risk of depression is not as clear, and a direct link between glucocorticoids used to treat the somatic illness and the occurrence of depression has been raised (2, 3). In our study, we found a much stronger association between glucocorticoid exposure and mania or delirium/confusion than between glucocorticoid exposure and depression. This supports the view that glucocorticoids have a role in inducing neuropsychiatric disorders.

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LAURENCE FARDET, M.D., PH.D.
Paris

IRENE PETERSEN, PH.D.
London

IRWIN NAZARETH, M.D., PH.D.
London

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Long-Term Maintenance With Intramuscular Ketamine for Treatment-Resistant Bipolar II Depression

TO THE EDITOR: Ketamine, an *N*-methyl-D-aspartic acid (NMDA) receptor antagonist, is being actively explored as a rapid treatment for resistant depression (1, 2), but its long-term efficacy has not been investigated. We report on two patients with bipolar II disorder who responded to intramuscular ketamine augmentation. Both patients provided consent for publication.

A 57-year-old woman with bipolar II disorder and attention deficit hyperactivity disorder (ADHD) had depressive episodes that did not respond to multiple adequate medication trials, including ECT. During the last depressive episode, she had 12 adequate antidepressant trials that failed to relieve her symptoms. Her current medications were venlafaxine (150 mg/day), lamotrigine (100 mg/day), and methylphenidate (40 mg b.i.d.). Her depressive symptoms (low mood, fatigue, anhedonia, and passive suicidal ideation) began to improve after the third infusion of ketamine (administered twice a week, 0.5 mg/kg over 40 minutes; weight=122 lbs, height=5'2"); however, her depression returned 10 days after the fifth and final infusion. Trials of oral ketamine (210 mg/day by capsule, three times per week) and intranasal ketamine (200 mg/mL, three sprays, three times per week) for 3 weeks each did not provide relief. Next, the patient tried 32 mg and then 50 mg of intramuscular ketamine, and she experienced complete remission of her depression within a few days. The schedule was empirically determined, and 50 mg i.m. every 4 days was continued for 5 months until she had partial relapse. The dosage was increased to 70 mg every 4 days, and she remained completely asymptomatic for 4 months. She experiences side effects of irritability, nightmares, and dissociative feelings.

A 48-year-old woman with a history of bipolar II disorder, ADHD, fibromyalgia, hypothyroidism, chronic depression, and persistent suicidal ideation for the preceding 5 years obtained no relief from aggressive pharmacological treatment with mood stabilizers, serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants, or monoamine oxidase inhibitors. She tried ketamine at 150 mg p.o. three times per week for 2 weeks with no benefit (weight=225 lbs., height=5'5"). While taking lamotrigine (150 mg/day), levothyroxine (75 µg/day), pregabalin (200 mg/day), armodafinil (250 mg/day), and oxcarbazepine (900 mg/day), she received 100 mg of intramuscular ketamine but did not tolerate the dissociative symptoms; the dosage was reduced to 50 mg, and treatment was repeated every 3 days with improvement after 1 week. She had a partial relapse after 6 months, and bupropion was added. While she has not reached remission, she is no longer suicidal and has continued to work for the past 6 months. Side effects included headaches and irritability.

These preliminary case reports indicate that intramuscular ketamine is a potential treatment for treatment-resistant bipolar depression. Oral ketamine has poor bioavailability (17%–20% compared with 93% intramuscular), and in these cases it did not produce any antidepressant effect. In contrast, intramuscular ketamine remained efficacious after months and was well tolerated, with adverse effects of moderate anxiety, irritability, dissociative feelings, and headaches. Intramuscular ketamine for treatment-resistant bipolar depression is worthy of further study to assess its long-term efficacy, adverse effects (cystitis, hepatotoxicity, or potential neurological effects), and possible risks of abuse and dependence.

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CRISTINA CUSIN, M.D.
Boston

GEORGE Q. HILTON, M.D.
Dover, N.H.

ANDREW A. NIERENBERG, M.D.
MAURIZIO FAVA, M.D.
Boston

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Correction

In the article "A Double-Blind Randomized Controlled Trial of N-Acetylcysteine in Cannabis-Dependent Adolescents," by Kevin M. Gray, M.D., et al. (Am J Psychiatry 2012; 169:805–812), Figure 3 was originally published online (in "AJP in Advance") with an incorrect scale for the y-axis. The figure appears as intended for the article's appearance in the August 2012 issue and in the online version posted as part of that issue.