The new age of treating depression: Psilocybin

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The search for the most effective treatment for Major Depressive Disorder (MDD) has skyrocketed following its continuous exponential growth over the last decade. Through this search one unresolved question persists: can alternative treatments such as psilocybin therapy be a replacement to traditional antidepressants? Current antidepressants work as “selective serotonin reuptake inhibitors” (SSRIs). SSRIs work by increasing serotonin levels in the brain which helps stabilize moods but they require daily dosing and cause immense amounts of painful side effects. However, psilocybin, a psychoactive compound found in mushrooms which can be synthesized, has shaken up the field of research with its promising attributes in initial studies. Psilocybin is a superior treatment for major depressive disorder compared to SSRIs due to its minimal dosing requirements, rapid symptom relief, and fewer side effects, which together improve adherence and enhance patients’ overall well-being.

Most people diagnosed with Major Depressive Disorder seek rapid symptom relief, a need not satisfied by traditional antidepressants that take weeks to work. Psilocybin offers an alternative outcome where patients are met with their needs due to its unique mechanism of action. Unlike SSRIs, which increase serotonin levels gradually by blocking its reuptake (NHS, 2021), psilocybin directly activates serotonin 5-HT2A receptors, healing neural circuits associated with self-reflection and negative thought patterns (NIH,2023). This allows psilocybin to improve symptoms quickly. A study on MDD treatment plans effects on serotonin receptors, it was found that psilocybin’s action on 5-HT2A receptors caused change mainly in the default mode network (DMN), which is the area of the brain causing depressive symptoms. This resulted in a ‘reset’ in the DMN which in turn gave patients symptom relief within days. The study also

showcased that SSRIs do not target the DMN, hence the longer wait for symptom relief.(Carhart-Harris, 2017). In 2021 the same research group ran a trial comparing psilocybin with escitalopram, where the patients received a 25 mg dose of psilocybin which according to figure 1 in the study led to a 6.6 point reduction in their depression scores on the "Quick Inventory of Depressive Symptomatology–Self Report (QIDS-SR)" in just one week, compared to a group of patients who took daily doses of 10-20mg of escitalopram over 6 weeks who had only 4.5 point reduction in the time period. This showcases how rapid psilocybin works compared to escitalopram. Figure 2 in the same study showcases that 57% patients that were treated with psilocybin showed clinical responses after just one dose (≥50% reduction in symptoms), compared to only 28% of the escitalopram group, highlighting the rapid efficacy of psilocybin. (Carhart-Harri, 2021). These results further support psilocybin's potential in delivering rapid relief to patients in dire need of immediate treatment more effectively than traditional SSRIs.

Adherence to daily antidepressant regimes is a critical barrier for MDD patients, often due to motivational and/or cognitive challenges inherent to the disorder. A cross-sectional study of over 400 MDD patients concluded that 52.9% of patients reported low adherence to their antidepressant medication (Al Jumah et al., 2014). In table 2 of the study, a MMAS-8 analysis (Morisky Medication Adherence Scale) showcased that 40.6% of patients admit to forgetting to take medication, and 46.8% stopped adhering to their medication without telling their doctors due to stigma/hassels. These findings are further supported by Figure 3 in a meta-analysis which reviewed several studies and showed that patients on weekly (QW) regimens had nearly double

the odds of adhering to their treatment plans compared to those on daily (QD) regimens, with an odds ratio of 1.90 (95% CI, 1.81–2.00). Both fixed-effects and random-effects models produced consistent results, underscoring the reliability of this association.(Iglay et al. 2015). Psilocybin's biweekly dosing schedule leverages this principle by minimizing the practical and emotional burdens of daily medication adherence. This combination of reduced dosing and fewer side effects directly addresses major barriers to adherence, offering a promising alternative that could improve treatment outcomes for MDD patients.

SSRIs are associated with a range of disruptive and persistent side effects, including fatigue, weight gain, and emotional blunting. These side effects often last as long as the medication is taken daily, leading to reduced patient satisfaction and adherence (NHS, 2021). In contrast, psilocybin's short-term administration significantly reduces the risk of prolonged side effects, enhancing overall well-being and improving treatment outcomes. Figure 3 from the same trial by Carhart-Harris in 2021 shows that 86% of participants given the dosage of psilocybin noticed notable reduction in side effects compared to only 40% in a traditional SSRI. Additionally, figure 4 showed that psilocybin-treated patients experienced less fatigue, weight gain, and emotional blunting, with 57% of patients improving their emotional range and 65% having enhanced social connection. By minimizing fatigue, weight gain, and emotional blunting, psilocybin not only improves treatment adherence but also enhances overall well-being, addressing one of the most significant challenges of traditional antidepressant therapy.

Psilocybin therapy can pose significant risks of psychological distress due to its psychoactive compounds, which may deter patients and complicate its accessibility. A qualitative

study analyzed practitioner and patient experiences during psilocybin therapy to assess the severity of emotional distress. The study documented adverse emotional responses, with Figure 1 showing that 61% of patients experienced psychological distress, and 28% described these effects as severe (Nordin, 2024). These responses, including fear, anxiety, and intrusive thoughts, often required immediate intervention from trained professionals**.** Unlike psilocybin, SSRIs induce only acute psychological distress as they do not have psychoactive compounds, making them a less emotionally disruptive option for managing depression. However, SSRIs' long-term use is associated with emotional blunting and a lack of trauma resolution, posing their own challenges. (Mayoclinic, 2024). This comparison raises questions about whether psilocybin can serve as a practical alternative for patients seeking a stable and predictable treatment experience.

