OPAB Research SC KQ3

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I. Screening considerations and tools for safety in psilocybin use

Psilocybin-containing mushrooms have a variety of physical and emotional impacts that will vary depending on the mindframe, setting, and personal physiology of each individual recipient. Most of these impacts are largely benign and transient, ending with the completion of psilocybin's metabolism in the body. However, there are certain conditions that deserve careful consideration and caution with use of psilocybin. Medical and mental health screening is necessary to optimize benefit and mitigate potential risks for psilocybin use in facilitated sessions. This section will discuss the potential complications of psilocybin use with a variety of health issues, and the screening tools that may be used to optimize psilocybin experiences and protect consumers.

II. Physical impacts of Psilocybin and Potential Implications

A. Concerns for Direct Psilocybin Impacts

i. Cardiac

Psilocybin mushrooms contain Phenylethylamine, a monoamine alkaloid that can elevate blood pressure and cause tachyarrhythmias (Beck et al. 1982). Due to potential increases in blood pressure and tachyarrhythmias, people with uncontrolled hypertension, aneurysms, heart disease, or tachyarrhythmias such as Wolf-Parkonsin-White Syndrome (Borowiak 1998) may be at increased risk for injury. Psilocybin and psilocin have been demonstrated to increase QTcF interval by a mean of 2.1 (6.6) milliseconds (Dahmane et al. 2021). There is a possibility that psilocybin and psilocin could act synergistically with other drugs that impact QTc-interval. People with long QT syndrome or other irregularities of heart rhythm and people taking medications that prolong QTc-interval may be at risk for exacerbation of arrhythmias and potential injury.

ii. Endocrine

Psilocybin's effect on blood glucose has only been studied in animal models. There is potential for mild hyperglycemia with psilocybin use (Steiner, Sulman 1963). People who take psilocybin may be at risk for transient episodes of hyperglycemia. Blood sugar monitoring in recipients with diabetes or other blood sugar dysregulation issues may be prudent to avoid hyperglycemia.

iii. Polypharmacy

Concomitant use of certain medications or drugs with psilocybin carries a variety of

risks depending on the pharmacokinetics of each drug class, interaction with receptors, impacts on metabolism, and epigenetic factors. DrugBank lists 436 potential Psilocybin/Drug interactions. Psilocybin is metabolized to the active form, psilosin by first pass hydrolysis by Alkaline phosphatase. Psilocin is then primarily glucuronidated by UGT1A10, and also oxidized by monoamine oxidase, Ceruloplasmin, Cytochrome oxidase, and aldehyde dehydrogenase, and other minor pathways.135, 157 Any medications that impact these metabolic pathways could change the rate of psilocybin and psilocin metabolism, and thus possibly change the intensity and duration of a psilocybin experience. People using drugs such as oral contraceptive pills158, the 4-anilinoquinazoline class of kinase inhibitors159, Cinacalcet160, Disulfiram161, Monoamine Oxidase Inhibitors, and others may experience differences in intensity and duration in psilocybin effects due to changes in the metabolism of psilocybin. Drugs that bind directly to 5-HT receptors or transporters may interfere with psilocybin binding. Examples include SSRI's, SNRI's, tricyclic antidepressants, buspirone, antipsychotics, and some muscle relaxers. Drugs such as antipsychotics that inhibit 5-HT2A receptors, likely the main site of action of psilocybin, may also have an impact on the intensity and duration of psilocybin effects.162 As noted above, psilocybin may prolong QTc interval. Drugs that prolong QTc interval may act synergistically with psilocybin putting those combining the two at risk for arrhythmia and injury.

iv. Gastrointestinal

Psilocybin can cause nausea, vomiting and diarrhea, likely due to strong agonistic affinity for and binding to 5-HT3 receptors (...) which play a role in gastrointestinal motility and nausea (Navari 2015). People living with bulimia may be triggered by the experience of gastrointestinal distress which may lead to difficult emotional states such as anxiety or grief. People with gastrointestinal sensitivity to other serotonergic drugs such as SSRI's may have stronger gastrointestinal symptoms with psilocybin use. People with gastrointestinal disease may have their symptoms exacerbated temporarily by psilocybin ingestion. The nausea and appetite suppression that may result from psilocybin use may cause difficulty in eating during a psilocybin experience.

v. Allergy

Most fungi including the psilocybin containing fungi contain chitin in their cell walls, which is known to cause allergy in some individuals, and mushrooms may contain multiple other antigens that cause allergic reactions (Koivikko and Savolainen 1988). People with a known mushroom allergy are at risk for allergy and anaphylaxis with the use of psilocybin containing mushrooms. However, synthetic psilocybin products with no mushroom extractives may still be possible for use, depending on the nature of the allergy.

