

Positive Clinical Psychology & Technology – Master of Science

Psilocybin Use and its Effect on Well-being in Healthy Individuals– A Scoping Review

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Abstract

Introduction: Research in the field of positive psychology posits that only a small part of the general population exhibits complete mental health, also referred to as “flourishing”. Therefore, novel interventions to promote well-being are needed. A growing body of evidence suggests that psilocybin, a psychoactive compound that induces mind-altering effects, can evoke long-lasting increases in well-being. This scoping review employed a multifaceted conceptualization of well-being, to examine how psilocybin use affects well-being and related sub-concepts in healthy individuals. Moreover, it was investigated which factors influence the relation between psilocybin use and well-being, what research protocols have been employed and what underlying mechanisms have been proposed in existing studies.

Methods: A comprehensive literature search in line with the PRISMA guidelines was conducted. Scopus, PubMed, PsycInfo, Web of Science, and Google Scholar were searched for peer-reviewed articles about psilocybin and well-being.

Results: Studies were rather heterogenous in regard to study objectives, study design, study procedure, sample size and psilocybin dosage. Eight experimental studies, one follow-up study, two cross-sectional survey studies, and one qualitative interview study were included in the review. In all studies, psilocybin use led to positive well-being-related outcomes for the majority of participants. Self-acceptance, positive relationships and meaning/purpose in life were facets of this studies’ well-being conceptualization that seemed to be particularly positively affected by psilocybin use. In studies that ensured psychological screening and preparation, physical comfort, social support and an appropriate dosage of psilocybin, adverse effects were rarely reported.

Discussion: This scoping review provided preliminary evidence for beneficial effects of psilocybin on well-being and related sub-concepts such as self-acceptance, positive relationships and meaning/purpose in life. Ego-dissolution, unity, connectedness, and mystical-type experiences are interrelated concepts that seem to be crucial for explaining such positive well-being-related effects of psilocybin. Future research should employ more diverse samples, comprehensive well-being measures and rigorous double-blind, placebo-controlled, crossover experimental designs with standardized dosages. Under conducive conditions, the use of psilocybin may contribute to healthy human functioning, through broad and sustained improvements in a variety of well-being concepts.

Introduction

Problem Statement

Although a large part of the global population is not formally diagnosed with a clinical disorder, it is widely acknowledged nowadays that the absence of mental health disorder does not automatically imply positive mental health (Lamers, Westerhof, Bohlmeijer, Ten Klooster, & Keyes, 2010). According to Keyes (2002), complete mental health, also referred to as “flourishing”, not only comprises the absence of mental illness but also the presence of positive emotions and adaptive psychological and social functioning. In the United States, for example, only 20% of the adult population can be categorized as flourishing (Keyes, 2005). This underscores the need for novel interventions to promote well-being in a sustainable and efficient manner among the general population.

In this regard, an approach to increase well-being that has seen a resurging research interest particularly in the past decade is the use of psychedelic drugs. Such substances have the ability to induce profound mystical or spiritual experiences, with potentially transformative effects (Else, 2017). For psilocybin, one of the most widely researched psychedelic drug, there is a growing body of evidence suggesting that the use of this substance can potentially result in a long-lasting increase in well-being, life satisfaction, meaning in life, and general healthy psychological functioning (Gandy, 2019). This study seeks to give an overview on the current state of research on the effect of psilocybin on well-being in healthy individuals, employing a multifaceted conceptualization of well-being.

What Is Psilocybin?

Psilocybin is a psychoactive compound that can induce psychedelic effects (Griffiths, Richards, McCann, & Jesse, 2006). It is a tryptamine alkaloid that naturally occurs in a variety of Psilocybe mushroom species, also known as *magic mushrooms*. The substance exerts its effects mainly through agonist activity at the serotonin 5-HT_{2A} receptors (Gandy, 2019; Johnson, Hendricks, Barrett, & Griffiths, 2019). Along with lysergic acid diethylamide (LSD), mescaline and N,N-dimethyltryptamine (DMT), psilocybin is a classic psychedelic, which is defined as “a drug which, without causing physical addiction, craving, major physiological disturbances, delirium, disorientation, or amnesia, more or less reliably produces thought, mood, and perceptual changes otherwise rarely experienced except in dreams, contemplative and religious exaltation, flashes of vivid involuntary memory, and acute psychosis.” (Grinspoon & Bakalar, 1979, p. 9). After 30 minutes upon ingestion of psilocybin, the psychedelic state, also called *psychedelic trip*, commences and usually last around three and a

half hours, depending on the dose (Araújo, Carvalho, Bastos, Guedes de Pinho, & Carvalho, 2015). During the acute experience, significant mind altering effects can take place, also referred to as an altered state of consciousness (ASC; Studerus, Kometer, Hasler, & Vollenweider, 2011).

