Exploring Psychedelic Usage in Athletes and Attitudes Towards Psilocybin Use in Concussion Recovery

by

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We acknowledge and respect the lək̓ʷəŋən peoples on whose traditional territory the university stands and the Songhees, Esquimalt and W̱SÁNEĆ peoples whose historical relationships with the land continue to this day.

Exploring Psychedelic Usage in Athletes and Attitudes Towards Psilocybin Use in Rehabilitative Contexts in Sports Cultures

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Abstract

Introduction: Given the prevalence of sports-related concussions in athletes across Canada and the United States of America and the debilitating nature of persisting post-concussion symptoms, novel rehabilitation and symptom management approaches are necessary research endeavours. I include a scoping review that I co-authored on the literature pertaining to psilocybin's effects on cognition and creativity as a precursor to the empirical study of my thesis. This study aims to examine the willingness of the sports community to engage with psilocybin-assisted therapy (PAT) for concussion recovery and the management of persisting post-concussion symptoms (PPCS), while also providing current psychedelic use rates among a sample of athletes and examining the motivations for using psychedelics in this population.

Methods: Athletes and sports team staff completed an online survey through Qualtrics with three sections: demographics, substance use history, and attitudes and willingness to use/support PAT for concussion recovery. Path analysis was used to assess direct effects and mediations of age, education, past psychedelic use, personality openness (assessed using the Ten-Item Personality Inventory) knowledge, attitudes, and concussion history (athlete model only).

Results: This sample consisted of 175 respondents (n = 85 athletes; n = 90 staff) from Canada and the US. The most common substances used in the past year among athletes were alcohol (90.6%) cannabis (43.6%), and psychedelics (35.8%). However, regular psychedelic use (use $\geq$ 2 times per week) was quite low in athletes (7.5%). Just over half of our athletes had sustained a concussion at some point in their life with 64.6% of those athletes sustaining two or more concussions. The path analysis for the athlete model revealed significant paths from age to willingness (β = .19, SE = .01, p < .01), knowledge to willingness (β = .37, SE = .14, p < .01), attitudes to willingness (β = .33, SE = .11, p < .01), attitudes to knowledge (β = .34, SE = .12, p

< .01), attitudes to psychedelic experience (β = .52, SE = .38, p < .001), and knowledge to psychedelic experience (β = .46, SE = .33, p < .001). There were also significant indirect effects between past psychedelic experience and willingness (β = .17, p < .01), and past psychedelic experience and attitudes (β = .16, p < .01), where knowledge was a mediator between both interactions. The staff path model revealed significant paths from knowledge to willingness (β = .32, SE = .12, p < .01), attitudes to willingness (β = .32, SE = .11, p < .01), attitudes to knowledge (β = .51, SE = .09, p < .001), attitudes to past psychedelic experience (β = .27, SE = .38, p < .01), and knowledge to psychedelic experience (β = .27, SE = .38, p < .01). There was a significant indirect effect between past psychedelic experience and attitudes (β = .14 p < .05) with knowledge as a mediator.

Conclusions: The results of the survey found that many athlete respondents used psychedelics in the past year, but few athletes use them regularly. Of psychedelics used, psilocybin is the most commonly used and athletes reported using psychedelics primarily for personal improvement and mood enhancement. The results of the path analysis suggest that knowledge of psilocybin and attitudes towards psilocybin are predictive of both athlete and staff willingness to use or support PAT. These findings suggest that it may be feasible for researchers to begin clinical studies to examine if psilocybin has any effect on concussion recovery and PPCS.

Keywords: psychedelics, psilocybin, sports-related concussion, mTBI

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Prologue

This thesis consists of four chapters: an introductory chapter, a pre-registered scoping review, an empirical study, and an integrated discussion of all findings. The first chapter is a brief review on sports-related concussions, persisting post-concussion symptoms, psychedelics (specifically psilocybin) and a proof of concept arguing that psilocybin may have a role have in concussion recovery and the management of persisting concussion symptoms which is discussed. Together, this chapter reviews whether there is a potential avenue to explore PAT for concussion rehabilitation. The second chapter is derived from a scoping review that I co-authored which examines the literature as it pertains to psilocybin's effects on cognition and creativity. This review summarizes the literature and intends to act as a guide regarding psilocybin's acute and post-acute effects on six domains of cognition (foundational, lower order, higher order, social cognition, subjective) and creativity, the timeline of publications on these topics since 1994, and the most frequent institutions and researchers publishing on these topics. Importantly, this review showcases the overall safety of psilocybin for clinical use and found that psilocybin does not impair cognitive functioning long-term, an important consideration for psilocybin as a concussion recovery tool. This article has since been published in the *Journal of Psychopharmacology* (Bonnieux et al., 2023). These chapters complement one another as Chapter 1 provides a proof of concept regarding the potential use of psilocybin as a recovery aid for concussion and persisting symptoms while Chapter 2 displays the safety of using psilocybin in a clinical setting and the outcomes of psilocybin use on cognition. Ultimately, some overlap among these chapters is natural given that both articles are built upon the study of psilocybin with an emphasis on outcomes in cognition. Importantly, the scoping review highlighted a pertinent gap in the literature and understanding of psilocybin's long-term influence on

cognition. This is of relevance when assessing psilocybin's utility in aiding those suffering from sports-related concussions and persistent post-concussion symptoms which include high rates of cognitive impairment in domains of memory, attention, and concentration, to name a few. As such, the scoping review has provided the necessary background for this research which will further the pursuit of understanding psilocybin's long-term influence on cognition. Key future directions that were highlighted in the scoping review included further investigation of cognitive effects of psilocybin use and particularly as it pertains to clinical populations.

The third chapter builds off Chapter 1 and Chapter 2 by moving in the next natural direction. That is, because existing research (with both human and animals) offers insight as to how psilocybin may benefit those with concussion and our scoping review displayed that psilocybin does not impair cognitive functioning, we should now examine willingness of the sports community to incorporate psilocybin in concussion recovery for athletes. Chapter 3 describes the methodology and outcomes of the empirical study of this thesis and is formatted for publication in *The Journal of Applied Sport Psychology*. This chapter builds off the previous chapters by taking the first step in examining research with psilocybin for concussion in athletes, including psilocybin's role in cognitive symptoms following concussion. The third chapter describes the results of a survey study examining current psychedelic use rates among athletes, concussion and persisting post-concussion symptom frequency, and the willingness of the sports community to engage in this research. The findings of this study are intended to provide important future directions for researchers, clinicians, and the sports community to move forward with PAT for concussion recovery and persisting symptoms. Finally, Chapter 4 summarizes the results of the scoping review and the empirical study and offers recommendations to future researchers moving forward.

Chapter One: A Proof of Concept for Psilocybin's Role in Concussion Recovery and Symptom Management

Introduction

Sports-related concussions (SRC) are a form of mild traumatic brain injury (mTBI) that occurs while engaging in sports (McKeithan et al., 2019). In the United States of America, roughly 3.8 million sports-related brain injuries occur annually (De Stefano et al., 2020) while in Canada, available data from 2020-2021 via the Canadian Institute for Health Information (CIHI, 2020) identified almost 2000 emergency department (ED) visits for sports-related brain injuries. While most athletes fully recover within 7-10 days, approximately 10-30% of athletes will experience persisting post-concussion symptoms (PPCS) which typifies the long-term persistence (for weeks or even months) of clinical symptoms past this recovery time frame (Leddy et al., 2012; Ledreux et al., 2020; Makdissi et al., 2013, 2017; Sicard et al., 2021). Common psychological symptoms include anxiety and depression, irritability, and cognitive impairments in areas of executive function, memory, attention, concentration, language, cognitive stability, and flexibility (Covassin & Elbin, 2010; Karr et al., 2014; Ledreux et al., 2020). Physiological symptoms include headache, fatigue, and light and noise sensitivity (Ledreux et al., 2020). These symptoms can be greatly debilitating in athletes across multiple domains of life (i.e., interpersonal relationship, academics, work, leisure, sports) and can prolong the time before returning to work, school, and/or play. The purpose of this thesis is to delve into

the topic of concussion recovery and management of PPCS, specifically examining the potential use of PAT in this context. The empirical study in Chapter 3 will explore the willingness of athletes and sports staff members to engage in or support this alternative approach by which we aim to contribute to the ongoing discourse surrounding concussion rehabilitation and offer insights into novel avenues such as psychedelic therapy for managing PPCS.

Definitions

mTBI and concussion are often used interchangeably to describe a brain injury caused by direct or indirect force to the head, which results in symptoms in the domains of cognition, emotion, and sleep (Romeu-Mejia et al., 2019). The conceptual definition of SRC according to the Concussion in Sport Group (CISG) was updated at the Amsterdam 2022 International Consensus Statement on Concussion. This improved definition involves the following major points: (1) force is transmitted to the brain via a blow to the head, neck or body through sport or sport-related activities; (2) the resulting injury to the brain occurs through a neurotransmitter and metabolic cascade; (3) symptoms can onset rapidly or overtime and typically resolve within days but may persist; (4) injury is typically functional rather than structural and will not be seen on standard structural neuroimaging studies; and (5) clinical presentation is broad and diverse and may or may not include loss of consciousness (Patricios et al., 2023). Therefore, SRCs can be understood as a type of mTBI which are a serious injury that can significantly impact quality of life.

Given the complex nature of SRCs, symptom presentation, recovery time, and long-term outcomes are variable and unpredictable (Kim & Priefer, 2020). Parachute Canada, in collaboration with the Public Health Agency of Canada, outlines strategies for returning to normal activities following an SRC. These guidelines, the Canadian Guideline on Concussion in Sport, follow a stepwise order beginning with cognitive and physical rest followed by specific guidelines for returning to school, work, and sports in a safe manner (Ellis et al., 2019). While this protocol is standardized and evidence-based (Ellis et al., 2019), it is worth highlighting that the individualized nature of each SRC and the cognitive sequelae may benefit from a more individualized treatment approach for each patient. Moreover, those who develop PPCS do so despite following these protocols. As previously mentioned, the persistence of these concussive symptoms are debilitating and can worsen recovery outcomes long-term (Iverson et al., 2017). These findings may explain why improved rehabilitation approaches and managing PPCS are among the most requested areas of research among patients, clinicians, and researchers (Osmond et al., 2023; Patricios et al., 2023). It is because of these lasting impacts on patients that this line of research is a necessary endeavour.

The Pathophysiology of Concussion and Cognitive Complaints

Following a concussion, one of the most frequent neuronal events is diffuse axonal injury which constitutes the tearing of neuronal axons and small blood vessels (Kim & Priefer, 2020). Outcomes of concussion include ischemia, hypoxia, and various chemical and metabolic

disruptions (Giza & Hovda, 2014). A neuroinflammatory cascade is characterized by an immediate microglial response and rapid increases of interleukin (IL)-1β, IL-6 and tumor necrosis factor-α (TNF-α) within 24 hours of injury (Giza et al., 2018; Giza & Hovda, 2014; Krukowski et al., 2021; Madathil et al., 2018; Patricios et al., 2023; Romeu-Mejia et al., 2019). A neurometabolic cascade which intends to restore homeostasis instead results in an energy crisis characterized by membrane depolarization (paired with potassium efflux), the release of excitatory neurotransmitters, N-methyl-D-aspartate receptor activation, calcium influx, excitatory neurotransmitter breakdown, reactive oxygen species overproduction, and finally cellular damage as the final consequence (Giza et al., 2018; Giza & Hovda, 2014; Romeu-Mejia et al., 2019). Other outcomes of concussion also include cell death (the degree of which is dependent on the severity of the injury), dendritic degeneration, and impaired synaptic plasticity (Gao & Chen, 2011; Kim & Priefer, 2020; Patterson & Holahan, 2012; Romeu-Mejia et al., 2019). A frequent finding via neuroimaging studies is atrophy of the hippocampus long-term following concussion and repeated concussions (McDaid et al., 2021; Misquitta et al., 2018; Strain et al., 2015). McDaid et al. (2021) found that mice subjected to a single concussive event showed long-term synaptic effects in the hippocampus similar in degree to those subjected to repeated concussions, while Pinar et al. (2020) found that repeated concussions in rats impaired hippocampal-dependent spatial learning and memory. Moreover, Pinar et al. (2020) suggest that repeated mTBI may interrupt cognitive development in adolescent rats. Research in humans has

also identified the effect of mTBI on the hippocampus; Misquitta et al. (2018) found that hippocampal atrophy was associated with poorer performance on verbal memory tasks in former professional football players. Using this hippocampal example, it becomes clear that the consequences of this neuroinflammatory and neurometabolic cascade in the brain produce the characteristic symptomatology of concussion which include the physiological, cognitive and behavioural impairments (McDaid et al., 2021; McInnes et al., 2017; Misquitta et al., 2018). Ground-breaking research may consider treatment options which will help rectify this pathophysiology of SRC and thus manage the resulting symptomatology.

Psilocybin

Psychedelics (serotonin 2A [5-HT_{2A}] agonists) are serotonergic hallucinogens that elicit altered states of consciousness, mood, and perception (Nichols, 2016). The scientific community has entered an era of renewed interest in psychedelics for medicinal purposes, a period termed the “psychedelic renaissance” (Carhart-Harris & Goodwin, 2017; Nichols, 2020; Sessa, 2012). This renaissance began in the 1990s; since then, researchers have continued to examine the role of these substances in treating and aiding various psychological disorders such as treatment-resistant depression, end of life care, and addiction (Carhart-Harris et al., 2017; Davis et al., 2021; Griffiths et al., 2016; Johnson et al., 2014) with movements towards examining effects on somatic illness such as chronic pain and headaches (Andersson et al., 2017; Schindler et al., 2021, 2022). Of profound interest in this renaissance is psilocybin, a classic psychedelic that is

naturally produced by mushroom species across the world and when ingested is dephosphorylated into psilocin, the psychoactive metabolite (Daniel & Haberman, 2017; Nichols, 2016). Psilocin shares structural similarities with serotonin such that psilocin has a high affinity for the 5-HT_{2A} receptor where it preferentially induces its mechanism of action (Halberstadt & Geyer, 2011). Psilocin also binds to other 5-HT receptors such as the 1A, 2B, 2C, 6, and 7 receptors (Dinis-Oliveira, 2017; Halberstadt & Geyer, 2011; Ray, 2010). These receptors are densely populated within the prefrontal cortex and the hippocampus (Carhart-Harris & Nutt, 2017; Smausz et al., 2022), two regions of the brain that have vital roles in higher order cognitive processing. It is these associations that suggest inquisition to psilocybin's utility in improving cognitive dysfunction.

Necessarily, the safety of psilocybin has been questioned and is a point of considerable discussion when assessing its clinical utility. Though there were initial significant concerns about psilocybin's potential addictive properties or ability to be abused, research indicates that psilocybin actually has low potential for abuse (Rucker et al., 2018) given that it has no direct effect on dopaminergic signalling in the brain – a system that appears to be necessary for drug dependence (Johnson et al., 2018; Nichols, 2016; Passie et al., 2002). Psilocybin poses low risk for toxicity via respiratory depression and cardiovascular complications, and a lethal dose of psilocybin is more than 1000 times the effective dose (Johnson et al., 2018). If consuming psilocybin-containing mushrooms, it is almost impossible to overdose given the quantity needed

to ingest (Dodd et al., 2022). Of frequent concern are “bad trips” which are negative incidents that most commonly involve panic, paranoia, fear, agitation, anxiety, and mental confusion as a reaction to powerful, hallucinogenic experiences, and which pose the greatest risk with psilocybin use, according to self-reports (Bienemann et al., 2020). Other risks associated with psilocybin use include risks of inducing psychosis and/or mania which may persist long-term (Barber et al., 2022; Hendin & Penn, 2021). These risks can be mitigated by taking a controlled dose of psilocybin in a safe and controlled setting and with an appropriate mindset and expectations going in to the session (Johnson et al., 2008). A recent systematic review assessing the safety of psilocybin for the treatment of psychiatric highlighted the positive safety profile of psilocybin with few reports of minor adverse effects (Castro Santos & Gama Marques, 2021). The most frequently reported negative effects included anxiety, nausea, transient hypertension, and headaches, with the headaches occurring primarily during the session. Moreover, our recent scoping review (see Chapter 2) examining psilocybin’s cognitive effects indicated that psilocybin is well-tolerated and poses limited risk in healthy participants (Bonnieux et al., 2023).

Psilocybin’s Role in Concussion Recovery

Researchers recently conducted a Canada-wide initiative that incorporated patient, caregiver, and clinician input to identify the most important concussion research topics. In this study, effective symptom management was one of the three most prominent themes highlighted, and the prevention of prolonged symptoms was among the top ten (Osmond et al., 2023).

Importantly, the most common cause of concussion was through sports involvement, suggesting that these concerns are held among athletes. Moreover, conference attendees at the International Conference on Concussion in Sport recently voted on the biggest gaps and top research priorities: 50.8% of respondents voted for rehabilitation, 50.3% voted on recovery, and 49.3% voted on persisting symptoms (Patricios et al., 2023). Together, these projects highlight that the current research needs identified by patients and professionals regard recovery and rehabilitation protocols, as well as managing PPCS. Given these priorities, the examination of psilocybin as a novel symptom management approach may be welcomed by those affected by concussion.

While psilocybin has not been studied as a treatment or recovery tool for concussion, I propose that it has therapeutic potential to provide (1) assistance with immediate physiological consequences of the injury (i.e., by reducing pro-inflammatory changes and neuronal atrophy) with potential to subsequently improve cognitive impairments, and (2) assistance in treating mental health outcomes in PPCS, such as depressive or anxious symptomatology.

Anti-Inflammatory and Neurogenic Properties of Psilocybin

Given the association between neuroinflammation and persistent cognitive impairment following concussion (Clausen et al., 2009, 2011; Xiong et al., 2018), targeting inflammation resulting from SRC emerges as a promising strategy for managing symptomatology. The potential of this approach lies in its ability to mitigate or even reverse cognitive impairment by addressing the underlying neuroinflammatory processes that chronically persist, rather than the

immediate neuroinflammatory response which is necessary for neural regeneration and recovery (Xiong et al., 2018). Along these lines, the use of anti-inflammatory agents, particularly non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, has been suggested in the acute phases of concussion recovery (Patterson & Holahan, 2012). When used immediately post-concussion in animal models, ibuprofen has been shown to have strong anti-inflammatory abilities by inhibiting IL-6 and -1β which contribute to a pro-inflammatory environment in the brain (Bergold, 2016). These findings highlight that managing the inflammatory environment in the brain may be a useful avenue to pursue in improving concussion recovery and functional outcomes. Research suggests that 5-HT_{2A} receptor activation on neuronal cells could be a therapeutic target for neuroinflammatory injuries in the brain (Yu et al., 2008) – the receptor which mediates psilocin's therapeutic effect. Specifically, the authors note that the activation of the 5-HT_{2A} receptors may be particularly effective in managing inflammation due to TNF-a-mediated inflammation and may both prevent and treat inflammation.

As critical modulators of the neuroinflammatory environment, TNF-a, IL-1β, and IL-6 act directly on and are expressed by microglia resulting in an increased inflammatory microglial phenotype (Willis et al., 2020). While this phenotype is a necessary temporary measure to deal with the immediate cellular damage from the brain injury (Johnson et al., 2013), it is possible that microglia sustaining this inflammatory phenotype can contribute to the lasting cognitive and emotional symptoms through the excessive phagocytosis and pruning of synapses (Alawieh et

al., 2021). This microglial behaviour has been demonstrated in models of major depressive disorder and anxiety (Deng et al., 2020; Wohleb et al., 2018). Targeting and reducing the sustained inflammatory reaction of microglia may be one of the reasons why psychedelics have such strong therapeutic effect (VanderZwaag et al., 2023) and may contribute to their potential ability to treat PPCS.

Another potential avenue for psilocybin's therapeutic effect is via its neurogenic and neuroplastic properties, which may support cognitive recovery and depressive symptoms following brain injury (Khan et al., 2021). Research has found that psilocin, among other psychedelics, promotes neuritogenesis, which may be mediated by the 5-HT_{2A} receptor (Ly et al., 2018). Raval et al. (2021) found that a single dose of psilocybin induced persistent (six days) synaptogenesis in pig hippocampi and an acute decrease in 5-HT_{2A} receptor density which is hypothesized to be involved in the antidepressive effects of psilocybin. Finally, Shao et al. (2021) showed that one dose of psilocybin resulted in persistent increases in spinal density in the medial frontal cortex and that these effects are also mediated by the 5-HT_{2A} receptor. These findings are often discussed with relevance to symptoms of depression but may apply to other mood disorders and cognitive function. Psychedelics may also promote microglial expression of neurogenic mediators, such as brain derived neurotrophic factor (BDNF), thus leading to increased recovery from the cognitive impacts of TBI (VanderZwaag et al., 2023). Unfortunately, the long-term outcomes of psilocybin use on cognitive functioning are currently

under researched with few studies examining cognition beyond the acute phase of psilocybin intoxication (Bonnieux et al., 2023).

