

An episode of mania following self-reported ingestion of psilocybin mushrooms in a woman previously not diagnosed with bipolar disorder: A case report

Holly M. Hendin^{1,2} | Andrew D. Penn³ 

¹Department of Psychiatry, St. Joseph's Hospital and Medical Center, Dignity Health Medical Group, Phoenix, AZ, USA

²Creighton University School of Medicine, Phoenix, AZ, USA

³School of Nursing, University of California San Francisco, San Francisco, CA, USA

Correspondence: Andrew D. Penn, School of Nursing, University of California San Francisco, San Francisco, CA, USA.

Email: andrew.penn@ucsf.edu

1 | A CASE OF MANIA POSSIBLY INITIATED BY PSILOCYBIN INGESTION

NT is a 21-year-old female identifying woman who came to the office of her outpatient psychiatric provider a month after a hospitalization for a brief psychotic episode, later diagnosed as mania, that she believes was triggered by consuming a substantial amount of psilocybe cubensis mushrooms that she had taken recreationally. While she has a positive family history (father and paternal grandmother) of bipolar disorder, she herself had never had a manic episode or been diagnosed with bipolar disorder before this hospitalization. She notes that over the past 4 years she had been diagnosed with and treated for anxiety that had later developed into depression and PTSD following rape. Psychotherapy and SSRI medications were beneficial but did not lead to remission. Eight months prior to her manic episode, she was hospitalized for depression and suicidal ideation. She was placed on fluoxetine in the hospital and released after her acute symptoms resolved about a week later. A few weeks following the hospitalization and still on her fluoxetine, she sought treatment with rTMS (standard 6 weeks, 5 treatments per week) for treatment-resistant depression. At the facility that provided rTMS, she also received adjunctive ketamine infusion (6 infusions over 2 weeks offered at initiation of her rTMS treatment) to help with depressive symptoms. The ketamine did produce short-lived (e.g., hours to days) antidepressant benefit, but the rTMS resulted in remission of her depression. Following completion of her course of rTMS, the SSRI was discontinued.

NT had never previously consumed psilocybin and reports the psilocybin experience was pleasant and mystical. Drug effects resolved

about 5 hours after ingestion, and she describes having had a positive “after-glow” effect for a 1–2 hours following the end of acute drug effects. About 36 hours after ingestion of the psilocybin, NT’s thoughts began racing. She noted an irritable mood and was observed to have pressured speech. She was confrontational with family and required only 2–3 hours of sleep each night. These symptoms persisted for 4 days and then, in addition to her original symptoms, she also began to feel fearful of being sexualized by others. She stopped eating. After 3 more days of these symptoms, her boyfriend and family became concerned about her welfare and called the police. NT was placed on an involuntary psychiatric hold for 48 hours. She notes that at the time she felt she had special powers that allowed her to read and respond to other people’s energies, and that she could communicate with people through telepathy. She became fearful that her boyfriend and family were intending to harm her, and tried to run away, but was sedated and restrained with haloperidol and olanzapine. She remembers akathisia following the administration of these antipsychotics, and she remembers calling out “Kill me, kill me, kill me” several times.

The inpatient psychiatric team diagnosed NT with a bipolar disorder because she met DSM-V criteria in both duration and symptoms for a manic episode (that was most likely psilocybin induced). She was admitted to an inpatient behavioral health unit and stabilized on lithium and aripiprazole. After 1 week she was transferred to a partial hospitalization program, and then to outpatient care. Because of adverse effects, we reduced and stopped lithium and aripiprazole and started lamotrigine monotherapy. She has not had any further psychotic symptoms; however, she has had one more period of an irritable mixed episode of mania lasting about a week that has since resolved with an increase in lamotrigine dose.

2 | CASE DISCUSSION AND IMPLICATIONS FOR CLINICAL RESEARCH

Psilocybin, the psychoactive substance contained in “magic mushrooms,” has received renewed attention in the psychiatric literature over the last two decades, especially with regard to the benefits of psilocybin when paired with psychotherapy for diseases such as PTSD, end-of-life anxiety, substance use disorders and depression.¹ There is mounting evidence to support the limited use of psilocybin as a catalyst for psychotherapy. While data support that psilocybin can be used safely in patients without a history of bipolar disorder or psychosis, patients with these conditions have been excluded from these studies, which presents a gap in knowledge.

Psilocybin is a naturally occurring prodrug (for psilocin) in psilocybe mushrooms and is structurally similar to serotonin. Psilocybin is believed to express most of its effects through direct 5-HT_{2A} agonism, with lesser agonism at the 5-HT_{1A}, 5-HT_{1D}, and 5-HT_{2C} receptors. Additional receptor and network effects of psilocybin have been reviewed elsewhere.²

Existing studies demonstrating the benefits of psilocybin in psychedelic-assisted therapy have excluded subjects who have a diagnosis of bipolar disorder. As the use of psilocybin moves from the lab to the office via possible FDA approval, the safety of psychedelic-assisted therapy among patients with bipolar disorder is an important consideration. Psychiatric diagnoses are inherently subjective and iterative as they progress along a developmental trajectory. For example, what is later diagnosed as schizophrenia or bipolar disorder may initially present as treatment-resistant depression, ADHD, a personality disorder, a brief psychotic episode, or obsessive-compulsive disorder. Further complicating diagnosis is that primary psychotic disorders can often co-occur with substance use, thus making diagnosis, causality and directionality of events difficult to ascertain. Cycloid psychosis, a proposed disorder not in DSM5, describes a pattern of psychotic symptoms that co-occur with affective symptoms. However, because the psychotic features emerged after psilocybin use (and after affective symptoms), this diagnosis would be excluded under criteria reviewed by El-Mallakh & Furdek.³ People with bipolar disorder have been excluded from studies primarily because of the concern that a psychedelic agent that serves as a full serotonin agonist or partial agonist could potentially evoke a manic or mixed episode.