This state constitutes profound changes in various perceptual modalities, mood, and cognition (Griffiths et al., 2006) and may result in a *complete mystical experience* also called *psychedelic peak experience* (Majić, Schmidt, & Gallinat, 2015). In therapeutic contexts, psilocybin is usually administered in a small number of high-dose psychedelic dosing sessions (Garcia-Romeu & Richards, 2018). After the acute effects of psilocybin subside, individuals may experience a state of elevated mood, enhanced interpersonal connection as well as decreased worry, stress, and anxiety; a phase commonly known as the *psychedelic afterglow* (Pahnke, 1969). These effects usually vanish after two to four weeks, but long-term beneficial effects may persist (Majić et al., 2015).

A Brief History of Psychedelic Use

From a historical perspective, naturally occurring serotonergic psychedelics have been used for centuries and are considered the oldest recreational drug, dating back to prehistoric time (Bruhn, De Smet, El-Seedi, & Beck, 2002). Psilocybin, for example, has been consumed by the Aztecs in religious healing ceremonies (Nichols, 2016). The substance was brought into the Western world by the American banker and amateur mycologist R. Gordon Wasson, who travelled to Mexico in order to document the traditional indigenous use of psilocybin mushrooms in 1955 (Johnson et al., 2019). By the end of the 1960s, hundreds of studies had explored the therapeutic potential of psilocybin and other classical psychedelic drugs such as LSD, DMT and mescaline (Grinspoon & Bakalar, 1981). Soon after, however, classical psychedelic drugs began to be taken recreationally in uncontrolled settings. They became heavily associated with the countercultural movement of the 1960s, and were depicted as dangerous drugs of abuse (Rucker, Iliff, & Nutt, 2018; Studerus et al., 2011). Consequently, psychedelics were placed in Schedule 1 of the United Nations (UN) Convention on Drugs in 1967, legally defining them as having no accepted medical use and the maximum potential for harm and dependence. Following their prohibition in most countries of the world, clinical research into the medical use of these substances soon ceased (Rucker et al., 2018).

Nowadays, psychedelic research is surging, with a renewed interest into clinical applications of these substances. This psychedelic renaissance was to a large part reignited in 2006, when the first modern clinical trial with psilocybin in healthy individuals was conducted

(Griffiths et al., 2006). Since then, psilocybin has been successfully utilized in numerous randomized controlled trials for treating a variety of psychiatric disorders, including depression and anxiety associated with terminal cancer (Ross et al., 2016), obsessive compulsive disorder (Moreno, Wiegand, Taitano, & Delgado, 2006), tobacco use disorder (Garcia-Romeu, Griffiths, & Johnson, 2014), alcohol use disorder (Bogenschutz et al., 2015), treatment-resistant depression (Carhart-Harris et al., 2016) and major depressive disorder (Carhart-Harris et al., 2021; Davis et al., 2021). As a consequence of promising results, the United States Food and Drug Administration granted “breakthrough therapy” status to the use of psilocybin for treatment-resistant depression (Reiff et al., 2020). However, the revival of interest in psychedelics has not been limited to its application for the treatment of psychiatric disorders. Modern era clinical trials have also explored the potential application of psilocybin in healthy individuals (e.g., Griffiths et al., 2006; Kometer et al., 2012; Kraehenmann et al., 2015; Rucker et al., 2022; Wittmann et al., 2007). Such research has been conducted with the aim to study neuropharmacological mechanisms related to time perception, emotional processing, or cognitive functioning and to examine acute and long-lasting psychological effects.