Mental Health Concerns in PPCS

Notably, mood symptoms are very common following a concussion (Lumba-Brown et al., 2023) and mood symptoms are more likely to occur following a concussion compared to an orthopaedic injury (Hoyle et al., 2020). Moreover, the risk of mood symptoms further increases in those with PPCS (Sicard et al., 2021). A recent study with a Canadian PPCS sample found that 35% of respondents endorsed elevated anxiety and/or depression symptoms. Furthermore, the authors identified a correlation between number of concussions and severity of anxiety and depression symptoms where more concussions were related to worse symptomatology (Doroszkiewicz et al., 2021). These findings have been corroborated by numerous other studies (Broshek et al., 2015; Guskiewicz et al., 2007; Guskiewicz & Broglio, 2015; Kerr et al., 2012). Moreover, a recent review summarized the frequency of depression in those with PPCS which called for improved mental health intervention throughout concussion rehabilitation in light of a strong correlation between PPCS and depressive symptoms (Lambert et al., 2022). Furthermore, suicide rates in athletes with a concussion history continue to rise and are highest within six-months post-concussion (Henry et al., 2017). While psychotherapy, such as cognitive behavioural therapy, is an appropriate treatment for mood concerns following concussion and in individuals with PPCS (Potter & Brown, 2012), it has also been suggested that selective

serotonin reuptake inhibitors (SSRIs) may provide relief from mood disorder symptoms and that brain injury, particularly mTBI, is not a contraindication for SSRI treatment (Silverberg & Panenka, 2019). Importantly, Silverberg and Panenka (2019) note that pre-emptive treatment of mental health outcomes, whether it's pharmaceutical or psychotherapy, may improve psychological, cognitive, and somatic symptoms in brain injury patients.

It is appropriate to consider the role that psilocybin may play in managing these prominent and debilitating mental health concerns in athletes with concussions, and this role that psilocybin may play has been recently discussed as a necessary avenue of research (Walton & Liknaitzky, 2022). In a study examining treatment preferences in patients with TBI and depression, researchers found that 91% of respondents would be willing to participate in herbal or alternative medicine to treat their depression (Fann et al., 2009). While this study did not query athletes, these interests may broadly apply to those with concussion. Evidently, there is room to explore the use of PAT for athletes with PPCS given the frequency of mood disorders in this population. Furthermore, psilocybin has already been demonstrated to be effective in individuals with anxiety and depression in life-threatening cancer and treatment-resistant depression (Carhart-Harris et al., 2017; Davis et al., 2021; Doss et al., 2021; Griffiths et al., 2016; Gukasyan et al., 2022; Rootman et al., 2021; Ross et al., 2016). The overwhelmingly positive effects with respect to psychological functioning and reduced mood disorder symptoms

further highlights the importance of examining psilocybin's therapeutic potential in those with PPCS.

Psilocybin Usage in Athletes and Attitudes Towards Use

Limited research exists on the current prevalence of psychedelic, and particularly psilocybin, use in athletes across variable levels of competition (i.e., recreational, club, varsity, national, professional). While it is illegal to sell psilocybin in most countries around the world, possession of these substances is being decriminalized in some major countries in the world, most notably in some cities and states throughout the US (MacCallum et al., 2022). Currently, none of the classic psychedelics are restricted by the World Anti-Doping Agency Prohibited List (WADA, 2023); this means that athletes may use psychedelics and not be in violation of anti-doping regulations. However, various leagues may make exceptions and deem any substance as prohibited according to that league (U.S. Anti-Doping Agency, 2021). While research does not yet indicate that psilocybin has performance enhancing or impairing effects for athletes, this is an area of concern which may influence individual league regulation and is an area necessary to examine further. Anecdotally, current and former athletes across sports suggest that psilocybin is frequently used by athletes currently playing and those retired for mental health purposes (Walton & Liknaitzky, 2022). Nevertheless, current data is limited on psychedelic use in athletes; the only existing paper to document psychedelic use in athletes focused on National Collegiate Athletic Association (NCAA) athletes and identified the highest rates of psychedelic

use in division three athletes, with 6.6% reporting usage (Green et al., 2001). However, this report was produced during the early phases of the psychedelic renaissance and more recent prevalence rates are needed. Substance use research in athletes appears to have largely neglected to capture psychedelic use otherwise.

Essential to the examination and implementation of PAT in athletes are the attitudes about psilocybin and willingness to incorporate this therapy into concussion and PPCS recovery protocols. To date there is no research examining the sports community's knowledge of or attitudes towards psilocybin or the willingness to use psilocybin for concussion recovery. However, Walton and Liknaitzky (2022) previously recommended that researchers understand the views of sports professionals towards the use of psychedelics for mental health prior to initiating clinical research.

To guide the attitudes and willingness examination in this thesis, I will follow the Theory of Planned Behaviour put forth by Ajzen et al. (2011). This theory asserts that one's general knowledge regarding the subject at hand has been found to be an unreliable predictor of intentions and behaviours. In their theoretical approach, these authors identified that the greatest predictors include attitudes, perceived social pressure to either engage or disengage, and perceived behavioural control (or ability to engage). These authors define attitudes as the beliefs about the probable outcomes of a behaviour. For the purpose of this thesis, we can understand attitudes towards PAT for PPCS as the beliefs about the probable consequences associated with

the use of PAT in PPCS. Consequently, intentions (or willingness) to use depend upon these beliefs and the consideration of whether the use of psilocybin is linked to a positive or negative outcome. Perceived social pressure to either engage or disengage is likely to be related to one's religious affiliation, race/ethnicity, level of athletic competition, gender, age, and other social groups with which one identifies. Finally, perceived behavioural control is related to geographical location, sport role, level of athletic competition, concussion history, current psychedelic use, and other factors that one believes enable or inhibit their ability to engage with psilocybin therapy. Because psilocybin is still a regulated substance in Canada and the USA, it carries a negative stigma associated with its use and a general lack of legal accessibility. Therefore, it is necessary to query athletes and sports team personnel directly about their perspective on psilocybin for rehabilitative purposes to inform clinical research that intends to examine and potentially implement these treatment options. Gathering this information will provide an understanding of the interest in the use of psilocybin therapeutically and concerns regarding use from athletes, coaches, and other staff.

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Chapter Two: Psilocybin's Effects on Cognition and Creativity: A Scoping Review

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Author Note

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[1*] As second author, my role included development of the initial rendition of this chapter followed by critical feedback to Justin Bonnieux in the subsequent versions. Furthermore, I assisted Justin in collaborative resolution of feedback provided by additional authors. In total, I contributed 40% of the overall work dedicated to this review.

Psilocybin's effects on cognition and creativity: A scoping review

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Abstract

Background: Research on psilocybin has become increasingly popular during the current psychedelic renaissance, which began in the early 1990s. Psilocybin's effects on mental health are promising and there are ongoing efforts to investigate its clinical implementation and its effects on cognitive processes.

Aims: The purpose of this study is to report trends in publications, methods, and findings from research examining the effects of psilocybin on cognition and creativity in adults.

Methods: We conducted an Open Science Framework preregistered scoping review, guided by the JBI Manual for Evidence Synthesis, on literature pertaining to psilocybin's effects on cognition and creativity.

Results: In the 42 included studies, psilocybin was primarily administered orally (83%) in a bodyweight-adjusted manner (74%) to healthy participants (90%). Of the few studies that explicitly reported safety outcomes (26%), only one reported serious adverse reactions. During the acute phase post-intake (i.e., minutes to hours), macrodoses tended to impair cognitive performance and creativity, whereas microdoses tended toward creative enhancement. The few macrodosing studies that included post-acute measures (i.e., 1–85 days) reported primarily null but some positive effects.

Conclusions: This scoping review identified a time-based variation of psilocybin macrodosing effects on cognition and creativity, in which impairment may be observed early post-intake but withdraw over time, and some positive effects may emerge afterward. These findings are limited by methodological concerns and inadequate assessment of long-term effects. We therefore recommend that future psilocybin research be conducted according to existing guidelines and include well-validated measures of cognition and creativity at multiple timepoints.

Introduction

Overview

Psychedelics elicit unique states of consciousness characterized by altered sensation, perception, cognition, and sense of self (Johnson et al., 2019; Nichols, 2016). There are two main groups of psychedelics: classic psychedelics which are serotonin 2A receptor (5-HT_{2A}R) agonists and non-classic psychedelics which have other varied mechanisms of action (Carhart-Harris et al., 2014; Mendes et al., 2022). Classic psychedelics include lysergic acid diethylamide (LSD), N,N-dimethyltryptamine (DMT), 5-Methoxy-N,N-dimethyltryptamine (5-MeO-DMT), mescaline, and psilocybin, which is the focus of this scoping review (Johnson et al., 2019; Lowe et al., 2021).

Psilocybin occurs naturally in over 200 species of fungi primarily of the genus *Psilocybe* (Nichols, 2020; Van Court et al., 2022). *Psilocybe* mushrooms, commonly referred to as "magic mushrooms," have been used by cultures around the world for thousands of years (Lowe et al., 2021; Nichols, 2020; Van Court et al., 2022). For example, Aztecs used them in healing rituals and religious ceremonies and ancient Hindu texts suggest their use in the ritualistic sacrament "soma" (Carod-Artal, 2015; Johnson et al., 2019; Nichols, 2020). Psilocybin is therefore considered an entheogen due to its use in mystical and religious contexts (Carod-Artal, 2015). While it is clear that psilocybin use spans millennia, its prevalence prior to the 20th century remains unknown (Johnson et al., 2019).

Scientific research into psychedelics began in the late 19th century and accelerated following Swiss chemist Albert Hofmann's discovery of LSD's psychedelic properties in 1943 (Hofmann, 2013; Johnson et al., 2019). It then expanded to include psilocybin after American amateur mycologist Gordon Wasson's experiences with psilocybin mushrooms in the Sierra

Mazateca of Mexico were published in 1957, sparking widespread public interest (Johnson et al., 2019). This research flourished until 1970 when psychedelics became regulated under the most restrictive schedule (schedule 1) of the United States Controlled Substances Act and, subsequently, under similar schedules worldwide (Belouin and Henningfield, 2018). These stringent regulations prompted an approximately 25-year period of limited advancement in psychedelic research (Belouin and Henningfield, 2018; Johnson et al., 2018).

Renaissance

After decades of considerable limitation, researchers once again obtained approval to administer psychedelics to humans in 1990 (Strassman, 1991, 1995), a year which also marks the beginning of a distinct increase in psychedelic publications more broadly (Solmi et al., 2022). Despite this, the first publication for a psychedelic trial in humans during this period did not appear until 1994 (Hadar et al., 2023; Strassman and Qualls, 1994), thus marking the beginning of the current "psychedelic renaissance" for the purposes of this review. Although the first human trial specifically involving psilocybin during this period was not published until 1996 (Spitzer et al., 1996), we chose 1994 as a start date to facilitate comparison with other psychedelic reviews (Bălăeţ, 2022; Sayalı and Barrett, 2023).

At the forefront of this renaissance is psilocybin (Lowe et al., 2021). While similar to other psychedelics in its psychological effects, its half-life of roughly 163 minutes upon oral ingestion is uniquely convenient (Passie et al., 2002; Swanson, 2018). In contrast, other psychedelics like LSD (roughly 306-minute half-life) and 5-MeO-DMT (roughly 16-minute half-life) produce experiences that are either too long-lasting or too brief for many clinical and research contexts (Barsuglia et al., 2018; Dolder et al., 2017). Furthermore, psilocybin has a relatively favorable safety profile (Hendricks et al., 2015; Lowe et al., 2021) and often carries less stigma than other

psychedelics such as LSD (Belouin and Henningfield, 2018; Fuentes et al., 2020). Recent findings have demonstrated psilocybin's promise for treating depression and anxiety in patients with life-threatening cancer (Griffiths et al., 2016), treatment-resistant major depressive disorder (Davis et al., 2021; Goodwin et al., 2023), and substance addiction (Bogenschutz et al., 2015, 2022; Johnson et al., 2017), even though these findings have been criticized due to small sample sizes and a paucity of long-term outcome measures.

Mechanisms of action

Serotonin (5-HT) is an important neurotransmitter that binds to cell membrane receptors to produce wide-ranging effects throughout the central nervous system (López-Giménez and González-Maeso, 2018). Upon ingestion, psilocybin is dephosphorylated into the psychoactive metabolite psilocin which is structurally similar to serotonin (see Figure 1; Nichols, 2020). It is this structural similarity that allows psilocin, like other classic psychedelics, to bind serotonin receptors and subsequently alter consciousness (Dinis-Oliveira, 2017). The prefrontal cortex, a brain region implicated in higher-order cognition including executive functions like planning, inhibiting, and problem-solving (Garcia-Barrera, 2019), has especially high concentrations of both 5-HT1A receptors, generally considered inhibitory, and 5-HT2A receptors, generally considered excitatory (Puig and Gulledge, 2011). Psilocin's psychedelic effects are primarily a result of it binding to the 5-HT2A receptor on neurons, thereby triggering increases in brain activity (Vollenweider and Kometer, 2010; Vollenweider et al., 1998) and network connectivity (Daws et al., 2022; Doss et al., 2021). However, recent work has emphasized the importance of non-neuronal brain cells, primarily microglia, in psilocin's cellular mechanism of action (Tay et al., 2017; VanderZwaag et al., 2023).Psilocin has no direct effect on dopaminergic systems and therefore lacks the reinforcement mechanisms necessary for dependence to occur (Nichols, 2016;

Dinis-Oliveira, 2017; Bienemann *et al.*, 2020). Furthermore, psilocybin is physiologically safe given its low toxicity and low risk of overdose – a lethal dose is estimated to be 1000 times greater than an effective dose (Gable, 2004). Despite this, "bad trips" (i.e., episodes characterized by intense negative emotions) remain a concern and can lead to dangerous behaviours. These types of experiences are most likely to occur when individuals are either not mentally prepared or are in a poorly controlled environment (Johnson, Richards and Griffiths, 2008; Pilecki *et al.*, 2021). Safety guidelines for clinical research involving hallucinogens outline precautions to minimize these risks (Johnson, Richards and Griffiths, 2008).

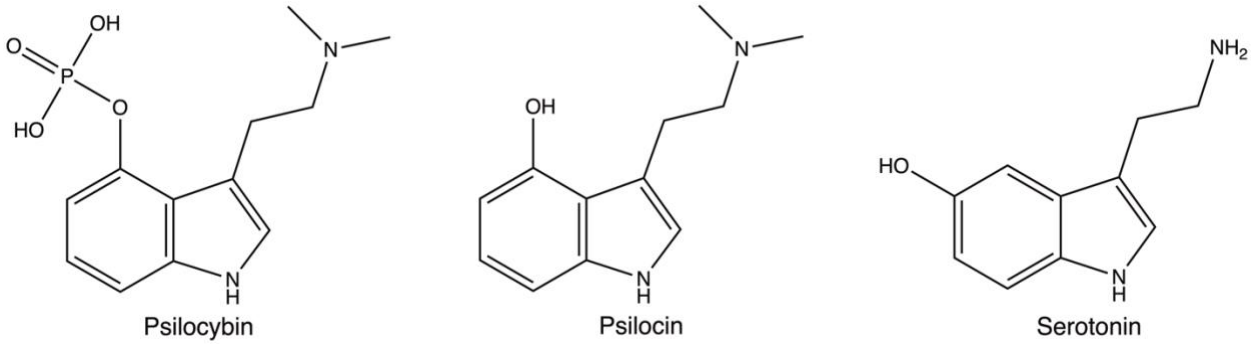

Figure 1. Chemical structures of psilocybin, psilocin, and serotonin. This figure was created using ChemDraw Prime software. Professional. Version 21.0.0.28. PerkinElmer Informatics, Inc © 1985-2022.

Psilocin has no direct effect on dopaminergic systems and therefore lacks the reinforcement mechanisms necessary for dependence to occur (Bienemann et al., 2020; Dinis-Oliveira, 2017; Nichols, 2016). Furthermore, psilocin is physiologically safe given its low toxicity and low risk of overdose—a lethal dose is estimated to be 1000 times greater than an effective dose (Gable, 2004). Despite this, "bad trips" (i.e., episodes characterized by intense negative emotions) remain a concern and can lead to dangerous behaviors. However, these types of experiences are most likely to occur when individuals are either not mentally prepared or are

in a poorly controlled environment (Johnson et al., 2008; Pilecki et al., 2021) and can be managed by following safety guidelines for clinical research involving hallucinogens (Johnson et al., 2008).

Cognition and creativity

Cognition is acutely altered by hallucinogenic "macrodoses" of psilocybin, typically ranging from ~130 µg/kg ("low-dose") to ~370 µg/kg ("high-dose") when taken orally (Barrett et al., 2018; Vollenweider et al., 2007), even though recent research suggests that adjusting doses by bodyweight is unnecessary (Garcia-Romeu et al., 2021). While Doss et al.'s (2021) open-label study in patients with major depressive disorder found improvements in cognitive flexibility 4 weeks post-psilocybin therapy, a recent double-blind, randomized, placebo-controlled study in healthy participants found no changes in cognition at 8, 29, or 85 days post-psilocybin therapy (Rucker et al., 2022). Contradictory findings such as these contribute to ongoing controversy regarding the long-term effects of psilocybin on cognition.

Psilocybin can also be taken in very low, sub-hallucinogenic "microdoses," typically ranging from ~100 mg to ~500 mg of dried mushrooms (of variable potency) taken orally, or about one-tenth to one-twentieth of a macrodose (Anderson et al., 2019; Kuypers et al., 2019; Polito and Stevenson, 2019). Anecdotal reports claim that microdosing psilocybin has many benefits including enhanced cognition and creativity (Lea et al., 2020), even though findings from research on this topic are mixed (Cavanna et al., 2022; Marschall et al., 2022; Rootman et al., 2021; Szigeti et al., 2021).

Although current psychiatric drugs often alleviate symptoms such as depression and anxiety, they seldom improve and sometimes impair cognition, as observed with selective serotonin re-uptake inhibitors in patients with depression (Millan, 2006; Millan et al., 2012).

Psilocybin studies showing improvements in psychiatric symptoms largely fail to consider its effects on cognition, even when assessing its use in populations with known cognitive impairments (Bogenschutz et al., 2015; Davis et al., 2021; Griffiths et al., 2016; Johnson et al., 2017). It is therefore unclear whether improved symptoms coincide with cognitive enhancement, impairment, or null cognitive effects. Measuring cognitive performance in clinical studies will not only improve our understanding of how psilocybin affects disease processes, but it will also guide us toward identifying new target populations. Furthermore, for clinicians who intend to engage in psychedelic-assisted therapy, knowledge of acute versus long-term cognitive outcomes will be important in guiding treatment decisions.

While researchers are increasingly incorporating measures of cognitive performance and creativity in psilocybin studies, we are unaware of any publications that synthesize these findings. Therefore, this scoping review presents trends in publications, methods, and findings from records published since 1994 (i.e., the beginning of the current psychedelic renaissance) that measure cognitive performance and/or creativity after psilocybin administration in adults.

Methods

Protocol and registration

This scoping review was conducted according to the JBI Manual for Evidence Synthesis: Scoping Review chapter (Peters et al., 2020) and is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021; Tricco et al., 2018). The review protocol was registered (Bonnieux et al., 2021) with Open Science Framework prior to its execution, which proceeded as planned except for adjustments to eligibility criteria.

Eligibility criteria

Inclusion criteria were studies published in English, French, or Spanish (i.e., languages known by the authors); studies published since 1994 (i.e., the beginning of the current psychedelic renaissance); empirical studies; studies limited to adult human participants; studies in which participants ingest psilocybin; studies in which one or more measure(s) of participants' cognitive performance/creativity is/are reported, and/or participants' subjective perceptions of their cognitive performance/creativity are reported, and/or participants' brain activity in response to cognitive performance/creativity task(s) is reported. Exclusion criteria were non-empirical studies (e.g., reviews, meta-analyses); animal studies; studies in which measure(s) of participants' cognition is/are not related to cognitive performance (e.g., changes in mood); studies in which participants' subjective perceptions of cognition are not related to cognitive performance (e.g., experiences of ego dissolution); studies in which participants' brain activity is not in response to a cognitive performance/creativity task (e.g., resting-state functional connectivity).

Search strategy

The following electronic databases were systematically searched on February 21, 2023 for records published since January 1, 1994: APA PsycINFO (EBSCOhost), MEDLINE (Ovid), Cochrane Central Register of Controlled Trials (Ovid), and Web of Science Core Collection (Clarivate). We developed a 2-concept comprehensive search in APA PsycINFO based on an analysis of a known set of articles on the topic. The two main concepts searched were psilocybin (intervention) and cognition/creativity (outcomes). The comprehensive search incorporated subject headings and keywords in addition to available database operators and Boolean operators

to enhance sensitivity. The APA PsycINFO search was first tested against a known set of studies before being translated to the other databases. The searches were developed by one author (JNB) and peer reviewed by another author (ZP), a librarian with expertise in evidence synthesis methods. See Supplemental Materials for the list of database segments queried in the Web of Science Core Collection and the search strategies as executed in each of the above databases.

Supplementary searches last performed on March 3, 2023 involved reviewing included studies' cited references and citing references using Google Scholar; searching for gray literature such as conference proceedings, dissertations, and theses; searching selected organizations' websites; and doing an incognito Google search. See Supplemental Materials for a comprehensive list of the resources consulted in the supplementary searches.

Article selection process

Electronic database search results were imported into Covidence systematic review management software (Covidence Systematic Review Software, 2021). In Covidence, duplicates were removed automatically. Titles and abstracts of the remaining records were screened for their relevance (see eligibility criteria above) by two authors (JNB and BV) independently. A third author (MGB) was then consulted to resolve disagreements. The full texts of the remaining records were reviewed for inclusion by the same two authors independently. The same third author was again consulted to resolve disagreements. Finally, supplementary searches were performed by a single author (either JNB or BV) to identify additional records for inclusion.

Data extraction

A data extraction form was developed to extract the following information from each included report: study name, year of publication, publication type, journal of publication,

authors, author affiliations, study design, sample size (placebo and psilocybin conditions only), participant characteristics, dosage and intake protocols, pre-intake protocols, acute phase protocols, post-acute phase protocols, study environment, intake to assessment intervals, assessment tools, neuroimaging methods, adverse effects reported, outcome directions, effect sizes, and funding sources and disclosures. Two authors (JNB and BV) used this form to complete the data extraction independently. Three authors (JNB, BV, and MGB) joined a working session to resolve inconsistencies between the two sets of extracted data.