vi. Inability to Provide Informed Consent

Psilocybin use has not been ethically studied in people with an inability to understand the details of taking psilocybin and to provide informed consent. The potential risk for poor outcomes due to confusion, hallucinations, and psychological distress is significant.

vii. Pregnancy

Psilocybin use in pregnancy has not been studied, however psilocin has been found to cross the placenta **IN RATS** (Law et. al. 2014).

viii. Renal

There is one confirmed case and some other scientific and anecdotal evidence of potential for acute kidney injury after psilocybin ingestion in some individuals (Raff, et al. 1992, Austin, et al 2019). People with renal disease using psilocybin may be at increased risk for further kidney injury and renal failure.

ix. Cerebral Hemodynamics

fMRI studies have demonstrated significant decreased blood flow to many areas of the brain during psilocybin use (Carhart-Harris et al. 2012, Lewis et al. 2017). People with brain-related arterial stenosis, decreased cerebral blood flow, or any condition leading to decreased blood flow to the brain may be at higher risk for hypoxia with psilocybin use. (IS THIS TOO MUCH EXTRAPOLATION?)

B. Medical conditions indirectly impacted by psilocybin use

i. Mobility Issues

Conditions such as Multiple Sclerosis, ALS, absent limbs or other mobility issues require a thorough discussion on facilitating comfort and safety. Because of changes in perception and proprioception, mobility can become more difficult after psilocybin ingestion. There may be an increased risk for falls, and the recipient should be monitored carefully to avoid injury.

ii. End of life care

End of life care is psychologically nuanced and often complicated by polypharmacy, mobility concerns, and organ system dysfunction. Hospice accompaniment and primary care provider involvement may be beneficial in coordinating end of life care with use of psilocybin.

iii. Pain

People with chronic or acute pain may have a reduction in their experience of nociception during and after psilocybin ingestion due to changes in inflammatory pathways and through stimulation of the 5-HT2A receptor. Recent trauma to the body resulting in wounds, fractures, sprains or other injury may necessitate extra assistance, and caution because the pain perceptions that are protective and prevent overuse are less apparent.

iv. Surgically implanted devices

People with ostomies, medication pumps, or other surgically implanted devices may require assistance with these devices because of alterations in perception and coordination.

v. Dizziness

Vertigo may be increased with psilocybin use warranting extra caution for those with inner ear disorders or other forms of vertigo who may need mobility assistance, and may have increased nausea.

vi. Vision Impairments

People who are blind or vision impaired may experience emotional distress due to changes in perception in other senses, such as proprioception, hearing and balance, and reports exist of psychedelics triggering visual hallucinations in blind recipients (Krill et al. 1968).

C. What mental health conditions are a concern for psilocybin use?

i. Psychosis and Schizophrenia

Many studies on psilocybin in the 1960's-90's focused around the potential use for the psilocybin experience as a model for psychosis and suggested that psilocybin use may lead to psychosis (Vollenweider 1998>>>>>>>). However, schizophrenia is largely considered a syndrome with multiple potential pathways and there are differences in brain function between those using psilocybin and those with schizophrenia such as opposing prefrontal cortex activation patterns (Arora and Meltzer, 1991; Joyce et al., 1993; Vollenweider et al., 1997) and opposite prepulse inhibition of the startle reflex (Carhart-Harris et al. 2012). in a population study of 130,000 US individuals, no increased risk for serious psychological distress, mental health treatment, suicidal thoughts, suicidal plans and suicide attempt, depression and anxiety in the past year were noted (Johansen, Krebs 2015). Psilocybin may induce temporary anxiety, fear, panic, dysphoria and paranoia for 6-8 hours after ingestion (Johnson et al., 2008); It is possible that psilocybin could exacerbate a current state of psychosis with these symptoms.

ii. Mania or Likelihood of Manic Induction

Gard, et al. found 15 cases of manic induction in the literature, advising caution with use in bipolar disorder (Gard, et al. 2021 **NOT YET PEER REVIEWED**). It is however notable that Bipolar experiences are a heterogenous group of disorders, and that there may yet be use for psilocybin in bipolar depression in individuals who have minimal experience of mania, or hypomania. Further research is needed in this area.

iii. Dissociative states???