Neurobiological Mechanism of Psilocybin

In order to get a better understanding of the psychological effects of psilocybin, it is useful to first consider the neural underpinnings and pharmacology of psychedelic states. Psilocybin and other classical psychedelic drugs mainly exert their effects at the serotonin 5-HT_{2A} receptor, where they act as agonists and thus stimulate the receptor (Nutt, 2019). An fMRI study investigating the neural correlates of the psychedelic state showed that the main effect of psilocybin is to decrease brain blood flow and blood oxygen level-dependent (BOLD) activity predominantly in the default mode network (DMN; Carhart-Harris et al., 2012). The DMN is a network of brain regions associated with metacognitive thinking, with reflecting on the past and future, and with mind wandering (Carhart-Harris et al., 2014). Interestingly, the connectivity of this network seems to be crucial for sustaining normal waking consciousness on the one hand, but it also limits conscious experience as it possibly restricts alternative brain states on the other hand (Carhart-Harris et al., 2014). Narrowed, internalized mental states are a key shared feature of a range of conditions that have been treated with psilocybin such as affective disorders or addiction (Nutt, Erritzoe, & Carhart-Harris, 2020). During a psychedelic experience, an entropic brain state is induced, the integrity of communication between brain regions of the DMN seems to be decreased and brain networks that usually function more independently are increasingly connected (Carhart-Harris et al., 2017; Tagliazucchi et al.,

2016). This leads to a compromised modular, but enhanced global brain connectivity, which is argued to allow individuals to think in new ways (Carhart-Harris et al., 2014). Furthermore, a recent study found that the pattern of increased connectivity across brain networks is sustained one month post-psilocybin use (Barrett, Doss, Sepeda, Pekar, & Griffiths, 2020).

A Multidimensional Conceptualization of Well-being

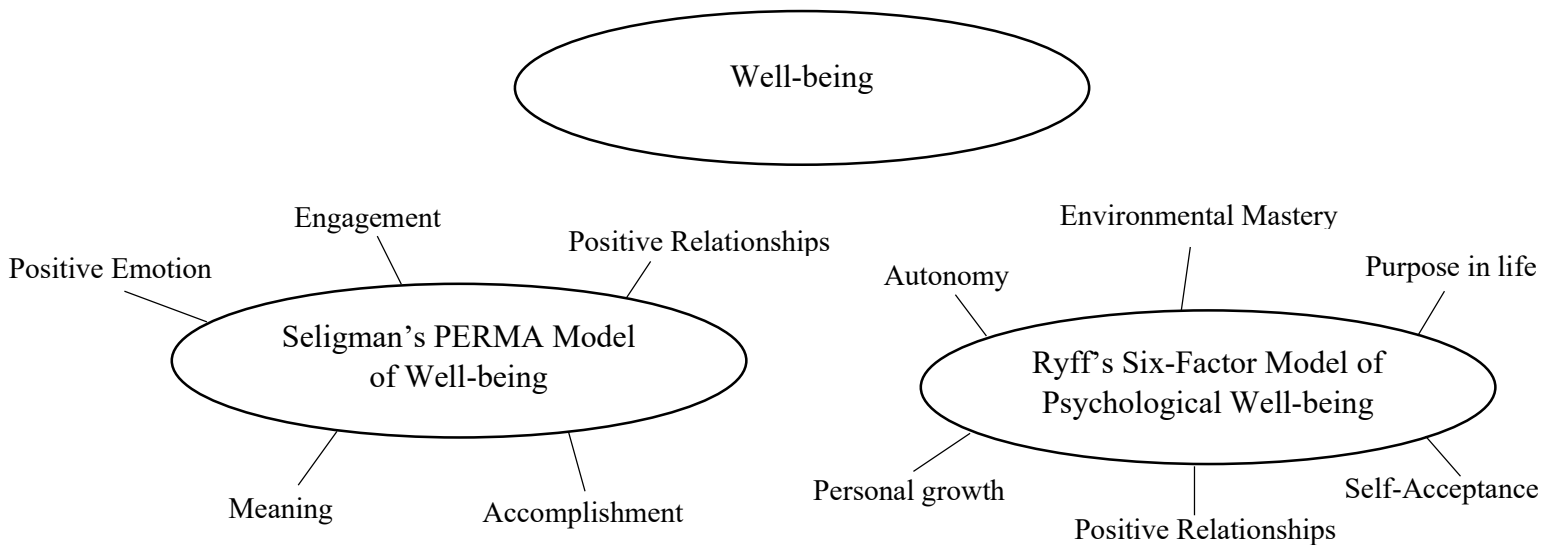
In order to examine how psilocybin can affect well-being, a clear conceptualization is first needed, since a variety of approaches to defining well-being exist in the literature, and a unified definition of the concept is lacking (Dodge, Daly, Huyton, & Sanders, 2012).