NT's manic episode, if induced by her consumption of psilocybin, may be due to the serotonergic activity of the psilocybin. Although NT had not experienced treatment-emergent mania with SSRI or rTMS treatments, it should be noted that unlike psilocybin which is a 5-HT_{2A} agonist, SSRIs exert most of their effect by inhibiting the serotonin transporter (SERT). A possible mechanism of action psilocybin-induced mania in a predisposed person (e.g., family history of bipolar disorder) could be the direct serotonin partial agonism of psilocybin in contrast to the indirect effect of an SSRI in increasing overall volume of available serotonin.

Further complicating the role of psilocybin in the induction of NT's mania is NT's intermittent use of recreational cannabis for 3 years prior to the manic episode. Cannabis use in young people predisposed

Key Message

As the use of psilocybin moves from the lab to possible FDA approval, the safety of psychedelic-assisted therapy among patients with latent or diagnosed bipolar disorder is an important consideration. The case of a young woman who experienced an episode of mania with psychotic features following the ingestion of psilocybin mushrooms raises questions about how to safely use this treatment in this population.

to bipolar or psychotic disorders has been associated with an earlier onset of bipolar disorder. Once symptomatic, patients with bipolar disorder who use cannabis tend to stay symptomatic longer than bipolar patients who do not use cannabis.⁴ It should be noted that NT had abstained from cannabis for several months prior to ingesting the psilocybin, and that she was not using cannabis when she consumed the psilocybin mushrooms. The likelihood of proximal effects of cannabis on the trajectory of her manic episode appears to be minimal. When substance use is present in bipolar episodes, multiple substances are often used and establishing clear correlation between mania and a single substance is difficult, at best, and causation almost impossible.

In the months prior to her manic episode, NT's depression had been treated with fluoxetine as well as rTMS both of which can induce mania in people with bipolar disorder.⁵ NT reported no symptoms of hypomania immediately following these interventions. Her last rTMS session and her last use of fluoxetine were 4 months before her manic episode, reducing the likely temporal relationship between these interventions and the emergence of mania. We do not believe that NT was symptomatic or pre-symptomatic with mania or hypomania prior to her use of psilocybin.

The burgeoning field of psychedelic-assisted therapy may offer help for those who have not benefitted from existing treatments. However, because of cautious exclusion of patients with bipolar or psychotic disorders from clinical studies, little is known about the effects of psilocybin on people diagnosed with bipolar disorder or schizophrenia. Further research is necessary to delineate the safety of psychedelic substances in people diagnosed with bipolar disorder. As psilocybin appears to be emerging as an effective treatment for unipolar depression, it will be critical to also study the possible efficacy of this compound in treating bipolar depression. Here, we can look to the rTMS literature for some guidance. Treatment emergent mania from rTMS in patients with bipolar disorder has been observed but the prevailing guidelines suggest that the risk of inducing mania is reduced by first treating patients with a mood stabilizer (e.g., lamotrigine) prior to initiating treatment with rTMS.⁵ If we used this guideline with psychedelic medicine, it could allow a large population of people (i.e., those diagnosed with bipolar disorder) to be safely treated with psilocybin-assisted therapy. Prospective research will be needed to determine if psilocybin can be used safely with bipolar patients and if the same

antidepressant effect is conferred in bipolar depression as has been demonstrated in unipolar depression.

Learning Points

- The influence of psilocybin on people with bipolar disorder is largely unknown because of the exclusion of bipolar patients from current psilocybin-assisted therapy trials
- Psilocybin might present a risk for treatment-emergent mania in patients with latent or diagnosed bipolar disorder
- The use of a mood-stabilizer prior to psychedelic-assisted therapy in patients with bipolar disorder may mitigate the risk and probability of psilocybin-induced mania, although further research is required

ORCID

Andrew D. Penn  <https://orcid.org/0000-0001-5552-7078>

REFERENCES

1. Luoma JB, Chwyl C, Bathje GJ, Davis AK, Lancelotta R. A meta-analysis of placebo-controlled trials of psychedelic-assisted

therapy. *J Psychoactive Drugs*. 2020;52(4):289-299. <https://doi.org/10.1080/02791072.2020.1769878>

2. Carhart-Harris RL, Roseman L, Bolstridge M, et al. Psilocybin for treatment-resistant depression: fMRI-measured brain mechanisms. *Nature Sci Rep*. 2017;7(1):13187. <https://doi.org/10.1038/s41598-017-13282-7>
3. El-Mallakh RS, Furdek C. Cycloid psychosis. *Am J Psychiatry*. 2018;175(6):502-505.
4. Kim S-W, Dodd S, Berk L, et al. Impact of cannabis use on long-term remission in bipolar I and schizoaffective disorder. *Psychiatry Investig*. 2015;12(3):349-355. <https://doi.org/10.4306/pi.2015.12.3.349>
5. Rachid F. Repetitive transcranial magnetic stimulation and treatment-emergent mania and hypomania: a review of the literature. *J Psychiatric Practice*. 2017;23(2):150-159. https://journals.lww.com/practicalpsychiatry/Fulltext/2017/03000/Repetitive_Transcranial_Magnetic_Stimulation_and.12.aspx

How to cite this article: Hendin HM, Penn AD. An episode of mania following self-reported ingestion of psilocybin mushrooms in a woman previously not diagnosed with bipolar disorder: A case report. *Bipolar Disord*. 2021;00:1-3. <https://doi.org/10.1111/bdi.13095>