RED LIGHT HOLLAND

Psilocybin Microdosing Report

Microdosing with psilocybin has become an increasingly popular trend in recent years. Psilocybin is a naturally occurring compound found in some species of mushrooms, commonly referred to as magic mushrooms or magic truffles. While psilocybin is widely known for its psychedelic effects, microdosing involves taking sub-hallucinogenic doses of it for therapeutic purposes.

As a medical doctor, you may encounter patients who are interested in or have already started microdosing with psilocybin. It is therefore useful to have a basic understanding of what microdosing is, and its potential benefits, risks, and considerations for dosing and protocols.

This report is written by Red Light Holland therapist and expert microdosing guide Jeff Hamburg and Red Light Holland CTIO and published psychedelic researcher Sarah Hashkes. For any questions please contact *sarah@redlight.co*.

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History of Microdosing

This practice seems to have started in modern times with Albert Hoffman, the chemist who discovered LSD-25. Hoffman lived to the healthy age of 102 and reportedly microdosed LSD. Hoffman was interested in low doses of LSD, which caught Dr. James Fadiman's attention[1]. Fadiman was also directed to the use of psychedelics by indigenous people as reported by both modern anthropologists as well as the 16th-century Jesuit priest Bernabe Cobo, who traveled through South America during the Spanish conquest of that continent. Cobo reports many instances of psychedelics being used during long hot walks in the jungle, or to help intensify the senses in order to hunt better[2]. It is clear that these must be descriptions of using lower doses as it is not practical to go hunting at night in the jungle on a high dose of psychedelics.

The Neuroscience Of Psilocybin

Psilocybin is considered a "classic psychedelic" which refers to a family of chemically similar substances that activate the 5ht2a serotonin receptor. Classic psychedelics do not cause dependency and generally have a very low risk profile[3]. Psilocybin actually gets broken down in the gut to psilocin which then activates the 5ht2a receptor[4].
The current scientific model explains the effects of classical psychedelics with the use of a neuroscientific framework called predictive coding. Predictive coding explains perception and action as a continuous process of combining the brain's previous knowledge with new incoming data by using Bayesian updating. It is proposed that an increased entropic state is created when top-down predictions in affected brain areas break up or decrease in strength due to hyper activation of 5-HT2A receptors in layer V pyramidal neurons.[5] When looking at neuronal correlates of brain waves psilocybin

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[1] Advances in Psychedelic Medicine: State-of-the-Art Therapeutic Applications by Michael J. Winkelman Ben Sessa MD, Chapter 16 Microdosing Psychedelics by James Fadiman and Sophia Korb. https://www.researchgate.net/publication/331321003_Advances_in_Psychedelic_Medicine_STATE-OF-THE-ART_THERAPEUTIC_APPLICATIONS

[2] Inca Religion and Customs By Father Bernabe Cobo

[3] Assessing the risk–benefit profile of classical psychedelics: a clinical review of second-wave psychedelic research By David Bender https://link.springer.com/article/10.1007/s00213-021-06049-6

[4] The pharmacology of psilocybin by Torsten Passie https://onlinelibrary.wiley.com/doi/abs/10.1080/1355621021000005937

[5] REBUS and the Anarchic Brain: Toward a Unified Model of the Brain Action of Psychedelics by Robin Carhart-Harris https://pubmed.ncbi.nlm.nih.gov/31221820/

reduces slower brain waves such as delta, theta, and alpha waves, which are considered an inhibitory signal connected to top-down predictions[6].
The result of consuming psilocybin is a brain that is more sensitive to bottom up sensory input and can more readily update its previous models.[7] This can allow for changes in top-down patterns that might have been created as an adaptive strategy to trauma. Due to the hyper sensitivity to sensory input it is important to prepare a "setting" conducive for healing when consuming psilocybin.

In animal research psilocybin has shown to increase neural plasticity and dendritic growth which is likely an important factor in long term positive effects.[8]

What Is Microdosing With Psilocybin?

