Letters to the Editor

Use of Clonidine for Behavioral Control in an Adult Patient With Autism

TO THE EDITOR: Hyperactive and impulsive behavior in patients with autism has been treated by behavioral management and pharmacotherapy (including neuroleptics, antidepressants, β blockers, and sedating agents). Recently, reports and our own clinical experiences have noted the efficacy of using clonidine, a centrally acting hypertensive agent, in the management of aggressive and violent patients of various types (1, 2). We wish to report a unique use of clonidine in an adult patient with autism and intermittent aggressive behavior who was on a complicated pharmacotherapy regimen.

Ms. A was a 26-year-old woman with a diagnosis of autism and intermittent explosive disorder. During her early life she lived in a highly structured institutional setting and demonstrated occasional behavioral dyscontrol—mostly episodes of violent and aggressive acts toward caretakers, other patients, and, especially, children. Four years before our consultation, and shortly after she was hospitalized for aggressive behavior (dragging a child by the hair), she was medicated with a regimen of phenobarbital, 240 mg/day. This treatment, in addition to a regimen of thioridazine, 200 mg/day; carbamazepine, 600 mg/day; and clonazepam, 2 mg/day, controlled her aggression except for violent outbursts occurring once or twice a month.

At the time of our consultation, staff and Ms. A's mother noted her to be sedated, less verbal, and occasionally aggressive. Attempts were made to lessen the phenobarbital dose but violent behavior emerged. In an attempt to maximize her level of alertness and control of her behavior, a plan was made to decrease the phenobarbital regimen and initiate clonidine therapy. Her phenobarbital treatment was gradually decreased over a 3-week period during which time oral clonidine was used in doses of 0.4–0.6 mg/day. Occasional outbursts occurred during this period, requiring restraints and as-needed doses of clonidine.

At the end of 4 weeks, Ms. A was placed on a regimen of transdermal clonidine, two 0.3-mg patches per week, insuring she received 0.6 mg/day. Her behavior improved. She became more verbal and alert, and her structured therapy continued without incident for several weeks. One weekend, when a clonidine patch fell off, she became violent, necessitating an emergency room visit and oral clonidine for management. Apart from this episode, she has remained cooperative, friendly, and generally without aggressive behavior.

Clonidine is an effective agent for behavioral dyscontrol in some patients. In one study of eight male autistic children, oral clonidine was found to "modestly improve" hyperactive and impulsive behavior. However, clonidine was not used in conjunction with other medications (3). Transdermal clonidine has also been effective with this population for symptoms of hyperactivity and impulsiveness (4). Its effect may be related to α receptor blockade reducing sympathetic outflow from the central nervous system, one mechanism thought to be operative in aggression (5, 6). In this patient, clonidine was used in conjunction with other medications to control aggressive and violent outbursts and obviated the need for a more sedating medication. This improved her overall quality of life. Further work on a dose-response relationship and the long-term efficacy of this drug in patients with autism and aggression needs to be pursued, since it is reported that tolerance may develop in some individuals. In addition, while transdermal medication could increase compliance and efficacy and produce constant blood levels, inflammation or irritation at the site may reduce the absorption of the medication.

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Risperidone, Serotonergic Mechanisms, and Obsessive-Compulsive Symptoms in Schizophrenia

TO THE EDITOR: Risperidone is a new atypical antipsychotic drug that is similar to clozapine and has a high affinity for serotonin ($5\text{-}HT_2$)-type receptors (1). Serotonin antagonism is proposed to contribute to the antipsychotic properties of both drugs and, in the case of clozapine, is believed to exacerbate obsessive-compulsive symptoms in schizophrenia (2). Risperidone may share this characteristic.

Mr. A, a 22-year-old single Caucasian, was first hospitalized at age 19 with paranoid and bizarre delusions, auditory hallucinations, poverty of thought and speech, prolonged staring, blunted affect, and catatonic posturing. After an 8-week hospitalization, he was discharged on a regimen of flupenthixol, 8 mg/day. As an outpatient, Mr. A continued to demonstrate negative symptoms but denied hallucinations or delusions. Obsessive-compulsive features were present, including hand washing six to eight times per day lasting 5–7 minutes at a time, as well as counting and

checking. Despite these symptoms, he worked part-time in a warehouse.

Mr. A discontinued his medication 9 months following discharge and his psychosis worsened. He was rehospitalized and initially treated with a regimen of loxapine, 100 mg/day; benztropine, 2 mg/day; and clonazepam, 1 mg/day. On the positive, negative, and general psychopathology subscales of the Positive and Negative Syndrome Scale (3), he scored 22, 30, and 54, respectively. In addition to hand washing, Mr. A was showering for 35 minutes. Loxapine treatment was discontinued and a regimen of risperidone initiated.