Generally speaking, it can be said that two opposing philosophical traditions rooted in ancient Greek philosophy are mainly relevant for today's conceptualizations of well-being: hedonism and eudaimonism (Ryan & Deci, 2001). In the hedonic view, well-being is equated with pleasure, comfort, and enjoyment. In the eudaimonic view, it is equated with pursuing meaningful goals and common good by means of exercising one's personal virtues and potentials (Delle Fave, Massimini, & Bassi, 2011). Most contemporary psychological models posit that well-being is constituted of both hedonic and eudaimonic components (Wagner, Gander, Proyer, & Ruch, 2019).

Two prominent and widely applied theories of well-being are the PERMA model by Martin Seligman, and the Six-Factor Model of Psychological Well-being (Ryff, 1989; Seligman, 2011; see Figure 1).

Figure 1

A Conceptualization of Well-being Informed by Seligman's PERMA model of Well-being and Ryff's Six-Factor Model of Psychological Well-being



The name of the PERMA model stems from the five elements that well-being consists of according to Seligman (2011), namely *positive emotion*, *engagement*, *positive relationships*, *meaning*, and *accomplishment*. *Positive emotion* is directly linked to related concepts such as happiness and life satisfaction. It is seen as the hedonic component of well-being (the “pleasant life”). It encompasses pleasurable emotions such as pleasure, rapture, ecstasy, comfort and warmth that are commonly referred to as subjective well-being. *Engagement* is about being in flow and the loss of self-consciousness during an absorbing activity (the “engaged life”). It means living in the present moment and focusing entirely on the here-and-now. *Relationships* encompasses feeling supported, loved and valued and having positive interactions with significant others. *Meaning* refers to the feeling of belonging to and serving something greater than oneself (the “meaningful life”). It may be pursued in various ways, for example through a profession, religion, creative endeavors, or political commitment. *Accomplishment* (or achievement) is referred to a sense of mastery and competence (the “achieving life”). It involves the concepts of perseverance and attaining goals.

According to the Six-Factor Model of Psychological Well-being, the six factors contributing to a person's psychological well-being are *self-acceptance*, *positive relationships with others*, *autonomy*, *environmental mastery*, *purpose in life*, and *personal growth*. *Self-acceptance* involves holding positive attitudes towards oneself. The concept of *positive relationships*, similar to Peterson's conceptualization, emphasizes the importance of warm and trusting relationships. *Autonomy* refers to qualities of independence, self-determination and

regulating behavior independent of social pressure. *Environmental mastery* involves being able to manage one's environmental factors and activities such as everyday affairs, to create situations that benefit personal needs, and to make effective use of opportunities. *Purpose in life*, similarly to Seligman's concept of meaning, encompasses a sense of directedness and a conviction that life holds meaning. Lastly, *personal growth* can be described as continually developing one's potential and welcoming new experiences. These two models serve as a useful basis for a multidimensional conceptualization of well-being which can be employed to investigate in what way well-being is affected by the use of psilocybin.

Psilocybin - Action Mechanisms and Positive Effects on Well-being

Despite the fact that several recent studies point towards a positive effect of psilocybin on well-being and its related sub-concepts (Carbonaro et al., 2016; Griffiths et al., 2018; Griffiths et al., 2011; Griffiths, Richards, Johnson, McCann, & Jesse, 2008; Griffiths et al., 2006; Haijen et al., 2018; Mans et al., 2021; Mason, Mischler, Uthaug, & Kuypers, 2019; Nicholas et al., 2018; Smigielski et al., 2019), the underlying action mechanisms are not fully understood (Andersen, Carhart-Harris, Nutt, & Erritzoe, 2021). In the early literature, it has been proposed that its positive effects are strongly tied to the ability of the substance to yield mystical-type experiences and profound existential insights (Pahnke, 1969). The concept of mystical-type experiences stems from Stace's (1960) work on mysticism, and is closely linked to virtually synonymous concepts of "spiritual", "religious", or "peak" experiences, which have been studied and conceptualized by a number of researchers (MacLean, Leoutsakos, Johnson, & Griffiths, 2012; Maslow, 1959; Pahnke & Richards, 1966).