Critical appraisal

Given that research examining the effects of psilocybin on cognitive performance and creativity has both mixed findings and mixed methodologies, our research team deemed it appropriate to critically appraise each of the 42 included reports using the 2018 version of the Mixed Methods Appraisal Tool (MMAT; Hong et al., 2018). First, two authors (JNB and BV) independently classified each report into one of the following five study design categories: qualitative research, randomized controlled trials (RCTs), non-randomized studies, quantitative descriptive studies, and mixed methods studies. Then, the same two authors met with a third (MGB) to resolve classification disagreements. Next, the same two authors independently rated each report on five quality criteria which varied depending on the report's study design classification. Responses for each criterion are either "yes" meets criterion, "no" does not meet criterion, or "can't tell" because appropriate information is missing. Lastly, the same three authors met to resolve disagreements in quality criteria ratings. Consistent with the MMAT authors' recommendation, no overall MMAT scores were calculated (Hong et al., 2018). Instead, a synthesis of the methodological concerns identified by the critical appraisal is presented in the Results section of this paper.

Data synthesis

Research into the effects of psilocybin on cognitive performance and creativity was characterized using the following data synthesis methods. First, we presented the timeline of publications using a cumulative frequency distribution. Second, we showed the institutions involved in research on this topic, the extent of their contributions, and the inter-institutional connections using a network analysis. Third, we presented the methodological characteristics of each report including psilocybin dosage and intake protocols. Finally, we synthesized findings from behavioral and subjective measures and extracted general themes from neuroimaging findings.

Statistically significant differences between psilocybin and baseline/placebo conditions were classified as either positive or negative findings depending on whether they reflected cognitive/creative enhancement or impairment. Nonsignificant differences between conditions were classified as neutral findings. Each finding was grouped into one of six categories based on the construct being measured. For instance, attention and vigilance were classified as foundational cognitive processes (e.g., Psychomotor Vigilance and Attentional Blink Tasks), inhibition and working memory as lower order cognitive processes (e.g., Digit Symbol Substitution and Trail Making Tests), planning and fluid intelligence as higher-order cognitive processes (e.g., Tower Test and Raven's Progressive Matrices), empathy and reactions to affective stimuli as social cognitive processes (e.g., Multifaceted Empathy Test and Ultimatum Game), convergent and divergent thinking as creative processes (e.g., Picture Concept and Alternate Uses Tasks), and self-reported changes in cognition as subjective findings (e.g., Visual Analog Scale [Concentration and Creative subscales], and the Five Dimensional Altered States of Consciousness Scale [Impaired Control and Cognition subscale]). Guided by categorizations

of both cognitive (Nigg, 2017) and creative (Kuypers et al., 2016) processes in the literature, all classifications were discussed until consensus was reached among three authors (JNB, BV, and MGB). Moreover, findings were characterized as having been measured during acute drug effects or after acute effects had subsided (post-acute).

Results

Included articles

1253 results were identified by the electronic database searches and 516 were removed as duplicates by Covidence (Covidence Systematic Review Software, 2021). The remaining 737 records were screened with an inter-rater agreement of 85% and Cohen's kappa of 0.56. Of the 129 records considered to be relevant, three (Ort et al., 2018; Paulus and Vollenweider, 2006; Vollenweider et al., 2006) could not be retrieved despite attempts to contact the authors via email. The remaining 126 full-text articles were reviewed for inclusion and interrater agreement was 78% with a Cohen's kappa of 0.52. Supplementary searches identified an additional 25 records of interest. After screening, seven of these were considered relevant and were sought for retrieval. Three of these had already been identified in the main database searches, leaving four to be added to the final list of included studies. A total of 42 reports were included in the review. The PRISMA flow diagram shown in Figure 2 summarizes each step of the search process. See Supplemental Materials for the full list of included reports.

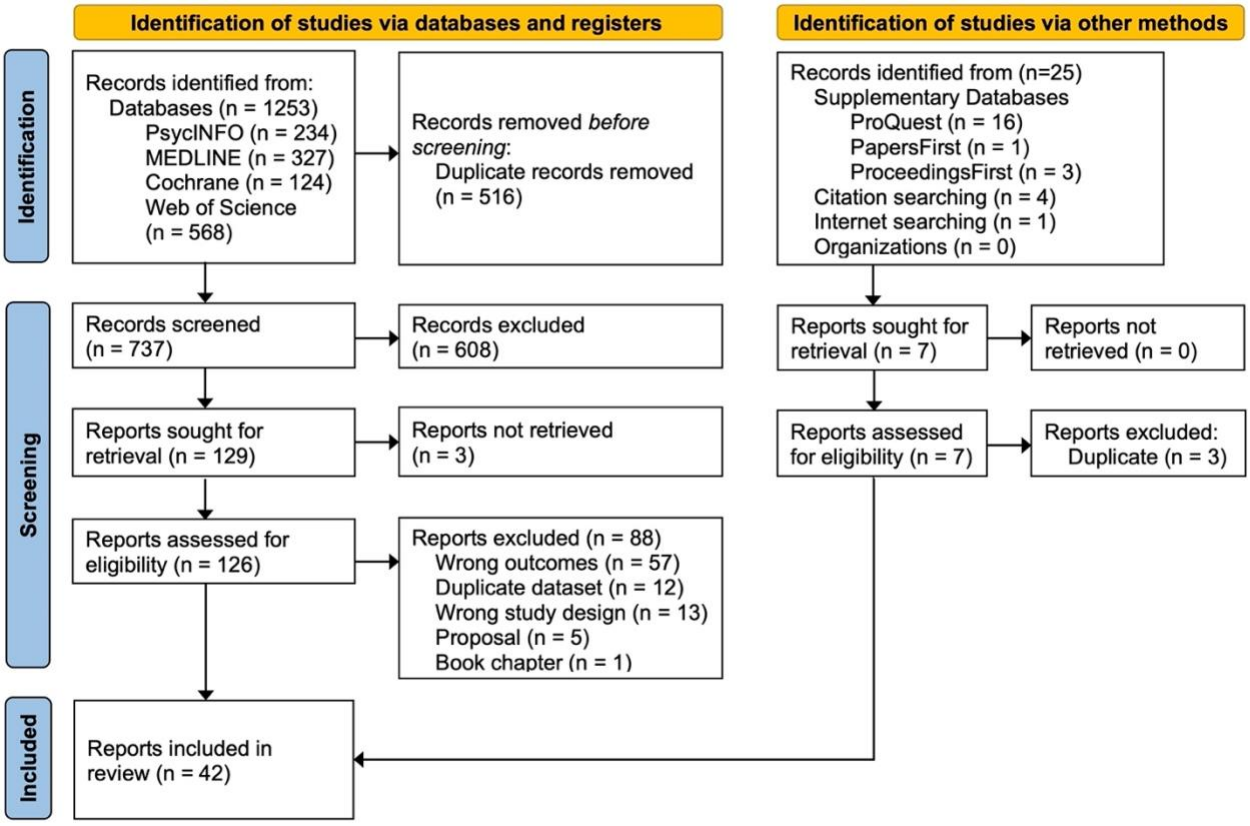

Figure 2. Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram.

Publication Timeline

Figure 3 shows the progression of publications from the first report meeting our eligibility requirements in 1996 to the 42nd in 2023. Major milestones in the broader psychedelic renaissance were added to provide additional context.

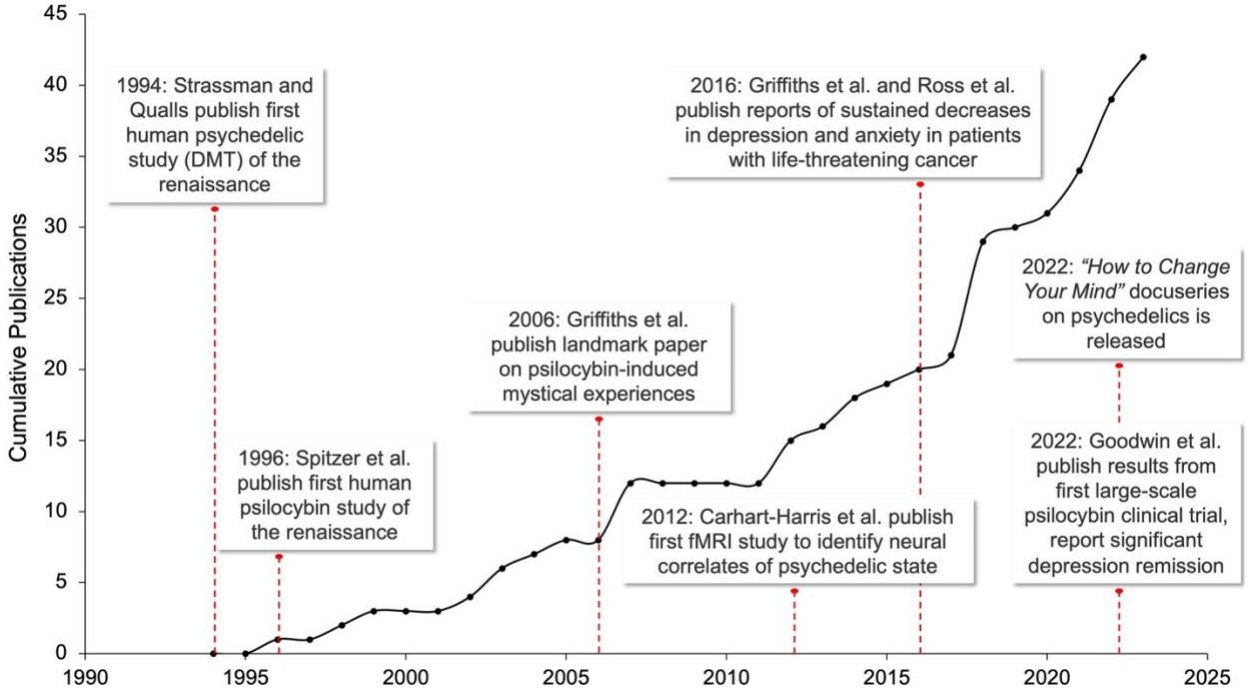

Figure 3. Publication timeline of included reports. Major milestones in the broader psychedelic renaissance were added to the figure using the following citations: Strassman and Qualls (1994), Spitzer et al. (1996), Griffiths et al. (2006), Carhart-Harris et al. (2012a), Griffiths et al. (2016), Goodwin et al. (2022), and Michael Pollan on the Psychedelic Renaissance and Netflix's New 'How to Change Your Mind' Documentary (Law, 2022).

Research institutions

The authors of the included reports were affiliated with a total of 87 institutions, as shown in Figure 4. Of these, Psychiatric University Hospital, Zürich, contributing to 31% of the included reports, and Heffter Research Center, Zürich, contributing to 19%, are the most prolific and their collaboration on 17% of the reports also makes them the most interconnected. These two institutions were especially productive in the beginning of the renaissance, with publications spanning from 1998 to 2022. Other institutions with notable involvement include Johns Hopkins University School of Medicine and University of California San Diego, each contributing to 10%

of the included reports. Geographically, institutions from the European Union are the most highly represented (n = 77) followed by the United Kingdom (n = 31), North America (n = 26), South America (n = 4), and Australia (n = 4).

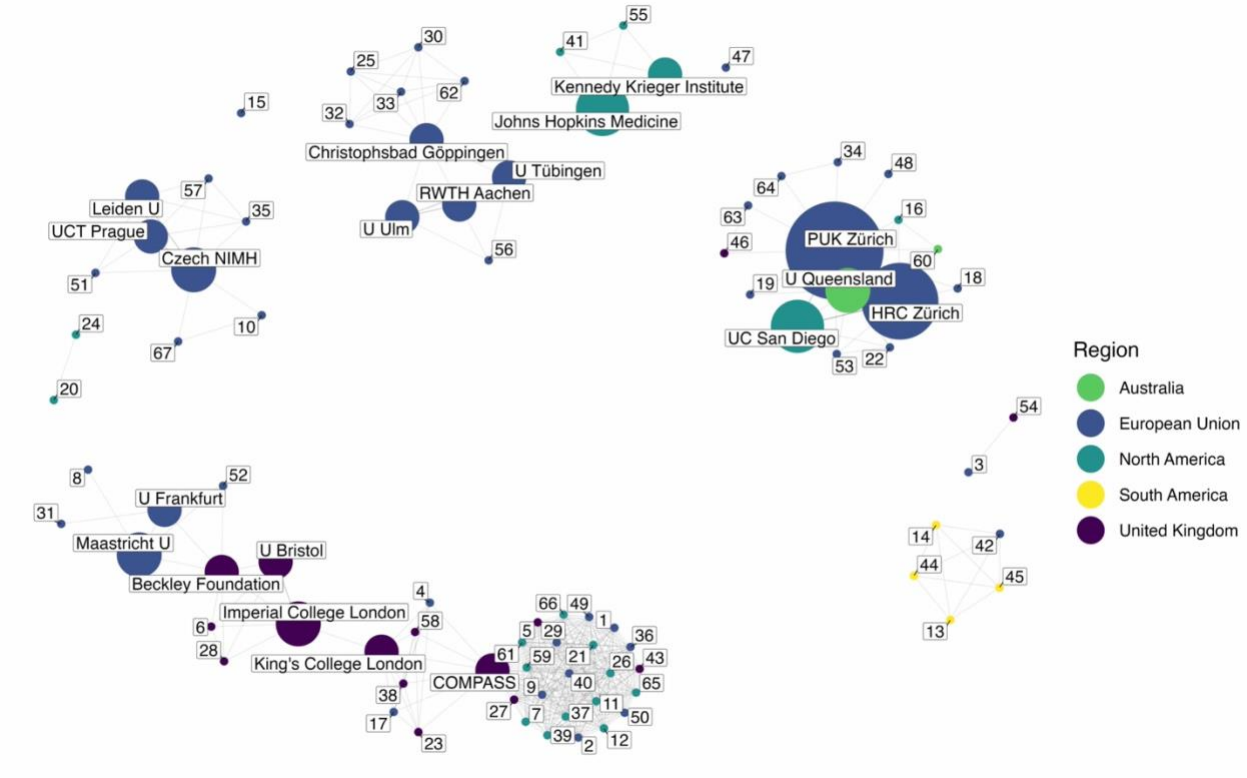

Figure 4. Network representing institutional affiliations (nodes) of included reports and their inter-connections (edges). Network was created in RStudio version 2021.09.0 using the Kamada-Kawai algorithm and the following R packages: psych (William Revelle), tidygraph (Thomas Lin Pedersen), tidyverse (Hadley Wickham), ggraph (Thomas Lin Pedersen), igraph (Gabor Csardi & Tamas Nepusz). See Supplemental Materials for the full institution names corresponding to the labels in the figure.

Study characteristics

90% of the reports included only healthy participants (three of which included only physicians and/or psychologists; Gouzoulis-Mayfrank et al., 1999, 2002; Spitzer et al., 1996), 7% included participants with major depressive disorder (Doss et al., 2021; Goodwin et al., 2023; von Rotz et al., 2023), and 2% included treatment-seeking smokers (McKenna et al., 2018). Sample sizes ranged from 8 to 233 participants (median = 20). 79% used a within-participant design, 10% used a between-participant design, and 12% used a mixed design. 83% included a placebo condition while 17% did not. 83% included at least one objective measure of cognitive performance and/or creativity while 17% included only subjective measures. 81% included only acute measures, 12% included only post-acute measures (ranging 1–85 days post-psilocybin administration), and 7% included both. Psilocybin administration protocols and dosages are presented in Table 1.

Table 1. *Methodological characteristics of included reports*

Report	Type of Report	Administration	Psilocybin Dosage
Barrett *et al.*, 2018	Journal Article	Oral	10 mg/70 kg (low), 20 mg/70 kg (medium), 30 mg/70 kg (high)
Barrett *et al.*, 2020	Journal Article	Oral	25 mg/70 kg (high)
Bernasconi *et al.*, 2014	Journal Article	Oral	170 µg/kg
Bravermanová *et al.*, 2018	Journal Article	Oral	~0.26 mg/kg (higher intermediate)
Cahn, 2007	Dissertation	Oral	125 µg/kg, 250 µg/kg

Carbonaro *et al.*, 2018	Journal Article	Oral	10 mg/70 kg, 20 mg/70 kg, 30 mg/70 kg
Carhart-Harris *et al.*, 2012	Journal Article	Intravenous	2 mg
Carter *et al.*, 2005	Journal Article	Oral	215 µg/kg
Carter *et al.*, 2007	Journal Article	Oral	215 µg/kg
Cavanna *et al.*, 2022	Journal Article	Oral	0.5 mg dried mushrooms (upper range microdose)
Doss *et al.*, 2021	Journal Article	Oral	20 mg/70 kg (moderately high), 30 mg/70 kg (high)
Duerler *et al.*, 2022	Journal Article	Oral	0.2 mg/kg
Gabay *et al.*, 2018	Journal Article	Intravenous	2 mg
Goodwin *et al.*, 2023	Journal Article	Unspecified	1 mg (control), 10mg, 25mg
Gouzoulis-Mayfrank *et al.*, 1999	Journal Article	Oral	0.2 mg/kg (up to a maximum of 15mg)
Gouzoulis-Mayfrank *et al.*, 2002	Journal Article	Oral	0.2 mg/kg (up to a maximum of 15mg)
Grimm *et al.*, 2016	Conference Abstract	Oral	0.16 mg/kg
Hasler *et al.*, 2003	Conference Abstract	Oral	45 µg/kg (very low), 115 µg/kg (low), 215 µg/kg (medium), 315 µg/kg (high)

Hasler *et al.*, 2004	Journal Article	Oral	45 µg/kg (very low), 115 µg/kg (low), 215 µg/kg (medium), 315 µg/kg (high)
Holze *et al.*, 2022	Journal Article	Oral	15 mg, 30mg
Kometer *et al.*, 2012	Journal Article	Unspecified	215 µg/kg
Kraehenmann *et al.*, 2015	Journal Article	Oral	0.16 mg/kg
Mallaroni *et al.*, 2023	Preprint	Oral	15 mg
Mason and Kuypers, 2018	Conference Abstract	Unspecified	0.17 mg/kg
Mason *et al.*, 2019	Journal Article	Oral	Average of 34.2 (SD 8.9) grams of truffles throughout the day (equivalent to 27.1 mg psilocin)
Mason *et al.*, 2021	Journal Article	Oral	0.17 mg/kg
McKenna *et al.*, 2018	Conference Abstract	Unspecified	30 mg/70 kg
Pokorny *et al.*, 2017	Journal Article	Oral	0.215 ug/kg
Prochazkova *et al.*, 2018	Journal Article	Oral	0.22g, 0.33g, 0.44g dried truffles
Prochazkova *et al.*, 2021	Preprint	Oral	~0.65g fresh truffles (low range microdose),

			~1g fresh truffles (mid-range microdose), ~1.5g fresh truffles (high range microdose)
Quednow *et al.*, 2012	Journal Article	Oral	260 µg/kg
Rucker *et al.*, 2022	Journal Article	Oral	10 mg, 25 mg
Schmidt *et al.*, 2012	Journal Article	Oral	115 µg/kg
Schmidt *et al.*, 2013	Journal Article	Oral	115 µg/kg
Spitzer *et al.*, 1996	Journal Article	Oral	0.2 mg/kg
Turton, Nutt and Carhart-Harris, 2014	Journal Article	Intravenous	2 mg
Umbricht *et al.*, 2003	Journal Article	Oral	0.28 mg/kg
Viktorin *et al.*, 2022	Journal Article	Oral	0.26 mg/kg
Vollenweider *et al.*, 1998	Journal Article	Oral	0.25 mg/kg
Vollenweider *et al.*, 2007	Journal Article	Oral	115 µg/kg, 215 µg/kg, 315 µg/kg
von Rotz *et al.*, 2023	Journal Article	Oral	0.215 mg/kg
Wittmann *et al.*, 2007	Journal Article	Oral	115 µg/kg (medium), 250 µg/kg (high)

Eighty-three percent of the reports indicated that participants were blinded to condition. Of these, only four (12%) assessed blinding integrity (i.e., whether participants were able to guess

which condition they had been assigned to) and, of these four reports, only one indicated that blinding was successful. Four additional reports (12%) commented on the importance of examining blinding integrity but did not assess it, noting this as a limitation.

Seventy-four percent of the reports made no mention of adverse outcomes, 12% reported no adverse outcomes, and 14% reported some adverse outcomes. Of the six studies (14%) that reported adverse outcomes, only one classified any as serious (Goodwin et al., 2023). These serious adverse outcomes occurred in 5% of participants with treatment-resistant depression and included suicidal ideation and intentional self-injury. Commonly reported non-serious adverse outcomes included headache, insomnia, and anxiety.

Critical appraisal

The full critical appraisal using the MMAT is presented in Supplemental Materials. Of the 42 included reports, 23 presented quantitative non-randomized studies, 18 were quantitative RCTs, and 1 was a qualitative study (Turton et al., 2014). There were several methodological concerns raised during the appraisal. Of the 23 quantitative non-randomized studies, just over half (n = 12) clearly demonstrated that participants were representative of the target population. Moreover, many (n = 9) failed to clearly demonstrate that they adequately accounted for confounds in their design and analysis. Of the 18 quantitative RCTs, 1 study did not perform appropriate randomization to groups and a majority (n = 10) failed to provide adequate information to determine if this was the case. Furthermore, two did not clearly demonstrate that outcome assessors were blind to the intervention provided. Lastly, a majority (n = 10) failed to provide adequate information to determine if groups were comparable in outcome measures at baseline.