No data exists in the literature examining dissociative states such as Dissociative Identity Disorder and psilocybin use. It is conceivable in individuals with DID that different personalities may present with different facets of the individual more prominently portrayed. This may create complications with facilitation, as different aspects of the individual may have different priorities, levels of fear or overwhelm, and response to the psilocybin. ((DID is more like group work.))

iv. Suicidal Intent

As evidenced by the research on depression and psilocybin, there is much potential for long-term healing. Psilocybin use may be life-saving in reducing depression, however could exacerbate anxiety and acute suicidal feelings during the psilocybin experience. A thorough discussion of safety measures with the recipient is warranted when working with acute suicidal ideation.

v. Homicidal intent

The alteration in mental and emotional states brought about by psilocybin can create increased emotional lability and volatility in some people. A person with acute homicidal ideation may have their experience exacerbated by psilocybin use.

D. Screening tools

i. Screening for Psychosis, Mania, Schizophrenia, and Dissociative States (Seiler et al. 2020)

Brief Psychiatric Rating Scale (BPRS)
https://www.smchealth.org/sites/main/files/fileattachments/bprsform.pdf?1497977629

Positive and Negative Syndrome Scale PANSS
https://www.psychdb.com/_media/psychosis/panss.pdf

Scale for the Assessment of Positive Symptoms (SAPS)

https://www.ncbi.nlm.nih.gov/projects/gap/cgi-bin/GetPdf.cgi?id=phd000837.1

Psychotic Symptom Rating Scale (PSYRATS)
https://core.ac.uk/download/pdf/204498869.pdf
Clinician-Administered Rating Scale for Mania (CARS-M)
https://www.neurotransmitter.net/CARS_M.pdf

ii. Bipolar screening
Hypomania Checklist (HCL-32) - Self Report
http://www.oacbdd.org/clientuploads/Docs/2010/Spring%20Handouts/Session%20220b.pdf

Mood Disorder Questionnaire (MDQ)
https://www.ohsu.edu/sites/default/files/2019-06/cmsquality-bipolar_disorder_mdq_screener.pdf

Composite International Diagnostic Interview (CIDI)
https://www.hcp.med.harvard.edu/ncs/ftpdir/CIDI_3.0_Bipolar_Screening_Scales_final.pdf
iii. Screening for Dissociative states

Dissociative Experiences Scale (DES)
https://www.hebpsy.net/files/ruZXkl5YGeKcvt6dBZpS.pdf
iv. Screening for Suicidality

ASQ Suicide Risk Screening tool
https://www.nimh.nih.gov/research/research-conducted-at-nimh/asq-toolkit-materials/asqtool/screening_tool_asq_nimh_toolkit_155867.pdf

v. Screening Tools to Assess Benefit

PTSD Checklist for DSM-5 (PCL-5)
https://www.ptsd.va.gov/professional/assessment/adult-sr/ptsd-checklist.asp

Patient Health Questionnaire (PHQ-9)

https://patient.info/doctor/patient-health-questionnaire-phq-9

Depression anxiety and stress scale

(DASS21; Lovibond & Lovibond, 1995)
https://maic.qld.gov.au/wp-content/uploads/2016/07/DASS-21.pdf

A study by Carrillo et al in 2018 found that a low-cost and effective machine learning algorithm applied to recipient speech patterns during intake can assess for the likelihood of psilocybin effectiveness in managing treatment resistant depression

GAD-7 (General Anxiety Disorder-7)
https://www.mdcalc.com/gad-7-general-anxiety-disorder-7

Demoralization scale
Kissane DW, Wein S, Love A, Lee XQ, Kee PL, Clarke DM. The Demoralization Scale: A Report of its Development and Preliminary Validation. Journal of Palliative Care. 2004;20(4):269-276. doi:10.1177/082585970402000402

Psychological Insight Questionnaire
(PIQ; Davis et al., 2021143; Davis et al., in press)

vi. Research Tools for tracking changes
The Oregon psilocybin program provides a rich opportunity to grow the body of knowledge about the impacts and benefits of psilocybin through voluntary surveys and symptom tracking pre-and post- use. In addition to using the above screening tools, the following may inform screening guidelines.

Well-Being Inventory

https://www.ptsd.va.gov/professional/assessment/documents/WellBeingAssessment.pdf

Well-Being Inventory Manual
https://www.ptsd.va.gov/professional/assessment/documents/WellBeingInventoryManual.pdf

Mystical Experiences Questionnaire (MEQ; (Barrett et al., 2015; MacLean et al, 2011)
https://www.ocf.berkeley.edu/~jfkihlstrom/ConsciousnessWeb/Psychedelics/States-ofConsciousness-Questionnaire-and-Pahnke.pdf

Challenging Experiences Questionnaire

Facilitator Experiences Questionnaire (FEQ)
Currently under research at the BAND lab at UCSF