The term "microdosing" exists in pharmaceutical and drug research, but it means something different than the common use of the word in the psychedelic context. The pharmaceutical definition of microdosing is "Less than 1/100th of the dose of a test substance calculated (based on animal data) to yield a pharmacologic effect of the test substance with a maximum dose of 100 micrograms."[9] This very low, subtherapeutic dose is used to study cellular response of substances. In common use, however, the term "microdosing" is usually understood in relation to a "full" dose of psychedelics, and is around 1/10 to 1/20 of such a dose.[10] The understanding of a "full dose" in psilocybin research varies between 15 - 30 mg.[11] Therefore, microdosing involves taking typically around 0.5 - 1 mg but potentially up to 2.5-3 mg on a regular basis. Due to variability in the amount of psilocybin in mushrooms[12] this can typically correspond to anywhere between 0.1 to 0.5 grams of dried mushrooms or 0.5 to 1 gram of fresh "truffles" (truffle is

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[6] Psilocybin-induced spiritual experiences and insightfulness are associated with synchronization of neuronal oscillations by Michael Kometer https://link.springer.com/article/10.1007/s00213-015-4026-7
[7] Perception is in the Details: A Predictive Coding Account of the Psychedelic Phenomenon by Sarah Hashkes https://cogsci.mindmodeling.org/2017/papers/0550/paper0550.pdf
[8] Psilocybin induces rapid and persistent growth of dendritic spines in frontal cortex in vivo by Ling-Xiao Shao https://www.sciencedirect.com/science/article/pii/S0896627321004232
[9] Chapter 6 - Clinical Pharmacokinetics and Drug Interactions by Nilanjan Saha https://www.sciencedirect.com/science/article/abs/pii/B9780128021033000067
[10] Advances in Psychedelic Medicine: State-of-the-Art Therapeutic Applications by Michael J. Winkelman Ben Sessa MD, Chapter 16 Microdosing Psychedelics by James Fadiman and Sophia Korb. https://www.researchgate.net/publication/331321003_Advances_in_Psychedelic_Medicine_STATE-OF-THE-ART_THERAPEUTIC_APPLICATIONS
[11] Optimal dosing for psilocybin pharmacotherapy: Considering weight-adjusted and fixed dosing approaches https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8056712/
[12] Psilocybin and psilocin levels in twenty species from seven genera of wild mushrooms in the Pacific Northwest, U.S.A. By Michael W.Beug https://www.sciencedirect.com/science/article/abs/pii/0378874182900137

the common name for sclerotia, a part of the fungi growing underground and utilized as the food reserve)

An outdated understanding of microdosing termed the practice “sub-perceptual”. However, many participants are “breaking blind” in research, as they can feel when they are microdosing[13]. This causes some to believe that microdosing is nothing more than a placebo. However the perceived effects of higher energy and better mood are precisely what many patients are looking for.

In a recent preprint that summarized 44 microdosing research papers, researchers found that microdosing is associated with identifiable subjective drug effects. Thus, the authors caution against describing microdosing as sub-perceptual. They suggest microdosing be defined as “sub-hallucinogenic with no loss of functionality.”[14]

Research shows that 3 mg of psilocybin activates around 40% of the brain’s 5ht2a receptors.[15] EEG research with a healthy population has shown that microdosing psilocybin can cause a reduction in slower theta brain waves similar to reduction in slower brain waves seen in higher doses although to a lesser degree[16]. Therefore it is likely that microdosing too can increase the brain's entropic state as seen in higher doses albeit to a lesser degree.

Potential Benefits Of Microdosing

While we need to be careful of the hype around microdosing and acknowledge that for a healthy population, current placebo controlled research shows mixed results and likely only transitory positive mood effects on the microdosing days[16], there is some evidence from placebo controlled trials in psilocybin or other classical psychedelics such as LSD that microdosing affects the brain and can potentially be beneficial for some people including at least some patient populations.

