Rapid Resolution of Obsessions After an Infusion of Intravenous Ketamine in a Patient With Treatment-Resistant Obsessive-Compulsive Disorder

To the Editor: Obsessive-compulsive disorder (OCD) is a leading cause of illness-related disability.[1] Identifying more effective treatments with faster onset of action would be a major advance. Medications thought to modulate the glutamate system are promising new agents; for example, open trials of riluzole, memantine, and minocycline as augmentation to serotonin reuptake inhibitors (SRIs) suggest that up to half of OCD patients may experience reductions in symptoms.[2–7] We chose to test intravenous ketamine (a noncompetitive *N*-methyl-D-aspartate [NMDA] receptor antagonist) in an OCD patient for 3 reasons: (1) it is known to modulate the glutamate system, having some mechanistic similarity to memantine[8]; (2) mice with a genetic deletion in a postsynaptic scaffolding protein (SAPAP3) have OCD-like compulsive behavior thought to be caused by increased NMDA activity, and ketamine

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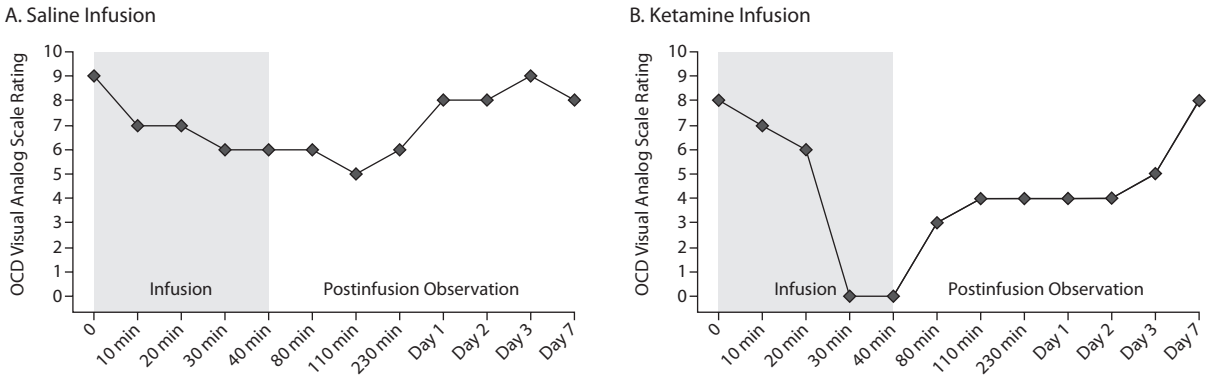
Figure 1. Assessment of Obsessions With the OCD Visual Analog Scale During a 40-Minute Infusion of Saline (A) or Ketamine (B)[a]



[a]Safety ratings were as follows: Brief Psychiatric Rating Scale and Young Mania Rating Scale = 0 at timepoints 0, 40, 80, 110, and 230 minutes and 7 days; Clinician-Administered Dissociative Scale = 1 at 40 minutes (feelings of unreality: "Things seem a little unreal, but I'm well aware of where I'm at") and = 0 at 0 and 230 minutes and 7 days. Yale-Brown Obsessive Compulsive Scale scores were as follows: baseline/day 0 (prior to saline) = 30; day 7 (7 days after saline) = 33; day 14 (7 days after ketamine) = 28.

decreases NMDA activity[9]; and (3) ketamine has been safely used in patients with depression and can relieve depressive symptoms in hours.[10,11]

The following case report describes the rapid resolution of obsessions in an OCD patient when she received ketamine in a double-blind crossover design of intravenous ketamine versus saline. To our knowledge, this is the first report to describe the use of ketamine in an OCD patient.

Case report. Ms A, a 24-year-old woman with *DSM-IV* OCD (and no other Axis I disorder) presented in May 2010 for treatment of her obsessions about symmetry/exactness (needing to have objects in the right place or else things do not "feel right") and associated repeating/checking compulsions. She spent nearly 8 hours per day managing her OCD symptoms, which interfered with her work and social relationships.

She was medically healthy and was not on medication due to the failure of 3 prior SRI trials: fluoxetine 60 mg/d, escitalopram 30 mg/d, and clomipramine 200 mg/d (each for over 3 months). Augmentation strategies were attempted unsuccessfully (ie, she refused a trial of an antipsychotic due to the possible side effect of weight gain and did not adhere to a trial of cognitive-behavioral therapy with exposure and ritual prevention). At baseline, she had severe OCD (Yale-Brown Obsessive Compulsive Scale[12] score = 30) and minimal depressive symptoms (Hamilton Depression Rating Scale[13] score = 7). Her sister has OCD, and her mother has depression. She provided written informed consent after a full explanation of the research procedures and their risks. The institutional review board approved the study.

In accordance with the protocol used in a prior depression study,[11] she received 2 double-blind intravenous infusions over 40 minutes given 1 week apart of saline or 0.5 mg/kg ketamine hydrochloride. An anesthesiologist provided continuous monitoring during the infusions. The patient's symptoms were assessed at baseline, every 10 minutes during the 40-minute infusions (to detect rapid changes in symptoms if they occurred), and at several postinfusion time-points (both on the day of the infusion and up to 1 week later) using the OCD Visual Analog Scale (OCD-VAS, a modified self-rating scale used previously to detect rapid changes in OCD symptoms[14–16]; we focused on obsessions, which are more readily assessed rapidly than compulsions).

Ms A reported minimal reduction in obsessions during the first infusion (placebo/saline) (Figure 1A) but complete cessation of obsessions during the second infusion (ketamine) (Figure 1B). Obsessions partially reemerged 40 to 230 minutes after the infusion (Figure 1B), plateauing until postinfusion day 2; the obsessions did not return to baseline levels until postinfusion day 7.

During both the saline and ketamine infusions, Ms A's vital signs remained within normal limits. At all time points, she denied symptoms of mania (Young Mania Rating Scale[17] score = 0), psychosis (Brief Psychiatric Rating Scale[18] score = 0), or intoxication (Visual Analog Scale for Intoxication[10] score = 0) using standard scales. During the saline infusion, she reported lightheadedness. During the ketamine infusion, she reported lightheadedness, dry mouth, and feelings of unreality (Clinician-Administered Dissociative States Scale[19] score = 1) that resolved 5 minutes after the infusion stopped.

This case report suggests that ketamine might have rapid antiobsessional effects that persist from 1 to 7 days after administration of an infusion, long after the drug has cleared. Limitations include the small sample size and the difficulties of blinding due to the psychoactive effects of ketamine. A larger trial is underway to further evaluate ketamine's efficacy, safety, duration of effect, and mechanism of effect. In sum, ketamine may provide a useful tool to study the glutamatergic mechanism implicated in OCD and, if proven effective, may help identify novel drug targets for this disabling illness.

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