Synthesis of results

A total of 254 findings (208 acute and 46 post-acute) from behavioral and subjective measures of cognitive performance and creativity were extracted from the 42 included reports. Acute effects on cognition and creativity were primarily negative (49%) and neutral (46%) as opposed to positive (5%). However, the 18 acute findings that assessed creativity following microdoses were exclusively neutral (67%) or positive (33%). Similarly, post-acute effects on cognition and creativity were most often neutral (72%) or positive (22%) and seldom negative (6%).

Figure 5 visualizes the dose–response relationship of the 200 behavioral findings (154 acute and 46 post-acute) that were compatible with this analysis: 2 positive, 4 neutral, and 22 negative acute findings were excluded because they were from subjective measures; 1 negative acute finding was excluded because it followed intravenous psilocybin administration thereby making dosage comparison with oral administration meaningless; and 18 neutral and 7 negative acute findings were excluded because they lacked adequate dosage information. Overall, the excluded acute findings were primarily negative (56%) and neutral (41%) as opposed to positive (4%), thus demonstrating a pattern of outcomes that is consistent with those included in the figure.

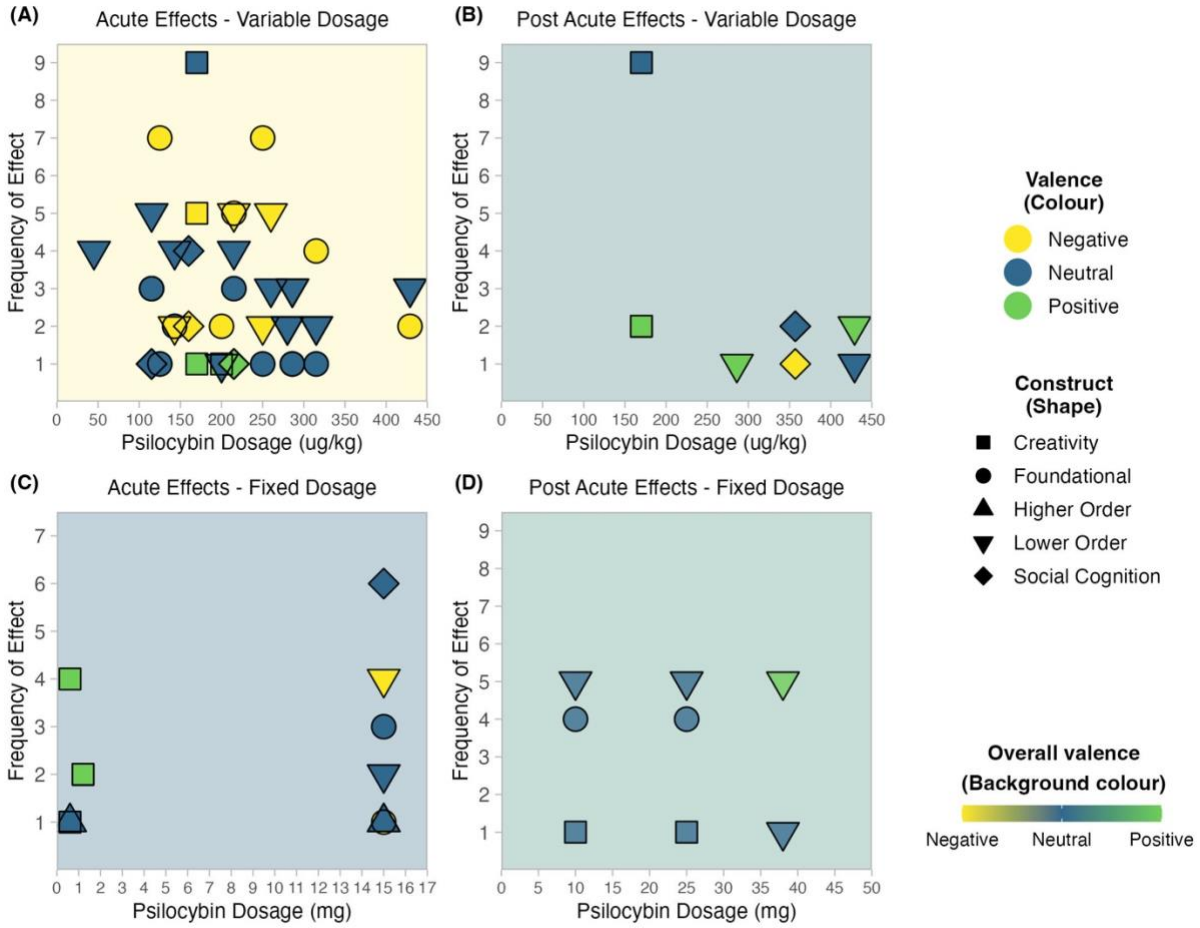

Figure 5. Cognitive performance and creativity outcomes according to psilocybin dosage. This figure contains four scatter plots showing cognitive performance and creativity outcomes measured during acute drug intoxication (plots a and c) or during post-acute phases (plots b and d). The horizontal X-axis shows psilocybin dosage administered in either a bodyweight-adjusted manner represented in µg/kg (plots a and b) or a fixed manner represented in mg (plots c and d). The vertical Y-axis shows the frequency of the reported outcome. The valence of each finding (negative, neutral, or positive) is indicated by the shape's color, and its corresponding construct (foundational, lower order, higher-order, social cognitive, or creative processes) is indicated by the type of shape. The overall valence of each plot was determined by subtracting negative from positive findings and dividing this by the total number of findings; the result of this equation was

used to create a background color. The plot was created in RStudio version 2021.09.0 using the following R packages: tidyverse, xlsx, psych, ggrepel, viridis, ggpubr, cowplot, and grDevices.

Effect sizes were reported in four (10%) of the included publications (Mallaroni et al., 2023; Mason et al., 2021; Prochazkova et al., 2018; Vollenweider et al., 2007). Mallaroni et al. (2023) reported the following significant negative outcomes with large effect sizes during the acute phase following a 15-mg psilocybin macrodose: increased reaction time on the Tower of London Test (a measure of higher-order executive function; d = 1.8), decreased correct (d = 1.45) and total (d = 1.5) responses on the Digit Symbol Substitution Test (a measure of lower order executive function), decreased correct responses on the Spatial Memory Test (a measure of lower order executive function) both immediately (d = 1.34) and 30 minutes (d = 1.43) following administration, increased reaction time on the Psychomotor Vigilance Task (a measure of foundational cognitive function; d = 0.81), and increased ratings of "impaired control and cognition" (a subjective measure of cognitive function; d = 1.93) on the Five Dimensional Altered States of Consciousness (5D-ASC) scale. Mason et al. (2021) reported significant impairments with large effect sizes during the acute phase following a 0.17 mg/kg psilocybin macrodose for the fluency measure (d = 0.80) on the Alternate Uses Task, and the fluency (d = 0.84) and convergent (d = 0.85) measures on the Picture Concept Task, and significant impairment with a medium effect size for the originality measure (d = 0.65) on the Picture Concept Task (all measures of creativity). The same study found that at 7-day follow-up, psilocybin resulted in significant impairment with a medium effect size for the convergent measure on the Picture Concept Task (d = 0.60) and significant enhancement with a medium effect size for the novel measure on the Alternate Uses Task (d = 0.52). Prochazkova et al. (2018) reported that approximately 90 minutes after taking a microdose of psilocybin, the

number of correct responses on the Picture Concept Task was significantly improved with a medium effect size (d = 0.49). Finally, Vollenweider et al. (2007) reported a dose-dependent pattern of significant negative acute effects of psilocybin macrodoses on Frankfurt Attention Inventory (FAIR; a measure of foundational cognitive processes) performance. This included large negative effects on performance capacity (FAIR P) scores after low (d = 1.03), medium (d = 1.27), and high (d = 1.17) doses, large negative effects on continuity of performance (FAIR C) scores after low (d = 0.86), medium (d = 1.13), and high (d = 1.13) doses, and large negative effects on performance quality (FAIR Q) scores after high doses of psilocybin (d = 0.95).

Eleven studies (26%) reported neuroimaging findings related to cognitive performance and creativity tasks. Five of these studies used electroencephalography (EEG) including examination of event-related potentials (ERPs), five used functional magnetic resonance imaging (fMRI), and one used positron emission tomography (PET). One common neuroimaging finding was that psilocybin decreased amygdala activation in response to emotional stimuli, as reported in three separate fMRI studies (Barrett et al., 2020; Grimm et al., 2016; Kraehenmann et al., 2015). Another common finding was that psilocybin acutely decreased task-induced P300 ERP amplitude (Bravermanová et al., 2018; Cahn, 2007; Kometer et al., 2012), with one study demonstrating that lower amplitudes were correlated with higher serum psilocin levels (Bravermanová et al., 2018). Psilocybin was also found to acutely decrease the following ERP amplitudes: N170 (Cahn, 2007; Schmidt et al., 2013), N100 (Cahn, 2007), and N200 (Kometer et al., 2012).

Discussion

Given that the current psychedelic renaissance has emerged from a period of stringent regulations, it is unsurprising that publications were scarce at first (Pilecki et al., 2021). Despite

this, research into the effects of psilocybin on cognition and creativity is on the rise, with half of the reports in this review being published since 2018. Compared to other topics like mental health, cognition remains understudied in the field of psychedelics; therefore, the relatively small number of studies included in this review represents a niche and novel sub-field within psychedelic research which offers important insight into psilocybin's clinical utility.

While regulatory bodies in the United States and Europe began approving psychedelic research in the early 1990s, European institutions like Psychiatric University Hospital Zürich and Heffter Research Center Zürich were unique in their inclusion of cognitive outcome measures during this period (Strassman, 1995). Over time, the list of contributing institutions has greatly expanded with notable involvement from Johns Hopkins University School of Medicine and University of California San Diego. As interest in this research grows and barriers to its conduct are removed, new opportunities for collaboration are bound to arise.

Unlike prior epochs which relied heavily on anecdotal evidence, the current psychedelic renaissance is characterized by more rigorous and reliable research methods (Sessa, 2012). This is reflected in our critical appraisal which identified nearly all of the included reports as quantitative, including 15 double-blind, randomized, placebo-controlled trials. Despite this, maintaining blinding with respect to drug condition represents an ongoing challenge for research with psychedelics due to their pronounced psychoactive effects (Muthukumaraswamy et al., 2021; Schenberg, 2021). While the majority (83%) of included reports had participants blinded to condition, only a small minority (12%) assessed blinding integrity (i.e., whether participants were able to guess which condition they had been assigned to), making it impossible to rule out placebo effects in most cases. Moreover, most studies were conducted with small samples

consisting entirely of healthy participants (90%), thereby limiting the conclusions that can be drawn as well as their generalizability to clinical populations.

Inconsistent psilocybin dosage and intake protocols represented an additional challenge for comparison across studies. Psilocybin was most often administered orally (83%), and dosages were typically body weight-adjusted (74%) despite recent research suggesting this to be unnecessary (Garcia-Romeu et al., 2021). Furthermore, dosages and their classifications (e.g., "high" or "low") varied substantially, indicating a lack of consensus regarding optimal dosing for different applications. "Set and setting," that is, how participants and their environment were prepared for the psilocybin experience (Gukasyan and Nayak, 2021), was also highly variable, with some studies failing to report on it altogether. To address these inconsistencies, we encourage researchers to adopt a fixed dosing regimen, as observed in recent publications (Goodwin et al., 2023; Rucker et al., 2022), and to consult existing guidelines for conducting psychedelic research (Johnson et al., 2008). Furthermore, authors should publish comprehensive procedures to facilitate replicability and comparison across studies.

Psilocybin's safety is an important consideration in both clinical and recreational settings. It is therefore noteworthy that the majority (74%) of included reports made no mention of adverse outcomes. Despite most reported adverse outcomes being categorized as non-serious (e.g., headache, nausea, anxiety, and increased blood pressure) and only one study reporting serious adverse outcomes (e.g., suicidal ideation and intentional self-injury) in a small minority (5%) of participants with treatment-resistant depression (Goodwin et al., 2023), the overall paucity of safety reporting makes firm conclusions from these data inappropriate. We therefore strongly advise researchers to explicitly state the observed safety and tolerability of psilocybin in future reports.

It is crucial that researchers and clinicians who intend to incorporate psilocybin in their work have a comprehensive understanding of the drug's effects on cognition. This is especially true when working with psychiatric populations who often present with cognitive impairments such as deficits in memory, attention, processing speed, and executive functions (DeBattista, 2005; Millan et al., 2012; Warren et al., 2021). Psilocybin's effects on creativity should also be considered, given anecdotal evidence of their occurrence (Lea et al., 2020) and associations between cognitive processes and creativity (Benedek et al., 2014; Wang, 2009). While it is important to consider these effects during acute drug intoxication, we argue that an understanding of long-term effects is paramount. Our synthesis discovered myriad acute but limited post-acute findings, thus identifying this as a significant gap in the literature.

Given psilocybin's hallucinogenic nature, it is unsurprising that macrodoses produced primarily negative acute effects on cognitive performance and creativity, as indicated by both objective and subjective measures. Despite this, microdoses tended toward acute creative enhancement, providing early support to anecdotal claims (Lea et al., 2020). Post-acute findings pertaining to macrodoses were mostly neutral and were more often positive than negative, suggesting that initial cognitive deficits are followed by a return to baseline and possibly even enhancement in some areas, although the limited number of post-acute findings and the heterogeneity of assessments limits the conclusions that can be drawn from these data. Moreover, it is important to consider that cognitive enhancement may occur as an indirect consequence of psilocybin's well-documented benefits for mood regulation (Heuschkel and Kuypers, 2020; Johnson and Griffiths, 2017).

It is germane to compare and contrast these findings with those that have been published in relation to other classic psychedelics. Two recent reviews (Bălăeţ, 2022; Sayalı and Barrett,

2023) reported that higher doses of classic psychedelics caused acute cognitive impairment. Both reviews also reported that creative enhancement was observed but that these findings were limited to studies involving psilocybin, LSD, and ayahuasca. It is worth noting that psilocybin is the most researched classic psychedelic with respect to cognition and creativity, with few studies to date examining how these constructs are affected by other classic psychedelics including LSD, ayahuasca, DMT, and mescaline. As psychedelic research progresses, it will be imperative that future reviews synthesize findings pertaining to the effects of these substances on cognition and creativity to inform researchers and clinicians of advancements in our understanding.

Evidently, there is a strong need for further exploration of cognitive and creative outcomes following psilocybin administration. It is our recommendation that researchers employ well-validated measures of the cognitive and creative processes most affected in the populations they are examining. Moreover, we advise researchers to include these assessments both acutely and at multiple post-acute timepoints, as observed in several recent studies (Barrett et al., 2020; Goodwin et al., 2023; Mason et al., 2021). Doing so will help elucidate the time-course of psilocybin's effects, thereby enabling clinicians to better prepare patients for changes in mental functioning that may occur after ingestion. Moreover, these data will help researchers identify populations that are more likely to experience favorable risk to benefit ratios from psilocybin and should thus be considered for future clinical studies.

Our findings support the notion that psilocybin is well tolerated and does not induce persistent deficits in cognition or creativity. This compendium is the most thorough to date and may be used to provide evidence to government and funding agencies for those considering the use of psilocybin in clinical populations in research or therapeutic settings, with a particular emphasis on countries where this research is greatly impeded such as Canada.

Limitations

One limitation of this scoping review is the moderate inter-rater reliability (McHugh, 2012) achieved by the two reviewers while selecting studies for inclusion at both the initial screening and full-text review stages. Despite this, having a third reviewer resolve any disagreements provided a robust mechanism to ensure that edge cases were given adequate attention and important inclusions were not missed.

Despite a recent surge in publications, research on this topic remains limited and the findings should therefore be considered preliminary. The possibility that discouraging findings, particularly those related to microdoses, remain unreported due to publication bias should be noted. More research is needed on long-term outcomes of psilocybin on cognition and creativity in addition to more detailed, objective cognitive assessments. In general, there was a lack of systematic reporting of the outcome measures such that means, standard deviations, and effect sizes were seldom provided, thereby making it difficult to compare raw scores across individuals, groups, and studies. These scores are commonly provided in cognitive research and can be useful to those with a broad understanding of the assessments. It is also noteworthy that few neuroimaging studies were included because many of those that were screened only collected resting-state rather than task-based data. Concerns have been raised regarding the use of resting-state, or task-free data, particularly under the influence of psychedelics (Doss et al., 2022). Given these criticisms, we recommend that researchers collect task-based neuroimaging data which can provide important insights into psilocybin's effects on specific mental processes, thereby improving our understanding of its potential clinical applications. Another limitation is the small number of institutions conducting this research. While it is unsurprising that few facilities are currently able to produce empirical research with psilocybin given worldwide

regulatory challenges, the field would benefit from a diversity of contributing institutions. Currently, the field's reliance on a core group of institutions to produce empirical research is stunting its growth; for psychedelic research to advance, greater collaboration between institutions is advised.

Conclusions

Research examining the effects of psilocybin on cognition and creativity has been expanding since the current psychedelic renaissance began in the early 1990s. As expected, findings from this research demonstrate that psilocybin macrodoses impair cognitive performance during acute intoxication. Interestingly, findings from microdosing studies suggest acute creative enhancement. Moreover, macrodosing studies that included long-term follow-ups found neutral and even positive effects on both cognitive performance and creativity. However, the limited number of long-term findings and the heterogeneity of assessments limit the conclusions that can be drawn from these data. We therefore recommend future research to include well-validated measures of cognitive performance and creativity both acutely and at multiple post-acute timepoints in well-controlled experiments guided by existing resources for conducting psychedelic research (Johnson et al., 2008). With thorough reporting of methodology and findings, including means, standard deviations, and effect sizes, future research can elucidate psilocybin's effects on mental processes of profound importance to both clinical and nonclinical populations.

Author contributions

JB led this research from initial conception to final execution. BV made substantial contributions from the execution of the systematic literature search onward. ZP provided expert consultation

pertaining to methodology. AGR provided expert consultation pertaining to psychedelic research. MGB supervised this research and made substantial contributions throughout. The writing of this article was led by JB with substantial contributions from BV and MGB. All authors reviewed and approved the final article for submission.

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Supplemental Materials

Supplementary Materials Table 1

Search Strategy in APA PsycINFO database accessed through EBSCO platform. Search last performed on February 21, 2023

#	Searches	Results
S1	TI (psilocyb* OR psilocin* OR ((magic* OR entheogen* OR psychedelic OR hallucinogen*) N3 mushroom*)) OR AB (psilocyb* OR psilocin* OR ((magic* OR entheogen* OR psychedelic OR hallucinogen*) N3 mushroom*)) OR KW (psilocyb* OR psilocin* OR ((magic* OR entheogen* OR psychedelic OR hallucinogen*) N3 mushroom*))	831
S2	DE “Psilocybin”	435
S3	S1 OR S2	837
S4	TI (cogniti* or metacognit* or "executive function*" or creativ* or memory or attention* or “problem solving” or “critical thinking” or “decision making”) OR AB (cogniti* or metacognit* or "executive function*" or creativ* or memory or attention* or “problem solving” or “critical thinking” or “decision making”) OR KW (cogniti* or metacognit* or "executive function*" or creativ* or memory or attention* or “problem solving” or “critical thinking” or “decision making”)	1,123,309
S5	DE "Cognition" OR DE "Cognitive Control" OR DE "Metacognition" OR DE "Executive Function" OR DE "Memory" OR DE “Short Term Memory” OR DE “Attention” OR DE "Problem Solving" OR DE “Critical Thinking” OR DE “Decision Making” OR DE “Creativity”	432,907
S6	S4 OR S5	1,192,829
S7	TI ("neural correlate*" or “neural basis” or "brain map*" or "network connect*" or "functional connect*" or "effective connect*" or connectom* or neuroimag* or "neuro-imag*" or "default mode network*" or "task positive network*" or "task negative network*" or "frontoparietal network*" or "central executive network*" or "salience network*" or fMRI or fMRIs or MRI or MRIs or “magnetic resonance imag*” or DTI or DTIs or "diffusion tensor imag*" or "diffusion tractograph*" or “fiber tractograph*” or "diffusion fractograph*" or echo-planar or echoplanar or tomograph* or "MR imag*" or "NMR imag*" or "magnetization transfer contrast imag*"	215,848

	or PET or “positron emission tomograph*” or EEG or EEGs or electroencephalogra* or ERP or ERPs or “event-related potential*” or MEG or MEGs or magnetoencephalogra* or fNIRS or NIRS or “near infrared spectroscop*”) OR AB ("neural correlate*" or “neural basis” or "brain map*" or "network connect*" or "functional connect*" or "effective connect*" or connectom* or neuroimag* or "default mode network*" or "task positive network*" or "task negative network*" or "frontoparietal network*" or "central executive network*" or "salience network*" or fMRI or fMRIs or MRI or MRIs or “magnetic resonance imag*” or DTI or DTIs or "diffusion tensor imag*" or "diffusion tractograph*" or “fiber tractograph*” or "diffusion fractograph*" or echo-planar or echoplanar or tomograph* or "MR imag*" or "NMR imag*" or "magnetization transfer contrast imag*" or PET or “positron emission tomograph*” or EEG or EEGs or electroencephalogra* or ERP or ERPs or “event-related potential*” or MEG or MEGs or magnetoencephalogra* or fNIRS or NIRS or “near infrared spectroscop*”) OR KW ("neural correlate*" or “neural basis” or "brain map*" or "network connect*" or "functional connect*" or "effective connect*" or connectom* or neuroimag* or "default mode network*" or "task positive network*" or "task negative network*" or "frontoparietal network*" or "central executive network*" or "salience network*" or fMRI or fMRIs or MRI or MRIs or “magnetic resonance imag*” or DTI or DTIs or "diffusion tensor imag*" or "diffusion tractograph*" or “fiber tractograph*” or "diffusion fractograph*" or echo-planar or echoplanar or tomograph* or "MR imag*" or "NMR imag*" or "magnetization transfer contrast imag*" or PET or “positron emission tomograph*” or EEG or EEGs or electroencephalogra* or ERP or ERPs or “event-related potential*” or MEG or MEGs or magnetoencephalogra* or fNIRS or NIRS or “near infrared spectroscop*”)	
S8	DE “Brain Connectivity” OR DE “Neural Networks” OR DE “Default Mode Network” OR DE “Neuroimaging” OR DE “Magnetic Resonance Imaging” OR DE “Functional Magnetic Resonance Imaging” OR DE “Diffusion Tensor Imaging” OR DE “Tomography” OR DE “Positron Emission Tomography” OR DE “Electroencephalography” OR DE “Magnetoencephalography”	178,492
S9	S7 OR S8	253,189
S10	S6 OR S9	1,341,946
S11	S3 AND S10	255
S12	S11 AND Limiters - Publication Year: 1994-	234

