

often of unusual nature. Despite the low rate of these hallucinations (0.08%–3%),<sup>4</sup> concerns may be raised over the use of non-benzodiazepine hypnotics, due to the diffusion of hypnotic drug prescriptions. Hallucinations with zolpidem are usually visual, template-like (a background abstract design), and mostly hypnagogic or hypnopompic. It was suggested that hallucinations may be secondary to rapid withdrawal and reintroduction of zolpidem.<sup>5</sup>

We report the case of a man with untreated bipolar I disorder and a history of benzodiazepine abuse who developed auditory command hallucinations after zolpidem overdose and subsequently enacted his misperceptual experience.

**Case report.** Mr A, a 32-year-old man, presented at a general hospital emergency department in January 2008 after stabbing himself. He reported mounting feelings of anxiety and inadequacy during the previous 20 days, with agitation, insomnia, depressed mood, nondelusional feelings of guilt, and impaired functioning. He denied alcohol or illicit drug intake; results of a drug screen test were negative. He had taken zolpidem 5 times during this 20-day period, and it was the only drug he took during this time. His prescribed dose was 10 mg prn, but on 2 occasions, he took 20 mg because he was not satisfied with the results obtained with the initial 10-mg dose.

The night prior to his presentation at the hospital, Mr A experienced severe agitation. This prompted him to ingest 40 mg zolpidem in about a half-hour. He suddenly felt overwhelmed, disoriented, and confused and started to perceive increasing background noise. He did not fall asleep and began to hear 2 conversing voices, one of which eventually commanded him to pierce his hands. He felt worthless and guilty, which prompted him to comply with the command. He stabbed his left hand with a knife, as he believed that he would thus expiate his guilt, but experienced no relief. His wife stopped him from continuing with the other hand. At psychiatric assessment, his hallucinations had subsided; overall, they lasted for 1 hour.

Mr A's psychiatric history began when he was 13 years old, with self-harming acts. At age 18, he reported a hypomanic episode followed by a depressive episode and heavy benzodiazepine abuse. Subsequently, he reported several depressive episodes, mostly with agitation and mixed features, alternating with periods of euthymia; for this reason, he was seen by many psychiatrists as an outpatient and was prescribed antidepressant drugs and benzodiazepines. He abused the benzodiazepines for a period of about 8 years, and he felt worse when taking antidepressants (increased anxiety, restlessness, and agitation). These "depressive" episodes were usually triggered by frustrating events and accompanied by self-mutilation episodes and benzodiazepine abuse. He had never experienced hallucinations, not even during his depressive episodes or his bouts of benzodiazepine abuse.

Past self-mutilation episodes consisted of self-cutting; they began when Mr A was 21 and, per patient report, ended when he was 27. The episodes occurred while he was lucid and conscious of what he was doing, and they generated relief. They were related to agitation during depressive mood states. The patient's clinical history revealed no sleep-related abnormal behavior.

Using *DSM-IV-TR* criteria, we diagnosed bipolar I disorder, most recent episode mixed, comorbid with borderline personality disorder and prescribed 800 mg/d lithium carbonate and 300 mg/d quetiapine. Mr A's mood rapidly improved; 1 year later, he is free from mood episodes and self-harm.

Self-stabbing may be viewed as continuous with past self-cutting and could have been modulated by the patient's psychopathology and was triggered by zolpidem overdose-induced psychosis. Zolpidem overdose did not induce sleep or myorelaxation in our patient, but rather worsened his agitation, also inducing confusion

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### Command Hallucinations With Self-Stabbing Associated With Zolpidem Overdose

**To the Editor:** Since Viscott's<sup>1</sup> original description of 7 patients who developed hallucinations while taking chlorthalidoxepoxide, there have been several reports of hallucinations with GABA<sub>A</sub>/benzodiazepine agonists. Some reports concerned nonbenzodiazepine hypnotics, like zolpidem<sup>2</sup> and zaleplon.<sup>3</sup> Hallucinations range from visual to auditory, kinesthetic, and somesthetic and are

and disorientation. A similar case was described in an elderly woman, who developed agitation, confusion, and both auditory and visual hallucinations with 20 mg zolpidem.<sup>6</sup> Cases of zolpidem-induced hallucinations are typically visual and usually occur when people are falling asleep or waking,<sup>5</sup> whereas in our case, auditory hallucinations occurred during a bout of agitation. The patient was taking no drug for mood disorder and used only zolpidem on an as-needed basis. During the 20 days preceding his self-stabbing, he had taken 10 or 20 mg zolpidem on 5 occasions. This pattern of drug intake is consistent with the pattern described by Tsai et al.,<sup>5</sup> who suggested that rapid zolpidem withdrawal and restarting may alter GABA<sub>A</sub> receptor sensitivity and kindle hallucinations.

The mechanism of GABA<sub>A</sub>/benzodiazepine agonist-related hallucinations is unknown, but GABAergic abnormalities may have played a role in their emergence in our patient. Auditory hallucinations are believed to be influenced by activity in the superior temporal gyrus, and GABA<sub>A</sub> receptors were shown to be up-regulated in that brain region in schizophrenia.<sup>7</sup> Our patient's bipolar disorder originated in adolescence and went undiagnosed and untreated. There is evidence that early-onset bipolar disorder is associated with superior temporal gyrus abnormalities<sup>8</sup>; reduced superior temporal gyrus volume is also displayed by untreated patients with bipolar disorder.<sup>9</sup> It is therefore possible that structural and GABAergic neurochemical alterations in our patient could have contributed to the onset of auditory verbal command hallucinations.

Physicians should closely monitor patients with bipolar disorder, borderline personality disorder, or drug abuse potential when prescribing zolpidem, as the latter might sensitize GABA receptors in some of these patients and predispose to the development of hallucinations.

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