or other relationship relevant to the subject of this letter.

**REFERENCES**


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Memantine for Disruptive Behavior in Autistic Disorder

Sir: Medications affecting glutamate neurotransmission have become the focus of increasing interest in the treatment of severe neuropsychiatric disorders including schizophrenia, obsessive-compulsive disorder, and mood disorders. Glutamatergic dysfunction has been proposed as potentially important in the pathophysiology of autistic disorder. We report on an adult with autistic disorder whose disruptive behavior in the workplace improved during a trial of memantine, a low-affinity noncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist.

Case report. Mr. A, a 23-year-old man, was diagnosed with autistic disorder at age 2. He was initially referred to our clinic in 2004 for evaluation and treatment following his loss of 2 jobs secondary to reported harassing and intrusive behavior. Intense interest in coworkers had led to physically intimidating behavior and angry responses to supervisory intervention. Other than receiving a brief psychostimulant trial as a young child, Mr. A had received no prior psychoactive medication trials. Prior to the memantine trial, Mr. A was referred for neuropsychological testing, which estimated his cognitive abilities to be in the low-normal range.

Autistic disorder (DSM-IV-TR) represented Mr. A’s only psychiatric diagnosis. Additionally, he suffered from ulcerative colitis for which he took stable doses of mesalamine, azathioprine, and folic acid. Mr. A last suffered from acute symptoms associated with ulcerative colitis 8 months prior to beginning memantine. While taking memantine, the patient reported no gastrointestinal symptoms.

After a disruptive argument with supervisors on a new job, Mr. A was prescribed memantine, 5 mg at bedtime for 2 weeks, subsequently increased to 5 mg twice daily. At his follow-up visit, Mr. A complained that his morning dose was making him tired, so the dosing was changed to 10 mg at bedtime. He also stated that he felt calm at work, and he reported no further work-related conflicts. This positive effect was further confirmed during ongoing discussion with Mr. A’s job coach and parents, who noticed he appeared calm without disruptive behavior throughout the memantine trial. Overall, in addition to decreased disruptive behavior, the patient also exhibited decreased social withdrawal and impulsivity during the memantine trial. After 8 months of treatment, Mr. A continues at the same job with no reports of disruptive behavior on the same dose of memantine.

Few reports on the use of glutamatergic agents exist in patients with autism. D-Cycloserine, a partial agonist at the glycine site of the NMDA glutamate receptor, showed efficacy for social withdrawal in autistic children and young adults in a single-blind, placebo-controlled pilot study. Memantine has been the subject of 1 report in 30 children and adolescents with a pervasive developmental disorder. That study reported improvement in motor planning, attention, language, and repetitive behaviors.

Memantine was chosen to treat our patient for several reasons. First, Mr. A was able to verbalize that his disruptive behavior closely followed confrontations with others when he had difficulty understanding what was being asked of him. Our hypothesis was that if memantine could improve our patient’s social skills or social use of language, factors precipitating disruptive outbursts could be eliminated. Second, we believed that long-term use of memantine would be associated with less deleterious side effects than other agents, including atypical antipsychotics. Finally, Mr. A was given a choice of treatments after discussion of our hypothesis and review of potential side effects associated with memantine in comparison to those associated with the atypical antipsychotics. Mr. A’s mother was also aware of our discussions, and she supported a trial of memantine prior to consideration of antipsychotics.

No previous reports have described the effects of memantine on disruptive behavior in pervasive developmental disorders. Further study is indicated to better define potential efficacy and safety of memantine in pervasive developmental disorders.

Drs. Erickson and Chambers report no financial or other affiliation relevant to the subject of this letter.

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