Supplementary Materials Table 2

Search Strategy in MEDLINE(R) ALL 1946 to February 20, 2023 database accessed through Ovid platform. Search last performed on February 21, 2022

#	Searches	Results
1	(psilocyb* or psilocin* or ((magic* or entheogen* or psychedelic or hallucinogen*) adj3 mushroom*)).ti,ab,kf.	1,542
2	psilocybin/	1044
3	1 or 2	1,759
4	(cogniti* or metacognit* or executive function* or creativ* or memory or attention* or problem solving or critical thinking or decision making).ti,ab,kf.	1,395830
5	cognition/ or metacognition/ or executive function/ or memory/ or memory, short term/ or attention/ or problem solving/ or decision making/ or creativity/	404,751
6	4 or 5	1,522,130
7	(neural correlate* or neural basis or brain map* or network connect* or functional connect* or effective connect* or connectom* or neuroimag* or neuro-imag* or default mode network* or task positive network* or task negative network* or frontoparietal network* or central executive network* or salience network* or fMRI or fMRIs or MRI or MRIs or magnetic resonance imag* or DTI or DTIs or diffusion tensor imag* or diffusion tractograph* or fiber tractograph* or diffusion fractograph* or echo-planar or echoplanar or MR imag* or NMR imag* or magnetization transfer contrast imag* or tomograph* or PET or positron emission tomograph* or EEG or EEGs or electroencephalogra* or ERP or ERPs or event-related potential* or MEG or MEGs or magnetoencephalogra* or fNIRS or NIRS or near infrared spectroscop*).ti,ab,kf.	1,249,437
8	brain mapping/ or connectome/ or functional neuroimaging/ or neuroimaging/ or default mode network/ or magnetic resonance imaging/ or diffusion magnetic resonance imaging/ or echo-planar imaging/ or positron-emission tomography/ or diffusion magnetic resonance imaging/ or diffusion tensor imaging/ or brain waves/ or	758,929

	electroencephalography/ or magnetoencephalography/ or spectroscopy, near infrared/	
9	7 or 8	1,488,672
10	6 or 9	2,840,004
11	3 and 10	373
12	limit 11 to yr="1994 -Current"	327

Supplemental Materials Table 3

Search Strategy in EBM Reviews – Cochrane Central Register of Controlled Trials January 2023 database accessed through Ovid platform. Search last performed on February 21, 2023

#	Searches	Results
1	(psilocyb* or psilocin* or ((magic* or entheogen* or psychedelic or hallucinogen*) adj3 mushroom*)).ti,ab,kf.	277
2	psilocybine/	7
3	1 or 2	277
4	(cogniti* or metacognit* or executive function* or creativ* or memory or attention* or problem solving or critical thinking or decision making).ti,ab,kf.	142,368
5	cognition/ or executive function/ or memory/ or memory, short term/ or attention/ or problem solving/ or decision making/ or creativity/	22,974
6	4 or 5	146,304
7	(neural correlate* or neural basis or brain map* or network connect* or functional connect* or effective connect* or connectom* or neuroimag* or neuro-imag* or default mode network* or task positive network* or task negative network* or frontoparietal network* or central executive network* or salience network* or fMRI or fMRIs or MRI or MRIs or magnetic resonance imag* or DTI or DTIs or diffusion tensor imag* or diffusion tractograph* or fiber tractograph* or diffusion fractograph* or echo-planar or echoplanar or MR imag* or NMR imag* or magnetization transfer contrast imag* or tomograph* or PET or positron emission tomograph* or EEG or EEGs or electroencephalogra* or ERP or ERPs or event-related potential* or MEG or MEGs or magnetoencephalogra* or fNIRS or NIRS or near infrared spectroscop*).ti,ab,kf.	84,215
8	brain mapping/ or connectome/ or functional neuroimaging/ or neuroimaging/ or magnetic resonance imaging/ or diffusion magnetic resonance imaging/ or echo-planar imaging/ or positron-emission tomography/ or diffusion magnetic resonance imaging/ or diffusion tensor imaging/ or brain waves/ or electroencephalography/ or	17,158

	magnetoencephalography/ or spectroscopy, near infrared/	
9	7 or 8	87,370
10	6 or 9	217,233
11	3 and 10	126
12	limit 11 to yr="1994 -Current"	124

Supplemental Materials Table 4

Search Strategy in Web of Science database (editions: A&HCI, ESCI, CPCI-SSH, CPCI-S, SCI-EXPANDED, SSCI) accessed through Clarivate platform. Search last performed on February 21, 2023

#	Searches	Results
1	**TS=(psilocyb* or psilocin* or ((magic* or entheogen* or psychedelic or hallucinogen*) NEAR/3 mushroom*))**	2,475
2	**TS=(cogniti* or metacognit* or "executive function*" or creativ* or memory or attention* or "problem solving" or "critical thinking" or "decision making")**	3,304,449
3	**TS=("neural correlate*" or "neural basis" or "brain map*" or "network connect*" or "functional connect*" or "effective connect*" or connectom* or neuroimag* or "neuro-imag*" or "default mode network*" or "task positive network*" or "task negative network*" or "frontoparietal network*" or "central executive network*" or "salience network*" or fMRI or fMRIs or MRI or MRIs or "magnetic resonance imag*" or DTI or DTIs or "diffusion tensor imag*" or "diffusion tractograph*" or "fiber tractograph*" or "diffusion fractograph*" or "echo-planar" or echoplanar or "MR imag*" or "NMR imag*" or "magnetization transfer contrast imag*" or tomograph* or PET or "positron emission tomograph*" or EEG or EEGs or electroencephalogra* or ERP or ERPs or "event-related potential*" or MEG or MEGs or magnetoencephalogra* or fNIRS or NIRS or "near infrared spectroscop*")**	1,671,391
4	**#2 OR #3**	4,764,082
5	**#1 AND #4**	584
6	**#5 AND** Timespan: 1994-01-01 to 2022-01-14 (Publication Date)	568

Supplementary Materials Table 5

Supplementary Search Methods. Searches last performed on February 22, 2022

Type	Resource(s)	Search Strings
Cited references	Reference lists of included studies	N/A
Citing references	Google Scholar	N/A
Conference proceedings	Web of Science (CPCI-SSH, CPCI-S)* PapersFirst (OCLC) ProceedingsFirst (OCLC)	(Psilocybin AND Cognition) OR (Psilocybin AND Creativity)
Dissertations & theses	ProQuest	(Psilocybin AND Cognition) OR (Psilocybin AND Creativity)
Specific website searching	Multidisciplinary Association for Psychedelic Studies (maps.org) Canadian Psychedelic Association (psychedelicassociation.net) Psychedelic Medicine Association (psychedelicmedicineassociation.org) MIND Foundation (mind-foundation.org)	N/A
General internet searching	Google (incognito mode)**	(Psilocybin AND Cognition) OR (Psilocybin AND Creativity)

*See Supplementary Materials Table 4 for full search strategy
**Screening was limited to the top 100 search results

Supplementary Materials Table 6

Network Analysis Institution Labels

Label	Institution Name	Frequency
PUK Zürich	Psychiatric University Hospital Zürich	13
HRC Zürich	Heffter Research Center Zürich	8
Johns Hopkins Medicine	Johns Hopkins University School of Medicine	4
UC San Diego	University of California San Diego	4
Czech NIMH	National Institute of Mental Health (Czech Republic)	3
Imperial College London	Imperial College London	3
Maastricht U	Maastricht University	3
U Queensland	University of Queensland	3
Beckley Foundation	The Beckley Foundation	2
Christophsbad Göppingen	Psychiatric and Neurological Hospital Christophsbad Göppingen	2
COMPASS	COMPASS Pathways PLC	2
Kennedy Krieger Institute	Kennedy Krieger Institute	2
King's College London	King's College London	2
Leiden U	Leiden University	2
RWTH Aachen	University of Technology (RWTH) Aachen	2
U Bristol	University of Bristol	2
U Frankfurt	University of Frankfurt	2
U Tübingen	University of Tübingen	2
U Ulm	University of Ulm	2
UCT Prague	University of Chemistry and Technology Prague	2
1	Aalborg University	1
2	Aalborg University Hospital	1
3	Aarhus University	1
4	Alzheimer's Center (AUMC) Amsterdam	1
5	Bethlem Royal Hospital	1
6	Cardiff University	1
7	Centre for Addiction and Mental Health (CAMH) Canada	1
8	Centre of Education and Science Cologne	1
9	Charité-Universitätsmedizin Berlin	1
10	Charles University Prague	1
11	Columbia University	1
12	Emory University School of Medicine	1
13	Favaloro University	1
14	Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI) Argentina	1
15	Goethe University	1
16	Harvard University	1
17	Helsinki University Central Hospital	1
18	Humboldt-Universität zu Berlin	1
19	Instituto di Neuroscienze del CNR (Pisa)	1
20	Johns Hopkins University	1
21	Kadima Neuropsychiatric Institute	1
22	Ludwig-Maximilian University Munich	1
23	Metis Cognition Ltd.	1

Label	Institution Name	Frequency
24	National Institute of Health (USA)	1
25	Neurology University Clinic (Magdeburg)	1
26	New York State Psychiatric Institute	1
27	Newcastle University	1
28	Oxford Health NHS Foundation Trust	1
29	Parc Sanitari Sant Joan de Déu	1
30	Psychiatric Clinic (RWTH) Aachen	1
31	Psychiatric Hospital Zürich	1
32	Psychiatric University Clinic (Heidelberg)	1
33	Psychiatric University Clinic (Tübingen)	1
34	Psychiatric University Hospital Zürich Department of Research	1
35	Ruhr University Bochum	1
36	Sant Joan de Déu Research Foundation	1
37	Sheppard Pratt	1
38	South London and Maudsley NHS Foundation Trust	1
39	Stanford University	1
40	Tallaght University Hospital	1
41	The Ohio State University	1
42	Tilburg University	1
43	Tyne and Wear NHS Foundation Trust	1
44	Universidad Adolfo Ibañez	1
45	Universidad de Buenos Aires and Instituto de Física de Buenos Aires (IFIBA - CONICET)	1
46	University College London	1
47	University Hospital Basel	1
48	University Hospital Zürich	1
49	University Medical Center Utrecht	1
50	University Medical Centre Groningen	1
51	University of Amsterdam	1
52	University of Basel	1
53	University of Bremen	1
54	University of Cambridge	1
55	University of Chicago	1
56	University of Cologne	1
57	University of Kassel	1
58	University of Manchester	1
59	University of Maryland School of Medicine	1
60	University of Southern Queensland	1
61	University of Toronto	1
62	University of Tübingen Institute of Pharmaceutical Sciences	1
63	University of Zürich	1
64	University of Zürich Medical School	1
65	UT Houston Medical School	1
66	UTHealth Harris County Psychiatric Center	1
67	Vilnius University	1

Supplementary Materials Table 7

Mixed Methods Appraisal Tool (MMAT) Version 2018: Criteria for Study Design Categories 1 to 3

Category of study designs	**Methodological quality criteria**	**Responses**			
		Yes	No	Can't Tell	Comments
Screening questions (for all types)	S1. Are there clear research questions?				
	S2. Do the collected data allow to address the research questions?				
	Further appraisal may not be feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.				
1. Qualitative	1.1 Is the qualitative approach appropriate to answer the				
	1.2 Are the qualitative data collection methods adequate to address the research question?				
	1.3 Are the findings adequately derived from the data?				
	1.4 Is the interpretation of results sufficiently substantiated by data?				
	1.5 Is there coherence between qualitative data sources, collection, analysis and interpretation?				
2. Quantitative randomized controlled trials	2.1 Is randomization appropriately performed?				
	2.2 Are the groups comparable at baseline?				
	2.3 Are there complete outcome data?				
	2.4 Are outcome assessors blinded to the intervention provided?				
	2.5 Did the participants adhere to the assigned intervention?				
3. Quantitative non-randomized	3.1 Are the participants representative of the target population?				
	3.2 Are measurements appropriate regarding both the outcome and intervention (or exposure)?				
	3.3 Are there complete outcome data?				
	3.4 Are the confounders accounted for in the design and analysis?				
	3.5 During the study period, is the intervention administered (or exposure occurred) as intended?				

Supplementary Materials Table 8

Critical Appraisal of Included Records using the Mixed Methods Appraisal Tool (MMAT) Version 2018

Record	Study design category	Screening questions		Methodological quality criteria (vary according to study design category)					Comments
		S1	S2	1	2	3	4	5	
Turton et al., 2014	1	No	No	No	No	Yes	Yes	Yes	Exploratory study; objectives clearly stated but no specific research question. Data collection methods are adequate to address the stated objectives.
Bravermanova et al., 2018	2	Yes	Yes	Can't tell	Can't tell	Yes	Yes	Yes	
Carbonaro et al., 2018	2	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	
Cavanna et al., 2022	2	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
Doss et al., 2021	2	Yes	Yes	Yes	Can't tell	Yes	No	Yes	
Duerler et al., 2021	2	Yes	Yes	Can't tell	Yes	No	Yes	Yes	
Goodwin et al., 2023	2	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	Extremely low dose psilocybin (1mg) was used as a control instead of placebo.
Gouzoulis-Mayfrank et al., 1999	2	Yes	Yes	Can't tell	Can't tell	Yes	Yes	Yes	
Gouzoulis-Mayfrank et al., 2002	2	Yes	Yes	No	Can't tell	Yes	Yes	Yes	
Grimm et al., 2016	2	Yes	Yes	Can't tell	Can't tell	Can't tell	Yes	Can't tell	
Holze et al., 2022	2	Yes	Yes	Can't tell	Yes	Yes	Yes	Yes	
Kometer et al., 2012	2	Yes	Yes	Can't tell	Can't tell	Yes	Yes	Yes	
Kraehenmann et al., 2015	2	Yes	Yes	Can't tell	Can't tell	Can't tell	Yes	Yes	
Mallaroni et al., 2023*	2	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
Mason et al., 2021	2	Yes	Yes	Can't tell	Can't tell	Yes	Yes	Yes	Randomization type is reported, but the tool used to achieve it is not described.

Record	Study design category	Screening questions		Methodological quality criteria (vary according to study design category)					Comments
		S1	S2	1	2	3	4	5	
Prochazkova et al., 2021*	2	Yes	Yes	Can't tell	Can't tell	Can't tell	Yes	Can't tell	Discrepancies between sample sizes reported in individual experiments and mega-analysis.
Rucker et al., 2022	2	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
Vollenweider et al., 1998	2	Yes	Yes	Can't tell	Can't tell	Yes	Can't tell	Yes	
von Rotz et al., 2023	2	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
Barrett et al., 2018	3	Yes	Yes	No	Yes	Yes	Yes	Yes	All participants had experience with psychedelics; this was not stated as the target population.
Barrett et al., 2020	3	Yes	Yes	No	Yes	Yes	No	Yes	
Bernasconi et al., 2014	3	Yes	Yes	Yes	Yes	Can't tell	Yes	Yes	
Cahn, B. R. 2007	3	Yes	Yes	No	Yes	Yes	Can't tell	Yes	
Carhart-Harris et al., 2018	3	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
Carter et al., 2005	3	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
Carter et al., 2007	3	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
Gabay et al., 2018	3	Yes	Yes	No	Yes	Yes	Yes	Yes	
Hasler et al., 2003	3	Yes	Yes	Can't tell	Yes	Can't tell	Can't tell	Yes	
Hasler et al., 2004	3	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
Mason et al., 2018	3	Yes	Yes	No	Yes	Yes	Can't tell	Yes	
Mason et al., 2019	3	Yes	Yes	Yes	Yes	No	No	Yes	
McKenna et al., 2018	3	Yes	Yes	Can't tell	Yes	Yes	Can't tell	Yes	
Pokorny et al., 2017	3	Yes	Yes	No	Yes	Yes	Yes	Yes	
Prochazkova et al., 2018	3	Yes	Yes	Yes	Yes	No	No	Yes	
Quednow et al., 2012	3	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
Schmidt et al., 2012	3	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	

Record	Study design category	Screening questions		Methodological quality criteria (vary according to study design category)					Comments
		S1	S2	1	2	3	4	5	
Schmidt et al., 2013	3	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
Spitzer et al., 1996	3	Yes	Yes	No	Yes	Yes	Yes	Yes	
Umbricht et al., 2003	3	Yes	Yes	No	Yes	Yes	Yes	Yes	
Viktorin et al., 2022	3	Yes	Yes	Yes	Yes	No	Can't tell	Yes	
Vollenweider et al., 2007	3	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
Wittman et al., 2007	3	Yes	Yes	No	Yes	Yes	Yes	Yes	

*Preprint

Included Reports

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Chapter Three: Exploring Psychedelic Usage in Athletes and Attitudes Towards Psilocybin Use in Concussion Recovery

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Author Note

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Exploring Psychedelic Usage in Athletes and Attitudes Towards Psilocybin Use in Concussion Recovery

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Exploring Psychedelic Usage in Athletes and Attitudes Towards Psilocybin Use in Concussion Recovery

Abstract:

Background: Psychedelics are receiving growing interest among clinical researchers for their effects on mood and cognition. Leading the psychedelic renaissance is psilocybin, one of the most widely studied classic psychedelics which has shown good safety and clinical benefit for major depression and substance use disorders. Athletes lead numbers in concussions sustained and often experience myriad symptoms, including cognitive and mood issues, which can persist for weeks or months in 10-30% of athletes. The growing research findings on psilocybin, particularly with psychiatric disorders, make it a potential symptom management option for athletes who have sustained a concussion and experience persisting concussion symptoms.

Methods: This study involved an online survey of athletes and sports staff in Canada the US to examine current psychedelic use rates, attitudes towards psilocybin, and willingness to use or support psychedelic-assisted therapy (PAT) for sports concussion and persisting symptoms. A path analysis was conducted in RStudio to examine the influence of predictor variables on willingness.

Results: This study included 175 participants (n = 85 athletes; n = 90 staff). The most common substances used in the past year among athletes were alcohol (90.6%), cannabis (43.6%), and psychedelics (35.8%). Regular psychedelic use (use $\geq$ 2 times per week) was quite low in athletes (7.5%). Attitudes towards psilocybin and knowledge of psilocybin were significant predictors for both athletes and staff members of their willingness to use or support PAT for concussion recovery. Athletes reported likely engaging in PAT (61.2%) and staff (71.1%) reported that they would support their athletes using PAT.

Conclusions: The results of this study suggest that the sports community is receptive to psilocybin-assisted therapy and athletes would be willing to engage in it for concussion recovery and/or the management of persisting post-concussion symptoms. Future research should examine the effects of psilocybin for PPCS to inform whether there is any impact. Other important concerns that must be addressed by researchers include long-term effects of psilocybin use.

Keywords: psychedelics; psilocybin; athletes; sports concussion; mTBI.

Lay Summary:

Psychedelics like psilocybin are gaining attention from researchers for their impact on mood and cognition. Athletes frequently experience concussions and long-lasting symptoms, making psilocybin a potential option to explore. An online survey of Canadian and American athletes revealed positive attitudes towards psilocybin and a willingness to try psychedelic-assisted therapy for concussion recovery.

Implications for Clinical Practice:

- With continued research using psilocybin and other psychedelics for clinical syndromes, it is unclear how patients feel about this potential treatment approach. In directly querying the intended patient population, clinicians can better understand concerns and interest in this treatment option.
- With sports-related concussions, athletes are at a heightened risk of cognitive impairment and increasing mental health concerns, particularly in athletes where symptoms persist. Psychedelic-assisted therapy may be an innovative rehabilitation approach to manage these outcomes.
- This study provides important next steps for researchers and clinicians who intend to examine and implement this treatment approach.

Exploring Psychedelic Usage in Athletes and Attitudes Towards Psilocybin Use in Concussion Recovery

Psilocybin's Role in Athlete Concussion Recovery

Background

Sports-related concussions (SRC) are a form of mild traumatic brain injury (mTBI) that occurs while engaging in sports (McKeithan et al., 2019). In the United States of America (USA), roughly 3.8 million sports-related brain injuries occur annually (De Stefano et al., 2020) while in Canada, available data from 2020-2021 via the Canadian Institute for Health Information (CIHI) identified almost 2000 emergency department visits for sports-related brain injuries. Although most athletes fully recover within 7-10 days, approximately 10-30% of athletes will experience persisting post-concussion symptoms (PPCS) which typifies the long-term persistence (for weeks or even months) of clinical symptoms past this typical recovery time frame (Champagne et al., 2023; Leddy et al., 2012; Ledreux et al., 2020; Makdissi et al., 2013, 2017; Sicard et al., 2021). Common psychological symptoms include mood dysregulation (i.e., anxiety, depression, irritability) and cognitive impairments in domains of executive function, memory, attention, and concentration (Covassin & Elbin, 2010; Karr et al., 2014; Ledreux et al., 2020). Physiological symptoms include headache, fatigue, and light and noise sensitivity (Ledreux et al., 2020). Both psychological and physiological symptoms can be greatly debilitating in athletes across multiple areas of life (i.e., interpersonal, academic, work, leisure, sport) and can prolong the time before returning to work, school, and/or sport (Champagne et al., 2023). Improved concussion rehabilitation approaches and managing PPCS are among the most requested areas of research from patients, clinicians, and researchers (Osmond et al., 2023;

Patricios et al., 2023). Therefore, the current study will explore the willingness of the sports community to engage in (as an athlete) or support (as a staff member) psilocybin-assisted therapy (PAT) for concussion recovery and PPCS in athletes. This study aims to contribute to the ongoing discourse surrounding concussion rehabilitation and offer insights into novel avenues such as psychedelic therapy for managing PPCS.

