

# Mania following ketamine abuse

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**Abstract:** Ketamine, a noncompetitive antagonist of the *N*-methyl-D-aspartate (NMDA) receptor, has multiple clinical uses. On the other hand, ketamine abuse or recreational use has been gaining increasing attention. Induction of mania and psychotic symptoms has been reported in a patient receiving IV ketamine therapy for reflex sympathetic dystrophy. We here report a 26 year-old man who abused ketamine by inhalation for 12 months and developed manic-like symptoms after ketamine use. This case suggests a possible relationship between manic symptoms and ketamine abuse. To the best of our knowledge, this may be the first report regarding mania after recreational use of ketamine.

**Keywords:** ketamine, mania, antidepressant, bipolar

## Introduction

Ketamine is a noncompetitive antagonist of the *N*-methyl-D-aspartate (NMDA) receptor, a major subtype of glutamate receptors. It has multiple clinical uses. Recent studies have shown that ketamine has antidepressant activity.<sup>1,2</sup> Induction of mania and psychotic symptoms has been reported in a patient receiving intravenous (IV) ketamine therapy for reflex sympathetic dystrophy.<sup>3</sup> Recently, ketamine abuse or recreational use has been gaining increasing attention.<sup>4</sup>

More recently, ketamine has become popular in many countries including USA as a “club drug”, often used by teens and young adults. However, whether ketamine abuse via other routes of administration such as inhalation can also induce mania remains unclear. We here report a patient who developed manic symptoms following ketamine abuse by inhalation. Ethical approval from a review board was not required for this case report, as the patient was under regular therapy and his case was not intended to be used for research. Patient consent was not required to report this case.

## Case report

A 26-year-old Han Taiwanese man had suffered from Tourette syndrome and obsessive-compulsive disorder since he was 12 years old and started to abuse ketamine by inhalation from 22 years old. He denied any mood disorder before using ketamine or other substance abuse/dependence until he started to abuse ketamine by inhalation. Initially, he took ketamine 5 g/wk for several weeks and then 10–15 g/wk for months (with a total duration of 12 months). Since his first time of ketamine use, he had experienced marked euphoria, labile mood, dissociation, and auditory hallucinations, and these symptoms vanished after hours. Even during the following 5 months after he stopped use of ketamine, he still had persistent elated mood, increased goal-directed activity with more energy, decreased sleep need, and fewer obsessive-compulsive behaviors. After the manic-like period, his mood gradually shifted to a depressive state. Approximately 7 months after stopping ketamine use,

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a major depressive episode occurred, with worsening of obsessive–compulsive symptoms. Therefore, he was followed-up at our outpatient clinic for 5 months. However, due to poor drug adherence and poor treatment response, he was then hospitalized to our psychiatric ward, where he achieved full remission from the major depressive episode and partial remission from obsessive–compulsive disorder with sertraline 200 mg/d and aripiprazole 10 mg/d for 3 weeks. He continued this treatment to keep a stable mood with minimal obsessive–compulsive symptoms for at least 21 months during outpatient follow-up.

## Discussion

The antidepressant effects of ketamine are believed to be related to the change in cortical excitability likely caused by cortical disinhibition<sup>5,6</sup> and reduction in the activity of inhibitory interneurons.<sup>7</sup> Acute changes in cortical excitability and glutamate release are proposed to initiate a sequence of biochemical and structural changes within cortical networks.<sup>8,9</sup> The abnormality may occur in people with bipolar tendency, whose glutamate receptors are hypersensitive or glutamate is overreleasing.

This case suggests a possible relationship between manic symptoms under recreational dosage and administration route of ketamine. According to the previous studies,<sup>2,10,11</sup> sub-anesthetic dose via intravenous-administered ketamine had rapid and robust antidepressant effects. Transient manic-like symptoms were noted in a few bipolar and unipolar depressed patients, but this transient mood elevation seems inconsistent with a persistent substance-induced syndrome.<sup>12,13</sup> That is, in these studies, the transient elevated mood did not meet the criteria for mania, in terms of the disease duration or the number of symptoms. Only one case report<sup>3</sup> shows the possibility of the induction of mania in a patient receiving intravenous ketamine therapy. However, the effect of multiple medication adjustments cannot be excluded.

There were some limitations in this case. First, bipolar tendency could not be entirely excluded in this patient although manic or hypomanic symptoms were not noted under antidepressant treatment. Second, we did not conduct screen tests for multi-substances; therefore, we could not prove the validity of his self-report.

To the best of our knowledge, this is the first report regarding mania after recreational use of ketamine. Further

research is warranted to replicate this finding and to elucidate the possible mechanism of ketamine-related mania symptoms. If the finding can be confirmed in the future, physicians should pay attention to manic symptoms in patients abusing ketamine.

## Disclosure

The authors report no conflicts of interest in this work.

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