

## Letter

## Benzodiazepines may reduce the effectiveness of ketamine in the treatment of depression

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To the Editor,

Ketamine is effective in the treatment of depression (Naughton et al., 2014). It is a glutamate *N*-methyl *D*-aspartate (NMDA) receptor antagonist, but leads to an increase in glutamatergic activity via the  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (APMA) pathways (Naughton et al., 2014). Benzodiazepines are often prescribed for depressed patients to reduce anxiety and assist sleep. They act as gamma-aminobutyric acid (GABA) receptor agonists.

We present a patient with depression whose response to ketamine was

modified, adversely, by the concomitant use of lorazepam.

A 57-year-old patient with bipolar disorder experienced a severe, prolonged episode of depression. There was no response to several antidepressants and antipsychotics. Lithium was effective in preventing mania but did not impact on the depression. In previous episodes, electroconvulsive therapy (ECT), repetitive transcranial magnetic stimulation (rTMS), lamotrigine and dexamphetamine had been unsuccessful.

The patient received 10 infusions of ketamine at a dose of 0.5 mg/kg while also prescribed lithium, fluoxetine, quetiapine and lorazepam 3.5 mg per day. The response to the first two infusions extended over 2–3 days. Subsequent infusions produced responses of no more than 24 hours. It was noted that the patient experienced a muted response to ketamine when lorazepam had been taken that morning. Lorazepam was withdrawn and the duration of the response to ketamine extended to several days, then to 10–14 days. There had been no other medication changes.

In animals, administration of ketamine causes increased metabolism in the limbic system, and this action is selectively blocked by administration of diazepam (Eintrei et al., 1999). Ketamine-induced dopamine release is similarly blocked by benzodiazepines (Irifune et al., 1997).

While this patient's response to the withdrawal of lorazepam may reflect a number of factors, it is possible that benzodiazepines reduced or blocked the antidepressant effects of ketamine. We suggest withdrawal of benzodiazepines be considered before ketamine treatment.

### Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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