The most common definition of concussion, often used interchangeably with mTBI, describes a brain injury caused by direct or indirect force to the head which results in symptoms in the domains of cognition, emotion, and/or sleep (Romeu-Mejia et al., 2019). The conceptual definition of SRC according to the Concussion in Sport Group (CISG) was updated at the Amsterdam 2022 International Consensus Statement on Concussion. This definition involves the following major points to describe a SRC: (1) force is transmitted to the brain via a blow to the head, neck or body through sport or sport-related activities; (2) the resulting injury to the brain occurs through a neurotransmitter and metabolic cascade; (3) symptoms can onset rapidly or over time and typically resolve within days but may persist ; (4) injury is typically functional rather than structural and will not be seen on standard structural neuroimaging studies; and (5) clinical presentation is broad and diverse and may or may not include loss of consciousness (Patricios et al., 2023).

The Role of Psilocybin

Psilocybin is a classic psychedelic that is metabolized into psilocin upon ingestion (Nichols, 2016). Psilocin has a greater affinity for the serotonin (5-HT) receptors and research suggests that the 2A subtype (5-HT_{2A}; Nichols, 2016) is a key mechanism of the psychedelic effects of psilocybin (Halberstadt & Geyer, 2011). Psilocybin has grown in popularity in recent years among researchers in an era termed the “psychedelic renaissance” (Carhart-Harris &

Goodwin, 2017; Nichols, 2020; Sessa, 2012). Researchers worldwide have examined psilocybin's effects on the symptoms and outcomes in a myriad of psychological disorders such as treatment-resistant depression, end of life care, and substance use disorders (Carhart-Harris et al., 2017; Davis et al., 2021; Griffiths et al., 2016; Johnson et al., 2014; Schindler et al., 2021, 2022). Given the important overlap with psychological disorders, a noteworthy scoping review summarized the research examining psilocybin's effects on cognition. The findings of this review indicate that psilocybin's effects on cognitive functioning occur in a time-based variation, suggesting that it does not impair cognitive functioning long-term despite the occurrence of cognitive impairments acutely (Bonnieux et al., 2023). These outcomes are often found in the absence of severe adverse side effects with psilocybin being found to display limited potential for abuse or toxicity and boasting notable safety overall when administered to carefully screened and prepared individuals in controlled settings (Bonnieux et al., 2023; Johnson et al., 2018; Nichols, 2016; Passie et al., 2002). This safety profile is especially important when considering use in clinical populations with a brain injury.

Although psilocybin has not been formally investigated in people with SRC, we hypothesize that psilocybin may benefit those with sports concussion and persisting symptoms through three primary mechanisms: (1) acting as an anti-inflammatory agent through 5-HT_{2A} receptor to limit prolonged neuroinflammation (Xiong et al., 2018; Yu et al., 2008); (2) inducing neurogenic effects in brain regions implicated in cognitive functioning (Catlow et al., 2013; Khan et al., 2021); and/or (3) by managing symptoms of anxiety and depression which are frequent after SRC and particularly in those presenting with PPCS (Carhart-Harris et al., 2017; Davis et al., 2021; Doss et al., 2021; Goodwin et al., 2023; Griffiths et al., 2016; Gukasyan et al., 2022; Rootman et al., 2021; Ross et al., 2016).

The Current Study

While current research highlights a theoretical proof of concept in examining PAT for SRC and PPCS (Bonnieux et al., 2023; Goodwin et al., 2023, 2023; Gukasyan et al., 2022; Khan et al., 2021; Ly et al., 2018; Xiong et al., 2018; Yu et al., 2008), it is unclear whether the sports community may be receptive to the use of psilocybin in concussion recovery. Therefore, we queried athletes and sports team personnel directly about their perspective on psilocybin for rehabilitative purposes to inform clinical research that intends to examine and potentially implement these treatment options. Moreover, we examined what variables are associated with willingness to use or support PAT for concussion recovery. A previous study in an American sample found that adults between the ages of 26-34 years old are more likely to engage in psilocybin use compared to adults 18-25 years old (Yockey & King, 2021). Additionally, respondents in this survey who had completed high school and/or college were more likely to report having used psilocybin (Yockey & King, 2021). In a sample of psychotherapists, attitudes and knowledge of psilocybin were positively correlated with willingness to recommend PAT to patients (Meir et al., 2023). Similarly, Melnikov et al. (2021) found that attitudes towards medical cannabis significantly influenced the likelihood that health care professionals would recommend medical cannabis as a treatment to their patients. Thus, variables such as age, education, attitudes, and knowledge emerge as important variables to examine in one's willingness to engage in or support PAT for concussion recovery. Gathering this information will provide an understanding of the interest and concerns from athletes, coaches, and other sports team staff regarding the therapeutic use of psilocybin.

To address these current gaps in our knowledge, this study used a descriptive online survey approach to address the following three objectives. The first objective is to provide an estimate of current prevalence rates of general psychedelic use among athletes in Canada and the

USA across levels of competition and the motivations for use. The second objective is to summarize the sports community's current attitudes and beliefs specifically about psilocybin and its therapeutic use for concussion recovery and managing persistent concussion symptoms. The third objective is to report the willingness of athletes to engage in psilocybin for the treatment of concussion and persistent symptoms and the level of support from sports team personnel for athletes interested in this treatment option.

Given the lack of research on this topic, we will examine current psychedelic use rates among athletes and motivations for use in athletes using an exploratory approach. Based on previous literature, it is hypothesized that age, education, knowledge, and attitudes will predict willingness to engage in or support PAT, and we will examine concussion history as an exploratory variable in the athlete sample.

Methodology

Protocol and Registration

The present study received ethics approval from the Research Ethics Boards at the University of British Columbia (UBC) and the University of Victoria (UVIC) through the harmonized ethics review process on March 9th, 2023. This harmonized review process is organized by UBC to coordinate ethics approval across institutions in the province of British Columbia. The study was conducted in accordance with the ethical guidelines set forth by the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans. The UBC REB approval number is *H22-03498* and the Board of Record REB approval number is *BC23-0060*.

This study was pre-registered through Open Science Framework on March 13th, 2023 before data collection commenced (VanderZwaag, 2023).

Participants

For this study, the population of interest included athletes and individuals involved as staff members to a sport team at any capacity (i.e., coach, trainer, or physical therapist) and at any level of competition (i.e., recreational, club, collegiate, etc.). Inclusion criteria were: (1) current involvement in a sports team as an athlete or a team personnel; (2) 18 years old or older; and (3) currently living within Canada and the USA. This study involved the completion of a three-part online survey.

Survey Section 1: Demographics and Clinical Information

Information was collected pertaining to age, gender, race/ethnicity, country and state/territory/province, level of education, religion, sportsmanship level, sport(s) currently engaged in, and role (athlete or team personnel). A brief personality inventory (Ten-Item Personality Inventory; Gosling et al., 2003) was used to examine the relationship between Big Five personality traits and the primary study variables. Concussion history was collected from athletes which included: (1) history of concussion (yes or no); (2) date of most recent concussion; (3) diagnosis by a medical professional (yes or no) and what type of professional diagnosed the concussion (if yes); (4) loss of consciousness (yes or no) and duration of (if yes); (5) experience of anterograde amnesia (yes or no); (6) experience of persisting concussion symptoms (e.g., headache, nausea, fatigue, sleep disturbance, light/noise sensitivity, etc.) and whether or not those symptoms persisted after returning to sport.

Survey Section 2: Substance Use Information

Information was collected from athletes pertaining to history of and current psychedelic use in addition to other drugs/alcohol. Questions included: (1) history or current use (yes or no); (2) psychedelic(s) of choice; (3) whether use is therapeutic or recreational; (4) frequency of use;

(5) approximate dosage; (6) method of intake; (7) motivations for use (mood enhancement, cognitive enhancement, pain management, relaxation, coping, etc.).

Survey Section 3: Attitudes and Beliefs Towards Psilocybin

Information was collected from athletes and sports team personnel regarding attitudes and beliefs towards psilocybin and willingness to incorporate it in PPCS recovery. Both the team personnel group and athlete group were asked about WADA regulation of psilocybin, current attitudes toward psilocybin, current knowledge of psilocybin, beliefs about addictive properties, perceived benefit of research on the topic, interest in learning more about psilocybin for medical use, and barriers to the implementation of PAT for concussion recovery in athletes. Athletes were queried on their willingness to *use PAT* for concussions recovery while staff were queried on their willingness to *support athletes using PAT*. Questions were ranked using a seven-point Likert scale. Full questions and Likert options can be found in Supplemental Materials.

Statistical Analyses

Descriptive statistics, including mean, standard deviation, skew, and kurtosis were calculated for the entire sample as well as each category (athletes/team personnel). Data was examined for outliers using the Mahalanobis Distance. To limit accidental omission of responses, we employed a request response validation if a question was not answered, with the option to skip the question if participants chose not to answer.

Two path analyses were conducted in RStudio version 2021.09.0 to test two proposed models (one for athletes and one for staff) developed based on prior literature and exploratory variables such as concussion history (for the athlete model only). The proposed models (see Supplemental Materials) were developed to test the effect of demographic variables (age and education), personality trait openness (measured through the TIPI), knowledge of psilocybin, attitudes

towards psilocybin, past psychedelic use experience, and concussion history (for the athlete model) on willingness to engage in or support PAT for persisting concussion symptoms. All other data analysis was conducted in SPSS Version 27.

Results

Missing data patterns were assessed using Little's Missing Completely at Random (MCAR) analysis. Based on the test results for athletes and staff, respectively, ($\chi^2 = 6.058$, df = 6, $p = .417$; $\chi^2 = 8.785$, df = 11, $p = .642$), there is no significant evidence to reject the null hypothesis of missing completely at random at $p < .05$. This indicates that the missing data (< 1%) are assumed to be missing completely at random with no systematic pattern of missingness.

Overall Respondent Characteristics

At the end of the data collection period (June 1, 2023), our sample consisted of 175 participants (Table 1), a majority of which were male (67.9%), Caucasian (59.4%), and from the United States (58.0%) between the ages of 18 to 76 years old, with a mean age of 30.52 years (SD = 9.02). Demographic information will be described separately for both the athlete and staff samples below and full demographics for the full sample, athlete sample, and staff sample can be found in Table 1.

Athlete Demographics

Our athletes sample consisted of 85 athletes ($M = 28.73$, $SD = 9.65$) with most athletes from the US (51.8%). The majority of athletes (65.2%) identified as Caucasian and most frequently played American football (17.6%), softball (17.6%), volleyball (16.5%), and soccer (11.8%). Most athletes played recreational ($n = 41$) and collegiate ($n = 37$) sports.

Staff Demographics

Our staff sample consisted of 90 staff members (M = 32.21, SD = 8.07) who primarily identified as male (65.6%) from the US (63.3%). Staff members were most frequently coaches (53.3%) at the collegiate level (38.2%) and the most common sport they coached was softball (22.2%).

Drug Use Findings

Overall

Just over half of our sample (50.8%) indicated using drugs or alcohol at some point in their life with the most frequent substance used among these respondents being alcohol (95.5%) followed by cannabis (55.1%) and psychedelics (41.6%). Over the past year, 87 participants (49.7%) indicated using drugs or alcohol, most frequently alcohol (93.1%), cannabis (43.7%), and psychedelics (34.5%). Finally, 71 participants (40.6%) indicated regularly using drugs or alcohol (defined as using two or more times per week) of which most reported using alcohol (63.4%), cannabis (28.2%), and tobacco (25.4%).

Athletes

The majority of athletes indicated using drugs at least once in their life (62.4%) while two athletes selected to not disclose their drug use history. Of those that reported using drugs at some point in their life (n = 53), all reported using drugs or alcohol within the past year and 56.5% of athletes indicated using drugs or alcohol regularly. The most commonly used substances in the past year were alcohol (90.6%), cannabis (43.4%), and psychedelics (35.8%) while the most commonly used substances regularly ($\geq$ 2 times per week) were alcohol (56.3%), cannabis (20.8%), and tobacco (16.7%). With respect to psychedelic use, 22.4% of athletes reported using psychedelics in their lifetime, 35.8% reported using psychedelics in the past year, and 7.5% reported using psychedelics regularly. The most common psychedelic used among athletes using

psychedelics was psilocybin (64.3%). The primary motivations for using psychedelic among athletes was personal improvement or general well-being (16.4%) and mood enhancement (12.3%).

Sports Team Staff

The majority of staff respondents indicated never having used drugs or alcohol in their lifetime (57.8%), while 40.0% indicated having used drugs or alcohol in their life, and two respondents indicated that they would prefer not to say. The most common substances used in the past year were alcohol (97.1%), cannabis (44.1%), and tobacco (41.1%). These were also the most common substances used regularly with 52.9% using alcohol, 32.4% using tobacco, and 29.4% using cannabis. Of those that used a substance at least once in their life (n = 36), 16.7% used psychedelics at some point in their life, 32.4% used psychedelics in the past year, and 5.9% used psychedelics regularly. The most commonly used psychedelic was psilocybin (52.6%), and psychedelics were primarily used for mood enhancement (16.2%) and PTSD or other trauma-related reasons (13.5%).

Psychedelic Use

Respondents who reported using psychedelics within the past year (33.7%) were asked about their patterns and reasons of use. Our participants primarily indicated using psychedelics a few times a year with the most common psychedelic used being psilocybin (59.6%). The reasons for use were most often for personal improvement (14.5%) and mood enhancement (13.6). Of participants who indicated using psilocybin, most reported some degree of improvement on their reasons for use. 16 respondents indicated using psilocybin for anxiety with 76.5% reporting some improvement to their anxiety (i.e., somewhat, moderately, or significantly improved anxiety) whereas 11.8% noted some degree of worsening (i.e., somewhat, moderately, or

significantly worsened). 16 respondents indicated using psilocybin for depression with 81.3% reporting improvement to their depression and 6.3% reporting worsening depression. 9 respondents indicated using psilocybin for trauma-related reasons with 100% reporting improvement. 13 respondents indicated using psilocybin for cognitive effects with 69.3% reporting improvement to their cognitive functioning and 23.1% reporting impairments to their cognitive functioning. 13 respondents indicated using psilocybin for stress-related reasons with 69.3% reporting improvement to their stress and 7.7% indicating worsening stress. 3 respondents indicated using psilocybin for concussion symptoms with 100% reporting improvement in their concussion symptoms. 10 respondents indicated using psilocybin for coping with 100% reporting improvement. 17 participants indicated using psilocybin for mood enhancement with 70.6% reporting improvement to their mood and 11.8% reporting worse mood. Lastly, 14 respondents indicated using psilocybin for personal improvement with 71.4% reporting improvement and 7.1% reporting worsened personal development.

Concussion History Frequency

Our survey found that 56% (n = 48) of our athletes had experienced at least one concussion. Of those athletes, 83.3% reported receiving a medical diagnosis of a concussion with 90% of these concussions being diagnosed by a physician. The most frequently endorsed concussion symptoms were headache (13.4%), nausea (10.9%), and fatigue (10.5%). Cognitive symptoms, such a feeling in a fog, feeling slowed down, memory complaints, and difficulties with concentration and attention were commonly reported among athletes with 29.3% of symptoms falling under the umbrella of ‘cognitive’ symptoms. Alternatively, mood symptoms only accounted for 6.1% of those experienced by athletes.

In our sample of athletes, persisting concussion symptoms occurred in 83% (n = 40) of those who reported a history of concussion. The most frequently reported persisting symptoms included headache (21.7%), nausea (10.8%), fatigue (10.8%), and sleep difficulties (10.8%). Again, cognitive symptoms were highly reported with 21.7% of persisting symptoms being cognitive while mood symptoms were less likely to persist (4.8%).

Attitudes Towards Psilocybin

Athlete Attitudes

Just over half of the athlete sample was familiar to some degree with psilocybin (56.5%) and almost a third of athletes had 'neutral' attitudes towards psilocybin, 'neutral' knowledge of psilocybin, and felt 'neutral' regarding the potential addictive or abusive potential of psilocybin. Interestingly, over half of athletes were interested in learning more about PAT for mental health, concussion recovery, and other medical concerns (55.3%) and felt that there was benefit in examining the medical use of psilocybin (57.6%).

Staff Attitudes

Just over half of team staff were familiar with psilocybin (54.4%), had favorable attitudes towards psilocybin (52.2%), and were knowledgeable of psilocybin (54.4%). Over half of team staff felt that psilocybin was addictive or likely to be abused (57.8%). Two thirds of staff felt that there was benefit in examining the medical uses of psilocybin (66.7%) and the majority of staff were interested in learning more about the medical uses of psilocybin (76.7%).

Psilocybin-Assisted Therapy Willingness

Athlete Willingness

Athletes were asked whether they would be willing to engage in PAT for PPCS if they were experiencing it themselves and research indicated that PAT was beneficial for this purpose.

23.5% of athletes indicated that they would be ‘very likely’ to engage in PAT. 22.4% and 15.3% indicated that they would be ‘likely’ and ‘somewhat likely’, respectively, to engage in PAT for this purpose (Figure 1D). 25.9% of athletes indicated that they would be ‘very unlikely’, ‘unlikely’, or ‘somewhat unlikely’ to engage in PAT for concussion recovery.

Staff Willingness

Sports team staff were asked whether they would be willing to support their athlete(s) dealing with PPCS in using PAT if research indicated that it was beneficial. 25.6% of staff indicated that they would ‘likely’ support this while 21.1% indicated they would be ‘somewhat likely’, and 24.4% ‘very likely’. 15.6% of sports team staff indicated that they would be ‘very unlikely’, ‘unlikely’, or ‘somewhat unlikely’ to support PAT for concussion recovery. (Figure 1E).

Perceived Barriers to PAT for Concussion Recovery

We queried athletes and staff regarding the barriers that they believed to be the most significant in implementing PAT for concussion recovery in athletes. A recurrent theme across athletes and staff were concerns regarding the long-term effects of psilocybin therapy with 24.0% of athletes and 24.7% of staff indicating this as a concern. Athletes highlighted the stigma from their coaches or other team staff (18.3%) as another prominent concern whereas staff believed access to psilocybin treatment (19.2%) to be a significant barrier.

Path Analysis

Correlations

Pearson correlations were conducted with the path variables of interest to examine any significant relationships, direction of relationships, and any especially strong relationships (i.e., multicollinearity). This was especially necessary for exploratory variables. Correlation

coefficients revealed that willingness to use PAT among athletes was significantly and positively correlated with psilocybin attitudes ($r = .57$, $p < .001$) and psilocybin knowledge ($r = .55$, $p < .001$). Willingness to support PAT as a staff member was also significantly and positively correlated with psilocybin attitudes ($r = .48$, $p < .001$) and psilocybin knowledge ($r = .49$, $p < .001$). All other correlations were not statistically significant. The full results of the correlation analysis are summarized in Tables 4 and 5.

Athlete Model

The model fit indices indicated a good fit to the data, $\chi^2 = 139.19$, df = 22, $p < .001$, CFI = .98, TLI = .96, RMSEA = .05. The results revealed significant direct paths from age to willingness ($\beta = .19$, SE = .01, $p < .01$), knowledge to willingness ($\beta = .37$, SE = .14, $p < .01$), from attitudes to willingness ($\beta = .33$, SE = .11, $p < .01$), attitudes to knowledge ($\beta = .34$, SE = .12, $p < .01$), attitudes to psychedelic experience ($\beta = .52$, SE = .38, $p < .001$), and knowledge to psychedelic experience ($\beta = .46$, SE = .33, $p < .001$). Past psychedelic use, concussion history, and education were not significant predictors of willingness. These findings suggest that higher levels of knowledge of psilocybin are associated with more positive attitudes towards psilocybin as well as greater willingness to use PAT. There was a significant indirect effect between past psychedelic experience and willingness ($\beta = .17$, $p < .01$) suggesting that knowledge mediates the relationship between these two variables. Similarly, there was a significant indirect effect between past psychedelic experience and attitudes ($\beta = .16$, $p < .01$) with knowledge as a mediator. See Figure 2.

Staff Model

The model fit indices indicated a good fit to the data, $\chi^2 = 99.51$, df = 18, $p < .001$, CFI = 0.99, TLI = 0.97, RMSEA = .04. The results revealed significant direct paths from knowledge to

willingness (β = .32, SE = .12, $p < .01$), attitudes to willingness (β = .32, SE = .11, $p < .01$), from attitudes to knowledge (β = .51, SE = .09, $p < .001$), attitudes to past psychedelic experience (β = .27, SE = .38, $p < .01$), and knowledge to psychedelic experience (β = .27, SE = .38, $p < .01$). There was a significant indirect effect between past psychedelic experience and attitudes (β = .14 $p < .05$) with knowledge as a mediator as well as a significant indirect effect between past psychedelic experience and willingness (β = .16 $p < .01$) mediated by knowledge. See Figure 3.