Stace (1960) describes the concept of a mystical experience as being composed of (1) feeling a sense of internal unity, the feeling of becoming one with all existing objects and persons, (2) a sense of sacredness, (3) a noetic quality, meaning that the experience is perceived as an encounter with ultimate reality, (4) a positive mood (feelings of awe, joy, and ecstasy), (5) transcendence of time and space, and (6) ineffability, meaning that the experience cannot be easily put into words. Pahnke's (1969) proposition seems to be supported by more recent studies as well, indicating that psilocybin use can lead to profound personal insights, which have the potential to provoke sustained positive changes in personality, attitudes, and values, and can lead to increased self-compassion, purpose in life, connectedness with oneself, others, and the world (e.g. Smigielski et al., 2019; Studerus et al., 2011; Watts, Day, Krzanowski, Nutt, & Carhart-Harris, 2017).

In one of the most prominent clinical trials investigating the effect of psilocybin in healthy individuals, Griffiths and colleagues (2006) employed a rigorous double-blind design to show that high-dose psychedelic experiences can reliably produce meaningful psychological experiences. The researchers administered psilocybin to healthy individuals with interest in spiritual practices and found that two months after the session, 67% rated their psychedelic experience to be among their most meaningful and spiritually significant event of their lives. Even after 14 months, about two-third of the participants still rated the experience as the most meaningful one of their lives and felt a persisting increased sense of well-being and life satisfaction (Griffiths et al., 2008). Participants also attributed sustained positive changes in prosocial attitudes and behavior to their experience, which was confirmed by community observer ratings.

Another study that examined retrospective survey data from individuals that had used psilocybin in the past year found that having a mystical experience was linked to high scores in positive changes such as increased gratitude and empathy, and low scores in negative changes such as anxiety (Russ, Carhart-Harris, Maruyama, & Elliott, 2019).

Similarly, in a survey of first-time psychedelics users in Finland, it was found that those with mystical experiences reported significantly more overall positive changes, especially pertaining to one's creativity and relation with nature and oneself (Kangaslampi, Hausen, & Rauteenmaa, 2020).

Furthermore, Studerus et al. (2011) pooled data from eight different trials involving psilocybin administration in healthy individuals and reported that 90% rated it as an enriching experience, and nearly 40% of the participants reported long-lasting positive change regarding their connection with nature and the environment.

Roseman and colleagues (2018) conducted a clinical trial on the efficacy of psilocybin for treatment-resistant depression and found that Oceanic Boundlessness (OBN)—a state conceptually closely linked to the mystical-type experience, characterized by feelings of blissfulness, insightfulness, disembodiment and experience of unity—was the main predictive factor for long-term positive therapeutic outcomes.

On a related note, Smigielski et al. (2019) administered psilocybin in a mindfulness group retreat and showed that the extent of ego dissolution, characterized by increased union with one's surroundings, dissolved ego boundaries, and a loss of the self (Nour, Evans, Nutt, & Carhart-Harris, 2016), predicted positive changes in psycho-social functioning of participants four months later. Furthermore, the experience of unity predicted a subsequent increase in self-acceptance and a sense of sacredness contributed to the change in appreciation

of life. These results have been interpreted as support for the notion that the temporary loss of the ordinary ego and self-boundaries induced by psilocybin, diminishes self-referential and egocentric processing and in turn fosters an altered perspective towards oneself, others and the environment (Smigielski et al., 2019).

On a more societal level, in a review on psychedelic drug use in healthy individuals, Elsey (2017) posits that psychedelic drugs such as psilocybin “may cater to a major human need for meaning, connectedness and purpose; needs which it may be argued are widely overlooked in Western, individualistic cultures” (p. 4).

Objectives

These findings indicate that psilocybin may have the potential to enhance the well-being of healthy individuals by bringing meaning, connectedness, and novel perspectives into people’s lives. Therefore, the objective of this scoping review is to provide an overview of contemporary research on psilocybin use and its effect on well-being in healthy individuals. Moreover, we aim to examine which factors influence this relation. The following research questions result from the previously formulated objectives:

- (1) How does psilocybin affect well-being in healthy individuals?
- (2) Which factors influence the relation between psilocybin use and well-being?