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[13] Psilocybin microdosing does not affect emotion-related symptoms and processing: A preregistered field and lab-based study by Josephine Marschall https://journals.sagepub.com/doi/pdf/10.1177/02698811211050556

[14] The emerging science of microdosing: A systematic review of research on low dose psychedelics (1955-2021) and recommendations for the field by Vince Polito https://pubmed.ncbi.nlm.nih.gov/35609684/

[15] Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels by Martin Madsen https://pubmed.ncbi.nlm.nih.gov/30685771/

[16] Microdosing with psilocybin mushrooms: a double-blind placebo-controlled study by Federico Cavanna https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9346139/

In a placebo-controlled study with obsessive-compulsive disorder (OCD) patients, symptoms were reduced after microdosing 1.7 mg of psilocybin per 70 kg.[17] It's also interesting to note that in an animal study using rodents, in which placebo effects are unlikely, microdosing DMT (another classical psychedelic) has shown positive effects on mood, anxiety, and fear.[18]

Self reporting large scale studies have found many potential benefits from microdosing that could help some patient populations:[19] [20] [21] [22] [23] [24] [25] [26]:

- Improved mood and well-being[19] [20] [21] [22] [23]: Some people report feeling more positive and content after microdosing, with a reduction in symptoms of anxiety, stress and even treatment resistant depression.
- Increased creativity [19]: Many people who microdose report an increase in creativity, with some even claiming that it helps them to overcome creative blocks.
- Enhanced focus, memory and productivity [19] [20] [23]: Microdosing seems to help some people concentrate better and work more efficiently, without feeling overwhelmed or stressed. Data from 115 users on Red Light Holland iMicro app who consented to share their anonymized data revealed that for every 5 year age decrease (or decrease in age group), people are 11% more likely to want to microdose to increase focus. This fits the global trend of younger people struggling with focusing their attention and presents the possibility that microdosing might help prevent some of the abuse of stimulants in our society.

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[17] Safety, tolerability, and efficacy of psilocybin in 9 patients with obsessive-compulsive disorder by Francisco A Moreno https://pubmed.ncbi.nlm.nih.gov/17196053/

[18] Chronic, Intermittent Microdoses of the Psychedelic N, N-Dimethyltryptamine (DMT) Produce Positive Effects on Mood and Anxiety in Rodents by Lindsay P Cameron https://pubmed.ncbi.nlm.nih.gov/30829033/

[19] Psilocybin microdosers demonstrate greater observed improvements in mood and mental health at one month relative to non-microdosing controls by Joseph M Rootman https://www.nature.com/articles/s41598-022-14512-3

[20] A systematic study of microdosing psychedelics by Vince Polito https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0211023

[21] Psychedelic Microdosing: Prevalence and Subjective Effects by Lindsay P Cameron https://www.tandfonline.com/doi/abs/10.1080/02791072.2020.1718250?journalCode=ujpd20

[22] Perceived outcomes of psychedelic microdosing as self-managed therapies for mental and substance use disorders by Toby Lea https://link.springer.com/article/10.1007/s00213-020-05477-0

[23] Might Microdosing Psychedelics Be Safe and Beneficial? An Initial Exploration by James Fadiman https://www.tandfonline.com/doi/full/10.1080/02791072.2019.1593561?needAccess=true

[24] Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches by Martin Andersson https://link.springer.com/article/10.1186/s12954-017-0186-6

[25] Analgesic potential of macrodoses and microdoses of classical psychedelics in chronic pain sufferers: a population survey, by Valerie Bonnelle https://journals.sagepub.com/doi/abs/10.1177/2049463721114962?journalCode=bjpb

[26] Microdosing psilocybin for chronic pain: a case series by Lyes Matthew https://journals.lww.com/pain/Citation/2023/04000/Microdosing_psilocybin_for_chronic_pain__a_case.5.aspx

- Reduced addiction[21]: Some people have reported that microdosing with psilocybin has helped them to overcome addiction to substances such as alcohol, tobacco, and opioids.
- Psychomotor performance for older population[19]: in a tapping experiment 55 year old and older microdosers improved their tapping speed.
- Reduction in cluster headaches and migraines[23] [24]: Smaller samples have shown some people with cluster headaches or migraines might benefit from microdosing. Their dose might need to be on the higher end.
- Chronic pain[25] [26]: There are documented reports and case studies that microdosing classical psychedelics including psilocybin can help manage chronic pain.
- Reduction in PMS and PMDD symptoms[23]: Smaller samples have shown potential benefits in reducing PMS and PMDD symptoms.
- Traumatic brain injury[23]: Smaller samples have shown potential benefits in reducing TBI symptoms.