Following 3 weeks of risperidone treatment up to a dose of 6 mg/day, his obsessive-compulsive symptoms worsened. He was washing his hands 15–20 times/day for periods in excess of 10 minutes. Showering occupied 1½ hours. Each shoelace was tied four or five times to get it "just right." However, his psychotic symptoms improved (scores of 8, 16, and 27 on the respective subscales of the Positive and Negative Syndrome Scale).

After 4 weeks of risperidone monotherapy, the serotonin reuptake inhibitor fluvoxamine, 100 mg/day, was administered as the sole concomitant medication. There were no adverse interactions with risperidone, and the patient's obsessive-compulsive symptoms abated dramatically over the subsequent 2 weeks. Hand washing diminished to his admission baseline frequency, with a shortened duration. Showering time decreased to 25 minutes. Mr. A reported a sense of relief, and his family found him to be socially responsive and prompt. Psychotic symptoms continued to be greatly diminished (scores of 7, 14, and 22 on the respective subscales of the Positive and Negative Syndrome Scale).

This case demonstrates that risperidone, like clozapine, can precipitate or exacerbate obsessive-compulsive symptoms in patients with schizophrenia, while acting as an effective antipsychotic. Fluvoxamine, which is a highly selective inhibitor of serotonin reuptake, was effective in ameliorating the obsessive symptoms and did not exacerbate the psychotic symptoms in this patient. The combination of a serotonin receptor blocker and a serotonin reuptake inhibitor appears to be antagonistic. However, risperidone exhibits 300–25,000-fold less affinity for 5-HT_1 subtypes than 5-HT_2 subtypes (1), and changes in serotonin receptors and reuptake sites in schizophrenia appear to occur in microanatomically distinct compartments (4). The interactions between risperidone and fluvoxamine in vivo are undoubtedly complex. Medications active with either component of the serotonin system may be efficacious in the treatment of schizophrenia, and judicious combination of these agents may be required to reduce unwanted effects.

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Nostalgia: A Swiss Disease

TO THE EDITOR: Recently, reviewing the papers of Dr. John Collins Warren of ether-operation fame, we were reminded that nostalgia was once considered a serious mental illness. Warren, in July of 1840, was called upon in Paris to attend Ellen Sears d'Hautville, a young married woman, pregnant and despondent, whose desire to return home to Boston was opposed by her Swiss husband. In the ensuing legal battle, Warren testified that the young woman was afflicted with "nostalgia": a state of mind that "proceeds from an unusual longing for the native country . . . . If the desire is opposed and cannot be gratified, it terminates in insanity, and sometimes produces death." The no doubt bewildered d'Hautville was further informed that the ailment is one to which the Swiss, his countrymen, were "particularly prone" (1).

The first detailed account of this illness appeared in 1688 in the doctoral thesis of Johann Hofer, who considered calling the condition "philopatridomania" but happily settled on "nostalgia" (from the Greek *nostos*, meaning "a return home," and *algos*, meaning "pain"). A second edition of Hofer's work employed a tongue twister: "pothopadrialalgia" (from the Greek *pothos* meaning "desire for what is absent or lost") (2). Cullen mentioned nostalgia in his work (3), and Parr's *Medical Dictionary* (London, 1809) classified it under Order VII Paranoiae. As a medical diagnosis, nostalgia retains its respectability, appearing in ICD-9 as adjustment reaction.

Warren's judgment that d'Hautville's countrymen were especially prone to nostalgia can be traced to Hofer's second edition, wherein one finds that a Swiss milking song ("Khue-Reyen" in German and "Ranz des Vaches" in French) could put homesick Swiss auditors over the edge. So readily could this music transform Napoleon's Swiss mercenaries into melancholy deserters or suicide victims that its playing was punishable by death (4).

Highlanders appear to have been more susceptible than lowlanders. We are told that Bosnian mountaineers conscripted into the Austrian army in the 1880s suffered like the Swiss; migrants from the mountains of Galicia in northwestern Spain experience a melancholia known as *morrina* or *saudade*. Some will recall from childhood readings (and with nostalgia) Heidi's low spirits when she was brought down from her mountain home.

Between 1820 and 1826, no fewer than 97 soldiers in the French army fell to this disease. But while Larrey, chief surgeon of the French army, recorded many similar cases in the retreat from Moscow, none occurred during Napoleon's Egyptian campaign (5).

An archivist making a rapid review of diagnoses made in McLean Hospital in Boston in the late 1840s failed to show that the diagnosis of nostalgia had been applied to a single patient during that period. We recall Yogi Berra's reported remark that he looked "forward to the future with great nostalgia."

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