Discussion

Psychedelic use by athletes has been scarcely documented, and to our knowledge, this is the most comprehensive and recent examination of psychedelic use in Canadian and American athletes. This is also the first survey to examine athlete willingness to engage in psilocybin-assisted therapy for concussion recovery and persisting concussion symptoms and staff willingness to support this treatment in athletes. Despite researchers discussing the clinical utility of psilocybin for athlete mental health, particularly in those with a history of concussion (Walton & Liknaitzky, 2022), research on this population has not been yet published. Moreover, some research indicates that psychedelics may be effective in concussion rehabilitation and the management of symptoms that often persist (Khan et al., 2021), but athletes continue to be a population understudied in the field. However, the use of psychedelics for mental health concerns in former athletes is being discussed in mainstream news with popular athletes such as former National Hockey League (NHL) players Daniel Carcillo and Riley Cote coming forward to discuss their experiences with psilocybin (Hall, 2023). As such, these anecdotal experiences suggest that this examination of psilocybin use in concussion recovery and persisting symptom management is a timely and worthwhile endeavor in psychedelic related research and this study may begin to pave way for the examination of psilocybin for acquired brain injury. Importantly,

the implementation of psilocybin for the management of PPCS would strongly depend on the willingness of the population to engage in this approach, thus this study represents an important early step prior to the commencement of clinical trials (Bonnieux et al., 2023).

In addressing the first research question, which aimed to assess psychedelic use among athletes and motivations for use, we found some evidence that there is current psychedelic use among athletes across levels of competition and that this sample of athletes favors psilocybin. Compared to a previous study with an American collegiate athlete sample and the only other survey to discuss athlete psychedelic use, we identified higher rates of psychedelic use in our sample (Green et al., 2001). This increase may in part be due to the rising discussion of psychedelics among researchers and mainstream media. Moreover, the aforementioned vocal discourse among former elite athletes may also fuel the increase of psychedelic use among our sample of athletes. In contrast to prior literature, the primary reasons athletes in our sample used psychedelics were for personal improvement and mood enhancement, compared to recreational or social reasons (Green et al., 2001). At this point, very few athletes indicated using psychedelics specifically for concussion symptom management, but of those that did indicate psychedelic use in the presence of symptoms that they identified as persisting symptoms, all self-reported that the psychedelic use had improved their concussion symptoms. Moreover, of respondents that used psychedelics for cognitive improvement, over half indicated that there was some level of improvement. However, it is important to note that these are self-reported improvements in the presence of naturalistic psychedelic use and thus may not be indicative of the true effects that psychedelics, and psilocybin specifically, may have on concussion symptoms and PPCS.

The second research question intended to examine the attitudes and beliefs towards psilocybin among athletes and sports team staff. While our sample endorsed primarily neutral attitudes towards psilocybin, respondents were somewhat familiar with psilocybin and knowledgeable about the medical uses of psilocybin. Staff were more likely to be concerned about the addictive properties of psilocybin or the ability of it to be misused than athletes were. Importantly, both athletes and coaches were concerned about the long-term effects of using psilocybin. Lastly, most participants were interested in learning more about psilocybin's potential use in mental health management and believed that there is benefit in examining psilocybin's use in PPCS management.

The key findings of this study and the subject of our third research question regards the overarching willingness of athletes to consider using PAT for PPCS if they had a concussion and the willingness of staff to support athletes using PAT for concussion recovery and persisting symptoms given that evidence indicates it is beneficial. These findings suggest that the athlete population may be receptive to PAT through concussion recovery and the management of PPCS even in the presence of generally neutral attitudes towards psilocybin. This openness suggests that it may be worthwhile to initiate a clinical trial with an athlete sample to examine the efficacy of psilocybin in the management of PPCS, specifically examining the effects on the cognitive and mood symptoms. Provided that nearly a quarter of our sample endorsed cognitive symptoms following their concussion and 6.1% endorsed mood dysfunction, it is worth examining whether psilocybin may offer relief for athletes who experience such symptoms.

While research with other clinical populations (i.e., treatment-resistant depression, life-threatening cancer, substance use disorders) suggest efficacy in managing symptoms with psilocybin, it is unclear whether these outcomes would translate in patients with brain injury.

Similarly, some research indicates cognitive improvement with psilocybin use or negligible cognitive outcomes, but many studies which examine these cognitive outcomes have often used healthy participants rather than clinical populations (Bonnieux et al., 2023), limiting the translatability directly to TBI patients. Nonetheless, these long-term outcomes represent a significant gap in the literature and were primary concerns of both athletes and staff in the implementation of PAT in athletes with concussions. Similar concerns were identified by over 40% of service members and veterans when asked about barriers to using PAT for PTSD and depression (Gray et al., 2022). Therefore, it is essential that researchers examine the long-term effects of PAT, particularly on cognitive functioning.

As shown in both path analysis models, knowledge about psilocybin plays a significant role in willingness to use or support PAT. Specifically, higher levels of knowledge of psilocybin were associated with more positive attitudes towards psilocybin as well as greater willingness to use and support PAT. By identifying the impact of knowledge on willingness for both athletes and staff, recommendations can be made to improve knowledge dissemination to the sport's community regarding psilocybin's safety and risks, current understanding regarding effects on athletic performance, as well as the proposed effects that psilocybin might have in helping manage PPCS. This knowledge dissemination to and broad discussion with those that this treatment approach intends to benefit (i.e., athletes, sports teams) will be paramount. Knowledge dissemination can include explaining the proposed mechanisms by which psilocybin may help concussion recovery and the management of cognitive and mood symptoms in PPCS, as well as discussing currently known long-term outcomes to address those concerns from athletes and staff. These findings highlight the importance of taking a *patient-oriented approach* in future research which will involve athletes and staff in the research process. Their involvement will

inform research design, development of treatment protocols, considerations for clinical implication, and concerns regarding sports performance and other long-term effects. Thus, we can ensure that the sports community's voice is heard, and that the results be more efficiently applied to those in need.

Limitations

It is important to acknowledge certain limitations of the present study. First, the reliance on self-reported data invites the potential for response bias which could lead participants to respond inaccurately or in a socially desirable manner. When surveying participants on drug use history and experiences, athletes may be hesitant to report their true experiences due to fears of potential consequences for drug use. Secondly, it is worth noting that athletes and sports team staff who responded to this survey may have done so out of personal interest or prior experience with psychedelics, potentially introducing a sample bias and inflated psychedelic use rates among athletes. Third, our survey found that almost half of our participants reported being drug naïve (i.e., never having used drugs or alcohol before). Subsequently, we found that respondents frequently selected 'neutral' for questions regarding attitudes, beliefs, and knowledge of psilocybin as well as interest in learning more and perceived benefit to research on psilocybin. While we provided a brief description of psilocybin that avoided any bias ("*The following questions focus on psilocybin which is a naturally occurring psychoactive substance found in* Psilocybe *mushrooms, also known recreationally as "magic mushrooms"*), additional information may have been necessary to provide drug naïve participants with a more comprehensive base for what psilocybin is for the next questions. As such, neutral responses may have been a result of a limited understanding of what psilocybin is and/or the current state of psilocybin research.

Conclusions

The findings of this study suggest a high level of receptiveness in the sports community towards using and supporting PAT for concussion recovery given evidence that it is beneficial. These findings highlight the feasibility of collaborating with the sports community to examine this innovative therapeutic approach. Importantly, knowledge about psilocybin emerges as a crucial factor influencing willingness, underscoring the importance of future initiatives that focus on fostering discourse between the scientific and sports communities. In bridging the gap between the communities and working in a collaborative approach, researchers can work to address key barriers identified by both athletes and staff members. Overall, this study indicates that conducting clinical research with athletes suffering from SRC and PPCS is a valuable research endeavor.

Tables

Table 1

Characteristics of Participants.

Characteristic	Athlete Sample *n* (%) and/or *M* (*SD*)	Staff Sample *n* (%) and/or *M* (*SD*)	Full Sample *n* (%) and/or *M* (*SD*)
Age	85 (48.6%) / 28.73 (9.65)	90 (51.4%) / 32.21 (8.07)	175 / 30.52 (9.02)
Gender			
Male	59 (69.4%)	59 (65.6%)	118 (67.4%)
Female	24 (28.2%)	30 (33.3%)	54 (30.9%)
Other	2 (2.4%)	1 (1.1%)	3 (1.7%)
Marital Status			
Single	44 (51.8%)	32 (35.6%)	76 (43.7%)
Married	41 (48.2%)	57 (63.1%)	98 (56.3%)
Education			
High School	3 (3.5%)	1 (1.1%)	4 (2.3%)
Some college or university	24 (28.2%)	16 (17.8%)	40 (22.9%)
Bachelor's Degree	33 (38.8%)	45 (50.0%)	78 (44.6%)
Master's degree or equivalent	14 (16.5)	20 (22.2%)	34 (19.4%)
Doctoral degree or equivalent	9 (10.6%)	8 (8.9%)	17 (9.7%)
Certificate program	1 (1.2%)	0 (0.00%)	1 (.6%)
Other	1 (1.2%)	0 (0.00%)	1 (.6%)
Ethnicity[a]			
White	58 (65.2%)	46 (43.4%)	104 (59.4%)
Latinx/Hispanic	12 (13.5%)	16 (15.1%)	29 (16.6%)
Indigenous	14 (15.7%)	14 (13.2%)	28 (16.0%)
Black	1 (1.1%)	8 (7.5%)	9 (5.1%)
East Asian	2 (2.2%)	5 (4.7%)	7 (4.0%)
Filipino	1 (2.2%)	5 (4.7%)	7 (4.0%)
Southeast Asian	0 (0.00%)	5 (4.7%)	5 (2.9%)
South Asian	0 (0.00%)	3 (2.8%)	3 (1.7%)
West Asian or North African	0 (0.00%)	3 (2.8%)	3 (1.7%)
Middle Eastern	0 (0.00%)	1 (0.9%)	1 (.6%)
Country			
Canada	41 (48.2%)	33 (36.7%)	74 (42.3%)
USA	44 (51.8%)	57 (63.3%)	101 (57.7%)
Drug History			
Yes	53 (62.4%)	36 (40.0%)	89 (50.8%)
No	30 (35.3%)	52 (57.8%)	82 (46.8%)
Prefer not to say	2 (2.4%)	2 (2.2%)	4 (2.4%)
Regular Drug Use[a,b]			
Alcohol	27 (50.9%)	18 (52.9%)	45 (51.7%)

Cannabis	10 (18.9%)	10 (29.4%)	20 (23.0%)
Tobacco	8 (17.0%)	11 (32.4%)	19 (21.8%)
Smokeless Tobacco	1 (1.9%)	2 (5.9%)	3 (3.4%)
Opiates	1 (1.9%)	1 (2.9%)	2 (2.3%)
Psychedelics	4 (7.5%)	2 (5.9%)	6 (6.9%)
Stimulants	0 (0.00%)	2 (5.9%)	2 (2.3%)
Anabolic Steroids	2 (3.8%)	1 (2.9%)	3 (3.4%)
None	10 (18.9%)	8 (23.5%)	18 (20.7%)
Other (Ketamine)	1 (1.9%)	0 (0.00%)	1 (1.1%)
Sport Level[a]			
Recreational	41 (33.9%)	22 (16.1%)	41 (33.9%)
Club	26 (21.5%)	42 (30.7%)	26 (21.5%)
Collegiate/Varsity	37 (30.6%)	34 (24.8%)	37 (30.6%)
National	9 (7.4%)	17 (12.4%)	9 (7.4%)
Professional	8 (6.6%)	22 (16.1%)	8 (6.6%)
Concussion History			
Yes	48 (56.5%)		
No	34 (40.0%)		
Don't know	3 (3.5%)		
Number of Concussions[c]			
1	15 (17.6%)		
2	9 (10.6%)		
$\geq$3	22 (25.9%)		
Don't know	2 (2.4%)		
None	37 (43.5%)		
Number of Concussion Symptoms[c,d]			
1-4	31 (64.6%)		
5-9	13 (27.1%)		
$\geq$10	3 (6.3%)		
None	1 (2.0%)		
Number of Persisting Concussion Symptoms[c,d]			
1	22 (45.8%)		
2	9 (18.8%)		
$\geq$3	9 (18.8%)		
None	8 (16.7%)		

Note. [a] Participants could select more than one option, [b] Indicates questions responded to only by participants who reported using drugs or alcohol in the past year, [c] Indicates questions responded to only by athletes (n = 85), [d] Answered only by athletes with a history of concussion (n = 48).

Figures

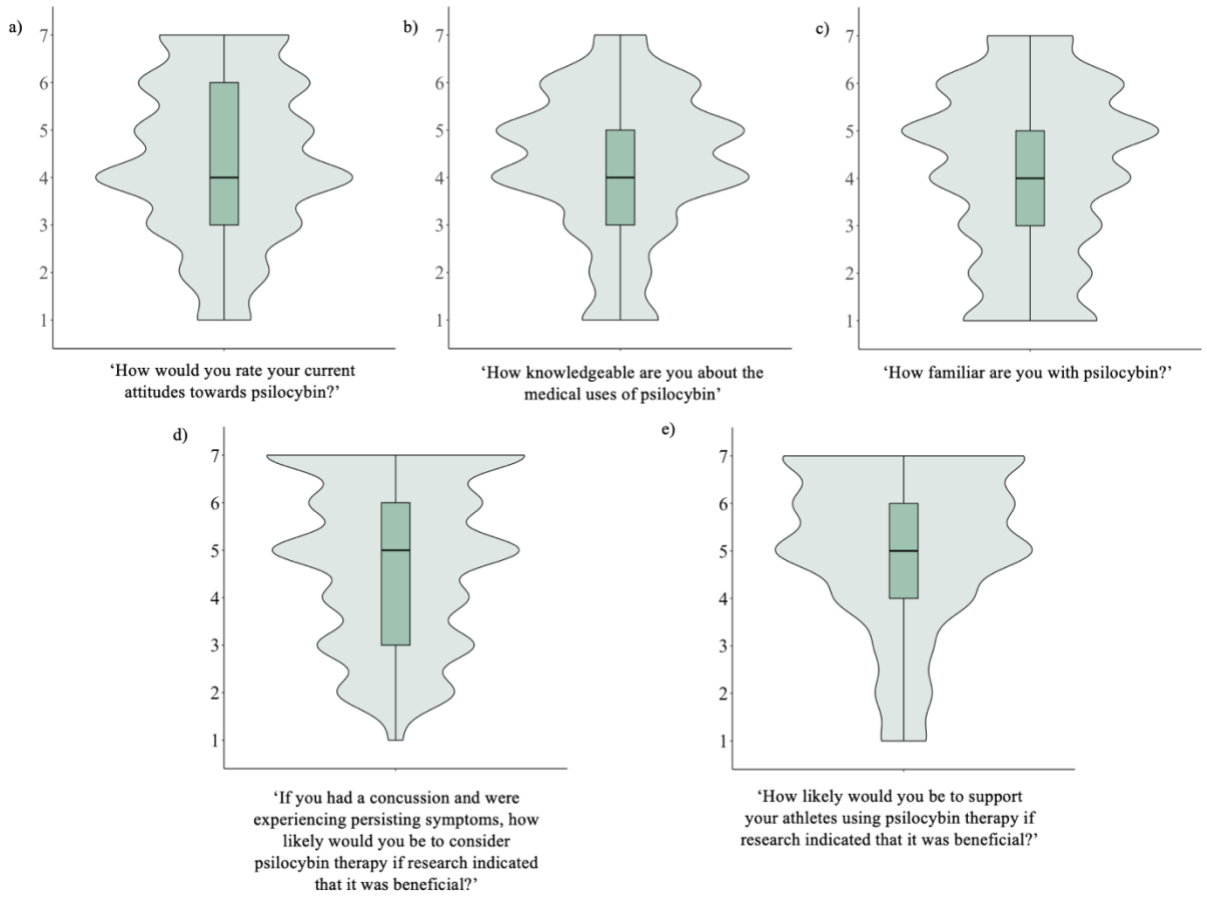

Figure 1. Violin plots displaying the density-based distribution of the Likert scale options for a) attitudes towards psilocybin, b) knowledge of psilocybin, c) familiarity with psilocybin, d) willingness to use PAT if you had a concussion (athletes only), and e) willingness to support athletes using PAT for concussion recovery (staff only). Each question was responded to according to a Likert scale ranging from 1 (lowest rating/agreement) to 7 (highest rating/agreement).

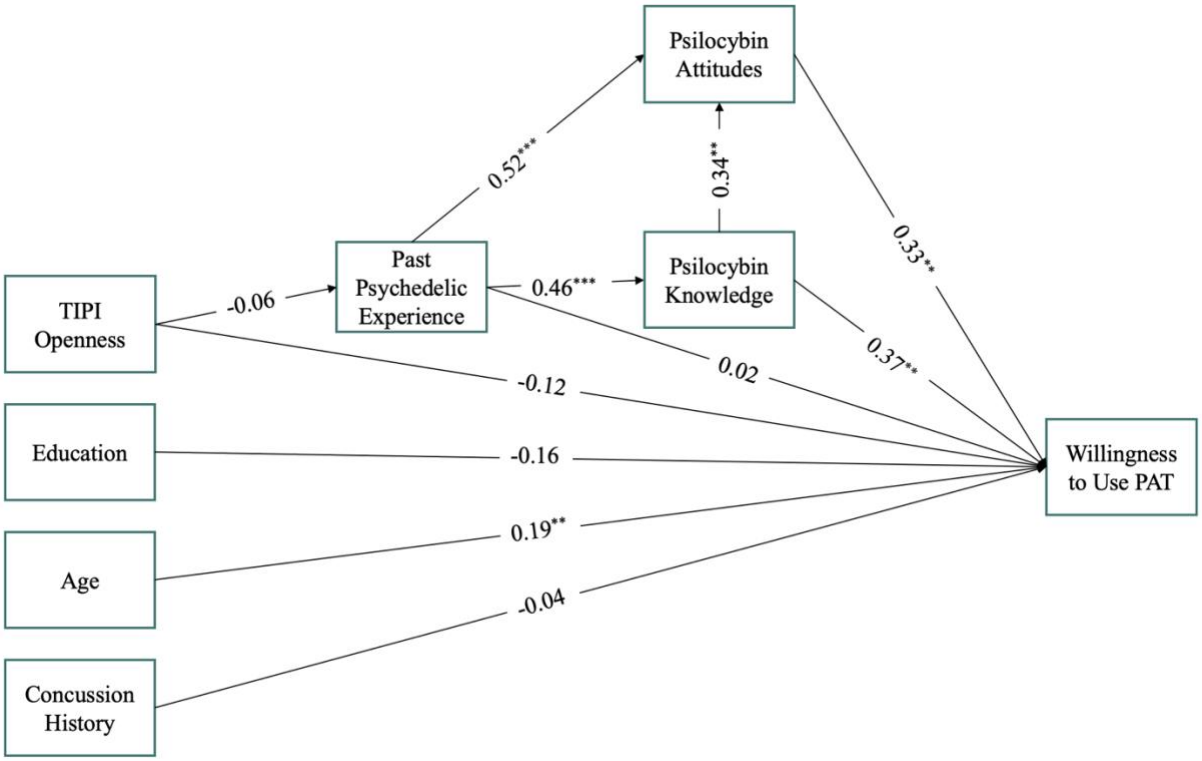

Figure 2. Path model with standardized coefficients for athletes. * indicates $p < .05$, ** indicates $p < .01$, *** indicates $p < .001$.

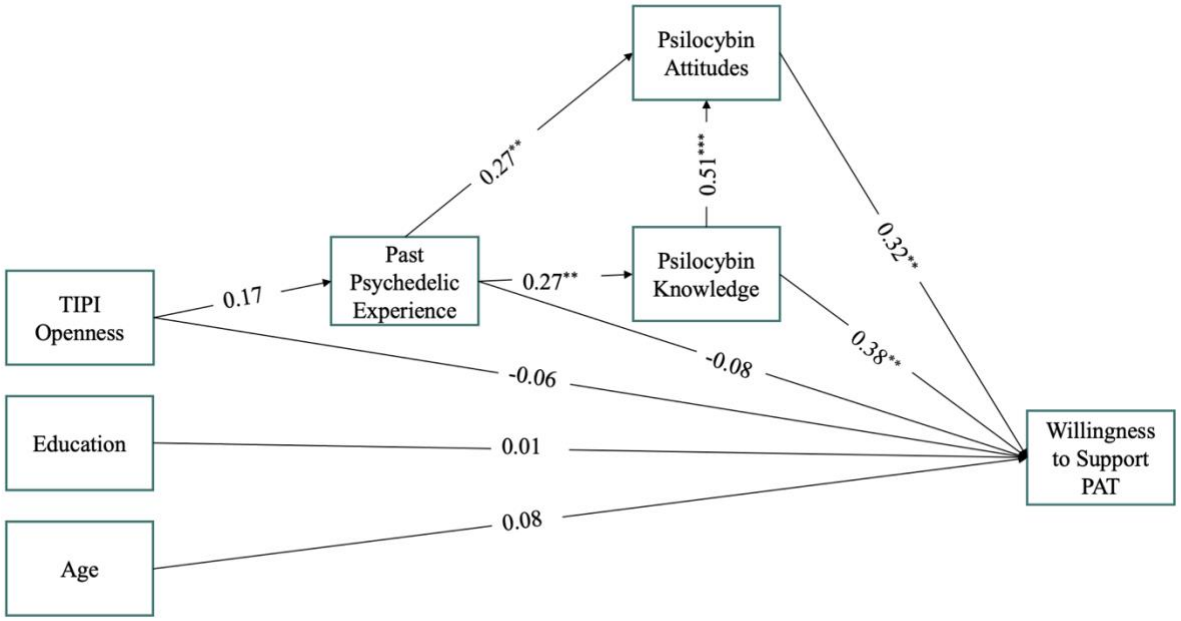

Figure 3. Path model with standardized coefficients for staff. * indicates $p < .05$, ** indicates $p < .01$, *** indicates $p < .001$.