There are a few other conditions with some case reports showing potentials benefits:

- Perimenopause or menopause symptoms.[27]
- Lyme Disease[28].

While many of the recorded benefits likely stem from breaking down of top down priors and inducing neural plasticity it is likely that other benefits stem from psilocybin having anti-inflammatory properties[29] and some researchers have speculated that some of the positive effects might be due to effect on the gut microbiome affecting the gut brain access[30] [31]

Potential Risks Of Microdosing

As we have seen microdosing with psilocybin is generally considered safe and tolerable but for some people there can be both physiological or psychological acute side effects which stop after halting microdosing[32]. Some of these side effects may be prevented with

[27] A Really Good Day: How Microdosing Made a Mega Difference in My Mood, My Marriage, and My Life By Ayelet Waldman.
[28] The Effectiveness of Microdosed Psilocybin in the Treatment of Neuropsychiatric Lyme Disease: A Case Study by Daniel Kinderlehrer https://www.tandfonline.com/doi/full/10.2147/IMCRJ.S395342
[29] Anti-Inflammatory Effects of Four Psilocybin-Containing Magic Mushroom Water Extracts in vitro on 15-Lipoxygenase Activity and on Lipopolysaccharide-Induced Cyclooxygenase-2 and Inflammatory Cytokines in Human U937 Macrophage Cells by Sanah Malomile Nkadimeng https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8352634/
[30] Psychedelic medicine: The biology underlying the persisting psychedelic effects Kim P.C Kuypers https://www.sciencedirect.com/science/article/pii/S0306987718313252
[31] Seeking the Psilocybiome: Psychedelics meet the microbiota-gut-brain axis by John R. Kelly https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9791138/#bib0084
[32] Motives and Side-Effects of Microdosing With Psychedelics Among Users by Nadia R P W Hutten https://academic.oup.com/ijnp/article/22/7/426/5509881

lower doses, not mixing with other substances like alcohol or cannabis or different protocols as we shall discuss in the How And When To Microdose section.

- Possible adverse reactions include: anxiety, feelings of paranoia, slight nausea, insomnia, drowsiness.[33]

Potential Drug Interactions

Psilocybin may interact with certain medications, including antidepressants and antipsychotics. Research has only been done regarding interaction of higher doses however it is important to be aware that the risks might also include microdosing.

- Lithium is especially known for its potential to cause seizures or increase the subjective effects of psilocybin and potentially trigger a psychotic break[34]. Oregon legal regulation prevents access to legal psilocybin services to anyone who is using lithium.[35]
- D2, antagonism alone, in the case of haloperidol, does not attenuate psilocybin's effects, and, in fact, exacerbates anxiety and produces dysphoria.[36]
- 5ht2a antagonists that directly block effects of psilocin might reduce the effectiveness of microdosing.[36]
- In traditional Ayahuasca ceremonies Maoi Inhibitors are combined with another classical psychedelic called DMT, as classical psychedelics do not increase serotonin there is little risk of this combination causing serotonin syndrome. [37]
- When blocking SERT serotonin transporter pharmacologically with escitalopram with a healthy population there was no attenuation of psilocybin's psychedelic effect. [38] Further evidence that SSRI's can successfully be combined with microdosing psilocybin comes from compass pathway's clinical trial with larger doses of Psilocybin for treatment resistant depression with patients that were also

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[33]Powerful substances in tiny amounts: An interview study of psychedelic microdosing by Peter Grahl https://journals.sagepub.com/doi/pdf/10.1177/1455072517753339

[34] Classic psychedelic coadministration with lithium, but not lamotrigine, is associated with seizures: an analysis of online psychedelic experience reports by Sandeep M. Nayak https://www.thieme-connect.com/products/ejournals/html/10.1055/a-1524-2794

[35]Public Health Division chapter 333 Psilocybin by Oregon Health Authority https://secure.sos.state.or.us/oard/displayDivisionRules.action?selectedDivision=7102