While psilocybin therapy can cause temporary psychological distress, such episodes are integral to its therapeutic process and often contribute to long-term healing. In a study where patients underwent two supervised psilocybin sessions over 12 months, figure 1 highlights that 75% achieved a clinical response (≥50% reduction in depressive symptoms), and 58% reached full remission despite some reporting discomfort. (Gukasyan,2022). This demonstrates that short-term distress, when managed in a controlled environment, facilitates breakthroughs rather than undermines efficacy. Additionally, psilocybin addresses underlying emotional trauma, unlike SSRIs, which often blunt emotions over time. These long-lasting benefits make psilocybin a safer and more transformative option for treatment-resistant depression when administered with proper oversight.

Psilocybin therapy offers a new perspective towards antidepressants for individuals with severe depression. Its minimal dosing requirements, sustained effect , and reduced side effects make it advantageous over daily antidepressant regimes that often lower overall well-being due to adherence challenges and undesirable side effects. Although psilocybin therapy currently requires controlled supervised dosing sessions, its long-lasting relief of symptoms make it a cost-effective and accessible option in the long-term. Expanding research and clinical trials on psilocybin safety, efficacy and accessibility could open new doors in the treatment of depression, especially for those who do not respond well to conventional antidepressants or therapies. Future studies should shift their focus on providing evidence to help understand the safety around psilocybin, optimizing its protocols to ensure safe use, to improve widespread use and lasting impact on mental health care.

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SCIE 113 Reflection Worksheet – Term Paper

Names of your peer reviewers: Cinar Ege Atar, Youssef Abouelseoud

1. Summarize, in your own words, the peer feedback that you received on your version 1.

Both reviewers appreciated the organization and clarity of my arguments, especially how I used evidence to back up my points about Psilocybin's benefits over SSRIs. They recommended a few improvements, such as using more transition words to create better flow between sections, citing sources narratively, and being more concise in summarizing evidence. One reviewer also suggested linking the methodology more clearly to the evidence in some cases.

2. Which pieces of peer feedback did you incorporate into your writing? Why? What changes did you make?

I worked on improving the flow by adding more transition words between paragraphs, as suggested. I also tried to summarize evidence more concisely to avoid making it too detailed and refined my citations to include a narrative style where appropriate

3. Which pieces of peer feedback did you <u>not</u> incorporate into your writing? Why?

I didn't focus heavily on explicitly linking the methodology to the evidence because I felt that my points were already supported well enough without needing to add that extra layer of explanation. Additionally, i already had concisely spoken on methodology a bunch.

4. What feedback did you receive that you could incorporate into other writing assignments (*i.e.*, something that is transferable)?

The suggestion to use more transition words and narratively cite sources is definitely something I can apply to other writing projects. These changes help make my writing clearer and more professional.

5. How helpful were your peer reviews with respect to improving your term paper?

- ❑ **Very helpful (THIS ONE)**
- ❑ Somewhat helpful

- ❑ Neutral
- ❑ Somewhat unhelpful
- ❑ Very unhelpful

6. Please comment on your response – why were the reviews helpful or unhelpful?

The reviews were super helpful because they gave me clear, actionable advice on how to improve both the content and style of my paper. The specific examples they provided made it easy for me to make the changes.

7. If your Turnitin report on version 1 of the term paper contained extensive highlighted passages (other than the title, references, or common technical phrases), briefly explain how you revised these passages when writing the final version.

I didn't receive extensive highlighted passages. But, I did double-check my citations to ensure everything was properly referenced.

8. Which section, component, or aspect of your writing do you think is the strongest? Why?

I think the strongest part of my paper is the way I organized my argument. Both reviewers noted that my points about rapid symptom relief, dosing schedules, and side effects were clear and supported well by evidence.

9. Which section, component, or aspect of your writing do you think has the most room for improvement? Why?

The transitions between sections still need some work. One reviewer pointed out that smoother transitions would help the paper flow better, so that's something I'll keep improving. Additionally, using more coherent evidence for everything that needs it.

10. Which section, component, or aspect of your writing would you like specific instructor feedback on?

I'd like feedback on how I summarized evidence and whether I found a good balance between being detailed and concise.

I would also appreciate some feedback on my logical flow of the paper and if it all comes together.

11. Please comment on your writing process – was there anything that you learned in SCIE 113 (or through events/workshops organized by the Faculty of Science) that helped you to write the term paper?

SCIE 113 taught me the importance of clearly connecting evidence to my claims through warrants. I learned that evidence isn't just about presenting data but about interpreting it to show how it supports the argument. This course also emphasized the need for reliable scholarly sources and proper citations, including narrative citations, to enhance credibility. Understanding how to evaluate and integrate evidence into my writing has been a key takeaway that I'll use in future assignments.