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Supplemental Materials

Attitudes and Willingness Section Questions

(1) “Which of these two statements do you think is correct? Option A: Psilocybin is restricted under the World Anti-Doping Agency. Option B: Psilocybin is not restricted under the World Anti-Doping Agency;

(2) “How would you rate your current attitudes towards psychedelics?” [Likert scale];

(3) “Please rate the accuracy of this statement: I am knowledgeable about the medical uses of psilocybin” [Likert scale];

(4) “Please rate the accuracy of this statement: I currently think that there is benefit in examining the medical use of psilocybin for athletes with persistent concussion symptoms” [Likert scale];

(5) “Please rate the accuracy of this statement: I think that psilocybin is likely to be abused and addictive” [Likert scale];

(6) “Which of the following do you believe to be the most significant barriers to psilocybin therapy in athletes with persistent concussion symptoms? [Various provided options with optional textbox].

The following question was presented to team personnel only: (1) “If an athlete had a concussion and experienced persistent symptoms, would you support them using psilocybin therapy if research indicated that it could be beneficial?”

The following question was presented to athletes only: (1) “If you had a concussion and symptoms were persisting, would you consider psilocybin therapy if research indicated that it could be beneficial?” [Likert scale].

Likert scale options

1 = Completely unfamiliar/unfavourable/unwilling … 7 = Completely familiar/favourable/willing

Supplemental Table 1

Means, standard deviations, and correlations with confidence intervals for regression variables in staff model

Variable	*M*	*SD*	1	2	3	4	5	6
1. Age	32.21	8.07						
2. Education	3.20	0.88	**.26*** [.06, .45]					
3. Psilocybin Attitudes	4.50	1.61	.14 [-.07, .34]	.05 [-.16, .25]	**.42***** [.23, .58]			
4. Psilocybin Knowledge	4.42	1.52	.07 [-.14, .28]	-.02 [-.23, .19]	**.29**** [.09, .47]	**.59***** [.44, .71]		
5. Willingness to Support PAT	5.11	1.67	.17 [-.04, .37]	.03 [-.18, .24]	.13 [-.08, .33]	**.48***** [.31, .63]	**.49***** [.32, .63]	
6. TIPI Openness	4.35	0.87	**-.33***** [-.51, -.13]	-.12 [-.32, .09]	.16 [-.04, .36]	.00 [-.21, .21]	-.04 [-.25, .17]	-.11 [-.31, .10]

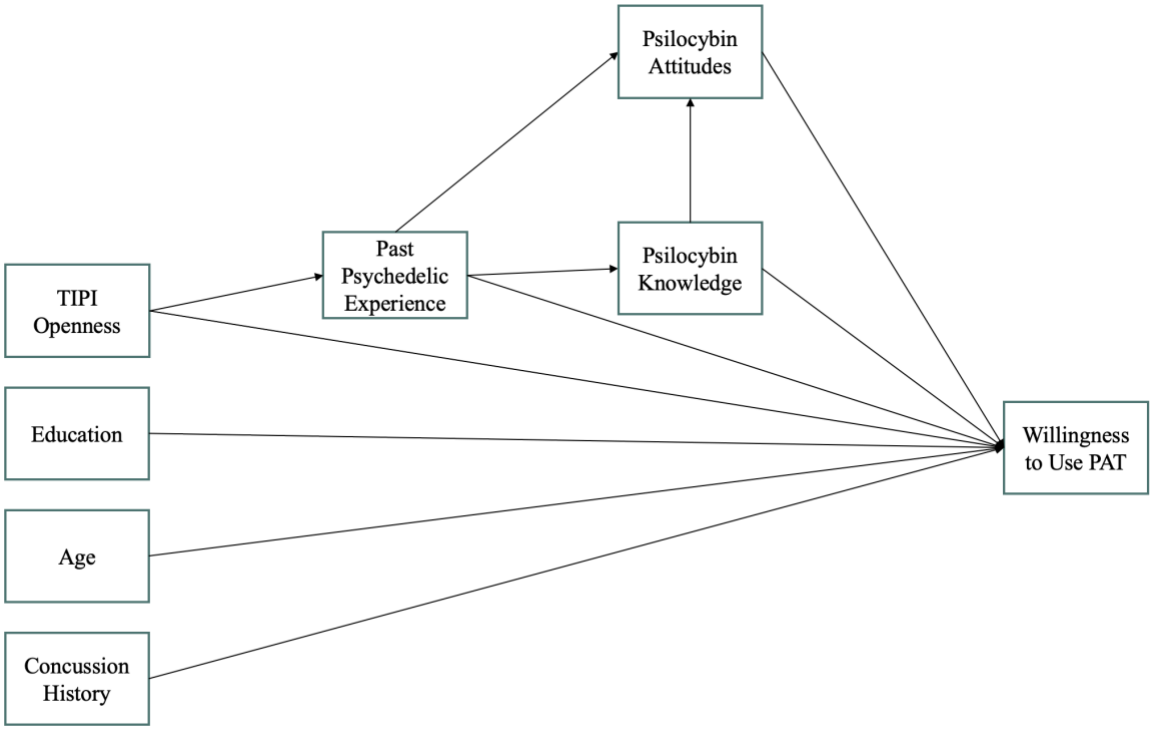
Note. M and *SD* are used to represent mean and standard deviation, respectively. Values in square brackets indicate the 95% confidence interval for each correlation. The confidence interval is a plausible range of population correlations that could have caused the sample correlation (Cumming, 2014). * indicates $p < .05$. ** indicates $p < .01$. *** indicates $p < .001$. TIPI = Ten-Item Personality Inventory. PAT = Psilocybin-Assisted Therapy.

Supplemental Table 2

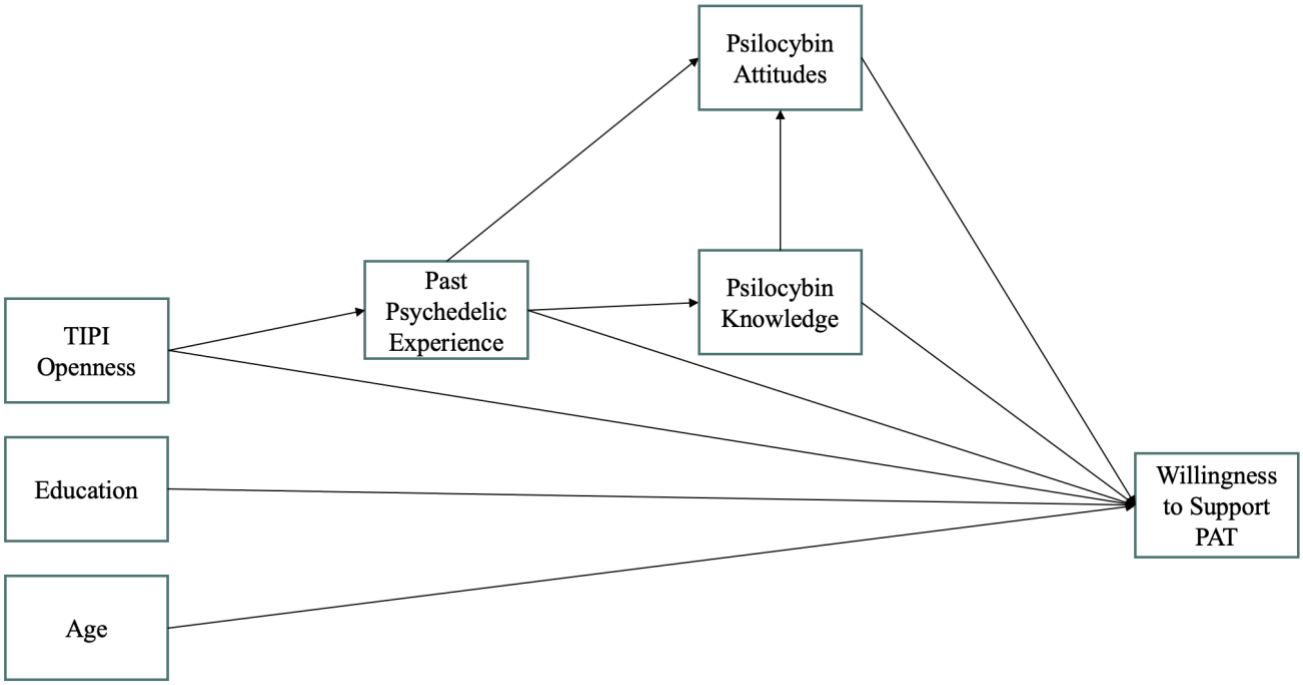
Means, standard deviations, and correlations with confidence intervals for regression variables in athlete model

Variable	*M*	*SD*	1	2	3	4	5	6
1. Age	28.67	9.61						
2. Education	3.12	1.14	.21 [-.00, .41]					
3. Number of Concussions	2.94	2.27	-.05 [-.34, .24]	-.14 [-.41, .16]				
4. Attitudes	4.29	1.72	.04 [-.17, .25]	-.06 [-.27, .15]	.36* [.08, .59]			
5. Knowledge	4.06	1.60	-.16 [-.36, .06]	-.06 [-.26, .16]	.08 [-.21, .36]	.58** [.42, .70]		
6. Willingness	4.83	1.72	.10 [-.12, .30]	-.19 [-.39, .02]	.03 [-.26, .31]	.58** [.41, .70]	.56** [.39, .69]	
7. TIPI Openness	4.38	0.77	.00 [-.21, .21]	-.01 [-.22, .20]	.06 [-.23, .34]	.09 [-.12, .30]	.06 [-.16, .27]	-.06 [-.27, .16]

Note. M and *SD* are used to represent mean and standard deviation, respectively. Values in square brackets indicate the 95% confidence interval for each correlation. The confidence interval is a plausible range of population correlations that could have caused the sample correlation (Cumming, 2014). * indicates $p < .05$. ** indicates $p < .01$. TIPI = Ten-Item Personality Inventory. PAT = Psilocybin-Assisted Therapy.



Supplemental Figure 1. Theoretical path model for athletes.



Supplemental Figure 2. Theoretical path model for staff.

Chapter Four: Discussions and Future Directions

Scoping Review Outcomes

The results of the scoping review offered valuable insights to our team when considering examining psilocybin's role in concussion recovery. The chief concern for this novel treatment approach is that we are intending to work with a clinical population that can suffer lasting cognitive impairments as a result of their brain injury. As such, it is paramount to be cognizant of any cognition-related effects that psilocybin may have, particularly detrimental effects. Therefore, it was necessary to first examine the current published literature with human participants to determine if the research suggests any trends in cognitive functioning when participants have been administered psilocybin. We found that, across the 42 included studies, psilocybin does not appear to impair cognitive functioning long-term. Importantly, psilocybin was found to be well-tolerated across studies, but it is worthwhile noting that only 26% of studies explicitly discussed safety outcomes. Our review did identify that some cognitive impairment can occur acutely, but importantly that these impairments are often minor and do not persist. Some examples of acute cognitive impairment included reduced reaction time and attention, which again returned to normal after the intoxication phase had passed. However, it is important to note that many of these studies worked with healthy populations and there were few studies which examined long-term outcomes. Despite these limitations, it is still reassuring that the existing literature suggests that psilocybin does not show any strong adverse effects on cognitive functioning and these outcomes provided a basis for moving forward with the survey study. Because our initial findings suggest that psilocybin is both safe and does not impair cognitive performance, the survey allowed us to address the second primary concern; that is, are athletes willing to use psilocybin for concussion recovery and PPCS *and* are staff members

willing to support their athletes through this treatment approach given that evidence suggests it is beneficial?

Discussion of Survey Results

This thesis provides the first in-depth discussion of the use of psilocybin for SRC and PPCS in athletes. Using an online survey approach, this study successfully addressed all three research questions: The first objective of this thesis was to describe the current patterns of psychedelic use and concussion rates in a sample of athletes. The second objective of this thesis was to examine the attitudes and beliefs of the sports community towards psilocybin. The final objective was to query the willingness of athletes to use PAT for concussion recovery/PPCS and the willingness of sports team staff to support athletes using PAT. Given the theoretical proof of concept discussed in Chapter 1, the purpose of the empirical study was to determine whether the sports community would be open to this examination of psilocybin as a novel treatment approach for concussion recovery and symptom management. This area of research is necessary and relevant prior to initiating clinical research on this topic to gauge the interest of the sports community (Walton & Liknaitzky, 2022) and will offer substantial direction to future researchers.

To my knowledge, the results of this survey provide the most comprehensive and thorough examination of psychedelic use among athletes across levels of competition to date (Walton & Liknaitzky, 2022), and thus, we hope these results offer valuable information to researchers who intend to pursue this line of research with athletes and is generally informative of substance use among athletes in Canada and the US across levels of competition. Concordant with current research, we found that alcohol and cannabis continue to be the most consumed substances among athletes (Exner et al., 2021; McDuff et al., 2019). The only published study to include

psychedelics as a drug category found that 5.6% of NCAA athletes reported using psychedelics in the past 12 months (Green et al., 2001). Of the athletes in our sample that reported playing at the collegiate or varsity level, 10.8% reported using psychedelics within the past year. These findings may suggest that psychedelic use is on the rise in athletes, particularly collegiate, which is not surprising given the psychedelic renaissance that society and research are experiencing. In their study, Green et al. (2001) found that the majority of athletes using psychedelics did so for recreational/social purposes and/or because it 'made them feel good'. Alternatively, many of our athletes reported using psychedelics to enhance their mood or for personal well-being/improvement. However, these findings are not surprising given that most media and research currently emphasizes the use of psilocybin and other psychedelics for mood and personal enhancement (Barrett et al., 2020; Davis et al., 2021; Teixeira et al., 2022). While some athletes did use them for concussion symptoms, these represented a small minority. Given that very few studies have discussed the potential use of psychedelics in brain injury, it was expected that few athletes would currently be experimenting with them for such purposes.

Importantly, we identified that most athletes in the present sample had sustained a concussion at some point in their life and the majority of these athletes had suffered three or more concussions. Moreover, 90% of the athletes who reported concussions said they had been diagnosed by a physician. Of athletes who reported a concussion history, 83.3% experienced at least one persisting symptom. While the use of a survey approach does not allow us to formally define persisting post-concussion symptoms in our sample, we can describe the frequency which symptoms appear to persist past returning to sport. These results indicate that many athletes engage in sports despite the continuance of their concussion symptoms which may worsen long-term outcomes. Therefore, given the rate of persisting symptoms, and the number of cognitive

symptoms that persist, research must consider the utility of psilocybin in PPCS recovery. Moreover, research suggests the PPCS treatment may benefit from multimodal approaches (Art et al., 2023; Haider et al., 2021). While psilocybin research is often combined with therapy, other lines of consideration include physical therapy interventions such as sub-symptom aerobic exercise (Art et al., 2023; Haider et al., 2021).

Our study described a high level of willingness to use or support PAT for SRC and PPCS, which offers important implications to the development of clinical research and to assess the feasibility of this research. Additionally, by understanding the leading concerns regarding PAT among athletes and staff, researchers can work to address these concerns via animal models and research with healthy and clinical populations. For example, research may examine the long-term impacts of psilocybin administration in healthy animal models and TBI models. Long-term outcomes should examine effects on mood, overall health, brain health, and cognitive performance. A central finding from this study is the important relationship between knowledge of psilocybin and willingness to engage in or support PAT. This study highlights the overall necessity of expanding knowledge dissemination regarding safety, clinical utility, and therapeutic effects of psilocybin to the sports community. Unexpectedly, it was found in our sample that trait openness was not related to willingness to use or support PAT, nor was it related to past psychedelic use. These outcomes are in conflict with previous work which suggests that lifetime psychedelic use is related to trait openness (Cavanna et al., 2021). However, these findings may be encouraging as this indicates that willingness to engage in or support PAT is not personality trait dependent, but rather it is heavily dependent on knowledge of and attitudes towards psilocybin. Therefore, anyone may be willing to engage in PAT if they are properly informed and educated on the safety, outcomes, and overall expectations of PAT.

Important results of the empirical study also involve the perceived barriers to implementing PAT voiced by athletes and staff. By understanding what athletes and staff consider to be the most substantial barriers, researchers can determine next steps in research and the overall feasibility of implementing PAT for concussion recovery. Interesting dynamics were identified from this survey question; while both athletes and staff identified uncertainty regarding long-term effects as the most substantial barrier, stigma from staff was the second most identified barrier. Alternatively, the second most frequent concern among staff was legal access to PAT. These athlete concerns may stem from societal stigma regarding the use of psychedelics, particularly as an athlete. Staff, however, appeared to be primarily concerned about logistical implementation of PAT for athletes. Logistical concerns may include long-term effects as well as legal accessibility and practical implementation in a sports context.

Future Directions

In considering future research directions, it is again worth noting that researchers, clinicians, and clients (i.e., athletes with concussions) place great importance on research that is examining rehabilitation and managing both acute symptoms and PPCS and have explicitly called for more research in these areas (Osmond et al., 2023; Patricios et al., 2023). While novel, PAT has the potential to address these priorities; moving forward, it is recommended that researchers use our findings from the scoping review and the empirical study to direct future research directions and begin engaging with the sports community. Important future examinations should work to examine more long-term outcomes of psilocybin use in clinical populations, particularly those with mTBI, on cognitive functioning. This would also address those concerns highlighted by our respondents that long-term outcomes are an important consideration for those who intend to engage in or support PAT.

While this is only one of a few pieces suggesting that there is room for psychedelics in athlete mental health care (Walton & Liknaitzky, 2022), as more current and former professional athletes discuss their personal use of psychedelics for mental health considerations, it is only natural that the field of psychedelic research will begin to incorporate the sports community. With recent reviews and commentaries discussing the role of psychedelics for brain injuries, it is expected that athletes with concussions will become a population of interest, given their increased risk of neuropsychological impairment. Research continues to assess the long-term cognitive impact of repeated concussions in athletes, such as increased risk of chronic traumatic encephalopathy (CTE), mild cognitive impairment and other neurodegenerative diseases (NDs) such as Alzheimer's disease (Bellomo et al., 2022; Ledreux et al., 2020; LoBue et al., 2020; Misquitta et al., 2018). It is, then, worth noting that over one third of our sample suffered two or more concussions. With poor concussion reporting among athletes, repeated concussions may occur more frequently.

CTE is considered to be a progressive ND that is unique to athletes who have sustained significant and repeated concussions (Stern et al., 2011). However, some researchers argue that it does not consist of a unique neuropathology nor does it affect only athletes; in fact, some researchers contest the existence of CTE at all (Iverson et al., 2019, 2023). While there is yet to be a strong consensus regarding the validity of CTE, it is worth noting that athletes who were eventually diagnosed with CTE typically presented with a number of physiological, cognitive, and behavioural symptoms (Galgano et al., 2016). These symptoms may vary in severity, but often include erratic behaviours, irritability, emotional distress, anxiety, suicidal or self-harm behaviours, confusion, and memory loss (Galgano et al., 2016). These symptoms have also been

reported in former athletes with concussion histories who have been diagnosed with Alzheimer's disease, Parkinson's disease, and mild cognitive impairment (Bellomo et al., 2022).

These types of symptoms are those that psychedelic therapy may help target and manage. Future research may study the effects of acute psilocybin administration, such as preventing the onset of such symptoms in the long-term as well as administering psilocybin to patients with a history of brain injury to manage present symptoms. While researchers are already considering the utility of psilocybin for NDs (Kozlowska et al., 2022) and believe that psilocybin may assist in managing the behavioural and psychological symptoms of these diseases (Garcia-Romeu et al., 2021; Saeger & Olson, 2022), the additional background of repetitive brain injury in athletes separates them from other ND patients and control patients. In athletes with repetitive brain injuries, NDs are thought to occur due to continued and significant cell death which subsequently leads to brain-wide atrophy in regions such as the hippocampus, amygdala, and frontal lobe (Asken & Rabinovici, 2021). As mentioned in Chapter 1, this may be a therapeutic target for psilocybin – that is, by managing cell death and subsequent atrophy in these regions, psilocybin may be able to offer some symptom relief or prevention in areas of cognitive function and mood. Other proposed mechanisms include synaptogenesis and modulating neuroinflammation, targeting two key pathologies of a number of NDs, neuropsychiatric disorders (Saeger & Olson, 2022) as well as SRCs (Giza & Hovda, 2014).

While some researchers have already proposed the use of psilocybin for NDs *or* for brain injury, it is this athlete population that often suffers subsequent ND-like pathology and impaired neuropsychological functioning that is a novel area of research that has not yet been examined. As research shows that almost 90% of former National Football League (NFL) players are diagnosed with CTE post-mortem (Mez et al., 2017), the impact of repetitive brain injury on

athletes cannot be overlooked and this area of research is strongly encouraged in the next steps in the psychedelic renaissance.

Conclusions

Using psilocybin as a concussion recovery aid and in the management of PPCS has the potential to offer significant relief to athletes with SRCs, particularly in domains of cognitive functioning and mood regulation. As identified in our scoping review, current research suggests that clinicians and patients do not need to be concerned about long-term cognitive outcomes from psilocybin therapy, but more research on this topic is encouraged. These promising findings allowed us to move forward with the descriptive online survey and while this did not involve directly examining psilocybin's effects on athletes with concussions, the importance of this simple survey study lies in the potential to inspire future research and advancements which may transform the treatment of mTBI, particularly sports concussions. Because we have demonstrated willingness within the sports community to use (by athletes) and support (from coaches) PAT for concussion recovery and PPCS, the natural next step is to engage in proactive discussions with the sports community and offer knowledge dissemination on the potential utility of this proposed treatment. Concurrently, researchers should begin engaging athletes in well-designed RCTs to examine psilocybin's effects on concussion symptoms and conduct long-term assessments of psilocybin's effects both therapeutically but also on important domains such as cognition and mood.

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