[36]Drug-drug interactions between psychiatric medications and MDMA or psilocybin: a systematic review by Aryan Sarparast https://link.springer.com/epdf/10.1007/s00213-022-06083-y?sharing_token=jK11E137Ql0TQ1eCnk29cPe4RwlQNchNByi7wbcMAY5CCdS-Ly4q6rEXtnSWflUbrRpCx4gBP7yEn9nUvw80dY2ZT2LA0J9VZ3heg4fOIH03zFvGRS_yjzMuqZdSRD_J9wF9e5EWOf4rcuj9wK1uonERzyKdi2VFsFnvDe6vjnI%3D

[37] Serotonin toxicity of serotonergic psychedelics by Benjamin Malcom https://pubmed.ncbi.nlm.nih.gov/34251464/

[38] Acute Effects of Psilocybin After Escitalopram or Placebo Pretreatment in a Randomized, Double-Blind, Placebo-Controlled, Crossover Study in Healthy Subjects by Anna M. Becker https://ascpt.onlinelibrary.wiley.com/doi/full/10.1002/cpt.2487

taking SSRI[39]. The successful results were similar to previous studies with patients that were not on an SSRI. However due to SSRI increasing serotonin levels which can increase 5ht2b receptor activation[40] there might be negative effects and heart valve risks in long term combination (seen next section for details on 5ht2b activation risks)

5HT2B Receptor Activation Risks

It is important to address a potential health risk of taking “microdoses” that are too high for prolonged periods. This is because psilocybin breaks down into psilocin, which also binds to the serotonin 5ht2b receptor which has been linked to valvupathalogies, specifically Valvular heart disease.[40] Our analysis of binding affinities suggests that in terms of binding affinity to the 5ht2b receptor, consumption of approximately 6 mg of Psilocin is comparable to doses seen in drugs like Fen-Phen that cause VHD[41]. Sixty mg of Fen-Phen has been found to be significantly dangerous, while about half the dose of fenfluramine (27 mg) has been shown to be safe after three months of daily use[42]. So far there has not been even one case report of VHD caused by microdosing psilocybin despite its growing popularity. However, while research has not yet affirmatively or negatively linked psilocin to heart damage, adding a clear maximum dose of 3 mg and forcing a break in microdosing every 3 months can help avoid any cumulative effects on heart valves and reduce any potential risk[40].

Pregnancy, Breastfeeding And Children

In some indigenous cultures pregnant and breastfeeding women as well as children consume classical psychedelics[43]. In Brazil after reviewing the evidence the government has decided it is up to parental discretion if children will consume a traditional classical psychedelic (Ayahuasca containing DMT)[43]. One research with adolescents using

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[39] The safety and efficacy of COMP360 psilocybin therapy as adjunctive treatment in treatment-resistant depression by Guy M. Goodwin
https://psychedelicalpha.com/wp-content/uploads/2023/02/COMPASS-Pathways-Poster-2022.pdf

[40] Classical psychedelics and NBOMS as serotonin 2b receptor agonists: Valvulopathogenic signaling pathways and cardiac safety concerns by Elias Roihuvuo
https://erepo.uef.fi/bitstream/handle/123456789/26985/urn_nbn_fi_uef-20220118.pdf?sequence=1

[41] Microdosing Safety And Recommended Usage Report For Measure 109 by Rohit Singh
https://redlightoregon.com/wp-content/uploads/2022/01/Microdosing-Safety-and-Recommended-Usage-1.pdf

[42] Fenfluramine HCl (Fintepla®) provides long-term clinically meaningful reduction in seizure frequency: Analysis of an ongoing open-label extension study by Joseph Sullivan
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7756901/

[43] Consumption of Ayahuasca by Children and Pregnant Women: Medical Controversies and Religious Perspectives By Beatriz Caiuby Labate
https://www.tandfonline.com/doi/abs/10.1080/02791072.2011.566498

Ayahuasca in traditional settings found positive psychological effects compared to their peer group.[44] Pregnant women and children consume smaller doses with the younger children's doses being potentially similar to a microdose[43]. Since there is very little research it is up to a medical professional to help patients calculate the potential risk and benefits and compare them to other treatment options to decide if they should try microdosing.

[44] Ayahuasca in adolescence: a preliminary psychiatric assessment by Dartiu Xavier De Silveria https://pubmed.ncbi.nlm.nih.gov/16149324/

How and When to Microdose

Research has not found a connection between weight, sex and size of effective dose when it comes to psilocybin[45]. The 5ht2a receptor can vary in the population and seems to decrease with age with most of the loss happening in mid life[46] therefore finding the effective dose for some might take some time. Data from 115 users on Red Light Holland iMicro app who consented to share their anonymized data showed that most people (35%) did not follow a strict protocol and microdosed whenever they felt it would be helpful[41].

Our recommendation based on the latest science reviewed in this report as well as our experience with clients in the Netherlands are to try microdosing for 8 weeks and follow these guidelines:

- Start with one microdosing capsule of 0.5 mg once every 3 days. This was the second most common practice in our research with 30% of participants following this protocol.
- Most people benefit the most from microdosing in the morning on an empty stomach or with a very light breakfast, preferably without coffee. Sugars, processed carbs, fruits, and coffee might decrease the effect of microdosing.
- If there are no positive effects or if feeling drowsy or tired after 2 weeks increase the dose gradually. Even at doses as high as 4 mg our research in the Netherlands[47] indicates most people do not experience open eye visual artifacts. However we do not recommend exceeding 3 mg on a regular basis.
- If there are no positive effects with the initial protocol of once every 3 days we recommend increasing microdosing to once every 2 days or the “Stamets” protocol of microdosing 4 days in a row and taking a break for 3 days. From the experience gained by our therapist in the Netherlands the Stamets protocol seems very effective so it is worth building up to that protocol if the other protocols don’t have a positive effect.
- Microdosing too late in the day or taking too high of a dose may hamper sleep at night.
- If feeling agitated, anxious or nausea, reduce the dose.

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[45] Optimal dosing for psilocybin pharmacotherapy: Considering weight-adjusted and fixed dosing approaches https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8056712/
[46] Greater Loss of 5-HT2A Receptors in Midlife Than in Late Life by Yvett I. Sheline https://ajp.psychiatryonline.org/doi/full/10.1176/appi.ajp.159.3.430
[47] Report on Psychedelic Concert In The Netherlands by Red Light Holland https://drive.google.com/file/d/1kP8kd-icdlo4NJN8XYDU4JrQkVWTU0Qi/view?usp=sharing

- For some people smaller doses can be used as a sleep aid as they may increase tiredness and bring about creative dreams.
- Patients with anxiety or those on the bipolar spectrum need to be especially careful not to start with too high doses.
- Those with bipolar symptoms would benefit from microdosing during down/depressed periods rather than during up/manic periods.
- Those on the autistic spectrum may need higher doses.
- For preventing cluster headaches or migraines higher doses may be needed.
- It is also recommended to pause microdosing every 8 to 10 weeks for a wee or two. In animal model's it has been shown that serotonin receptors build tolerance to classical psychedelics if taken too often or in too high of a dose.[48]
- Plasma concentration and subjective experience should peak by 90 min.[49] For those microdosing for the first time it is important to clear their schedule for at least 90 min and be able to access some support if their dose ends up having a stronger subjective effect then intended.
- The first hour post microdosing is crucial in determining a protocol. During this time, it is important to take note of what is happening in one's body. We recommend using our privacy first microdosing app www.iMicroapp.com to journal 30 min after dosing and then again at the end of the day.
- Combining journaling with a short mindfulness breathing exercise of even 3 minutes can be very helpful. An example of such an exercise can be found here: https://youtu.be/rOne1P0TKL8
- We highly recommend not driving for at least 3 hours after microdosing or while there is any subjective heightened sensation.

[48] Tolerance and Cross-Tolerance among Psychedelic and Nonpsychedelic 5-HT2A Receptor Agonists in Mice https://pubs.acs.org/doi/abs/10.1021/acschemneuro.2c00170

[49] Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels by Martin Madsen https://pubmed.ncbi.nlm.nih.gov/30685771/