Additionally, we explore what research protocols have been employed in studies on psilocybin use and well-being in healthy individuals, what underlying mechanisms of improved well-being have been proposed in literature and which facets of well-being are influenced by psilocybin use.

Methods

Overview

A scoping review was conducted to map out existing evidence, identify gaps in the research field, and provide implications for further research. Scoping reviews differ to systematic reviews in a number of ways. First, they usually give a broader overview of a specific topic, since research is usually included irrespective of study quality and study design (Arksey & O'Malley, 2005). This is useful if evidence on a topic is scarce (Tokgöz, Hrynyschyn, Hafner, Schönfeld, & Dockweiler, 2021) as it is the case for research on psilocybin and the effect on well-being in healthy individuals. Existing studies employ different study designs with highly heterogenous quality of evidence, and many lack standardized measures and rigorous models of well-being. Therefore, generalized claims about the effectiveness of such interventions, as one would expect in a systematic review, cannot be made. Hence, conducting a scoping review seems appropriate, since its aim is to provide an overview of the currently available evidence, which can point towards the need to employ more in-depth conceptualizations, and identify general knowledge gaps in a specific line of research (Tricco et al., 2016).

Literature Search

A comprehensive literature search in line with the PRISMA guidelines (Page et al., 2021) was conducted in November 2021. Scopus, PubMed, PsycInfo, Web of Science and Google Scholar were searched for peer-reviewed articles including experimental and non-experimental studies about psilocybin and well-being. To identify fitting studies, the search terms psilocybin and well-being (including its related sub-concepts described in Figure 1) were employed. The following search string was used in Scopus, PubMed, PsycInfo and Web of Science: psilocybin AND wellbeing (OR well-being OR "well being" OR autonomy OR "environmental mastery" OR "personal development" OR "personal change" OR "personal growth" OR "purpose in life" OR "life chang*" OR meaning* OR self-acceptance OR "positive emotions" OR "positive relations*" OR accomplishment OR engagement). A search of Google Scholar with the terms psilocybin and well-being was finally used to identify missing articles and check for comprehensiveness.

Inclusion and Exclusion Criteria

Inclusion criteria were studies that contain data about psilocybin and well-being or its sub-concepts (as shown in Figure 1) in healthy functioning participants. Exclusion criteria were studies that were not published in English, *microdosing* studies (the practice of consuming very low, sub-hallucinogenic doses), studies focusing on individuals with a clinically diagnosed illness (e.g., depression), studies about other psychedelic substances (e.g. LSD, Ayahuasca, or MDMA), studies solely examining positive outcomes not included in the conceptualization of well-being employed in this paper (e.g., empathy or mindfulness), and studies published prior to 1990, as many studies of this “first wave” of psychedelic research were criticized for containing methodological flaws (Wheeler & Dyer, 2020). The screening process was performed by one researcher independently. First, duplicates were removed and the title and abstract of search results were screened. Articles that did not match the inclusion and exclusion criteria were removed. The identified full-text articles were then further screened and assessed for eligibility.

Results

In total, 12 studies met the inclusion criteria and were considered in this review (see Figure 2). All studies entailed data about healthy individuals that have used psilocybin in the past and outcome measures related to well-being (e.g., subjective well-being, life satisfaction, positive mood). The initial search yielded 782 results. Duplicates were removed, and 273 results remained. After scanning titles and abstracts, 232 articles were excluded because they did not match the inclusion and exclusion criteria. Hence, 43 full-text articles were further screened and assessed for eligibility. Thirty-one articles were excluded for multiple reasons: first, several studies examined the effect of psychedelics in general and not of psilocybin specifically. In other studies, well-being or related constructs were measured but scores were not provided. Moreover, studies that solely reported positive outcomes unrelated to the conceptualization of well-being in this study were excluded. This was the case for studies focusing on concepts such as mindfulness, empathy, or nature connectedness. Lastly, some studies solely focused on neurobiological measures and were therefore removed. The selected studies are presented in Table 1 and are further described below.

Figure 2

Prisma Flow Chart

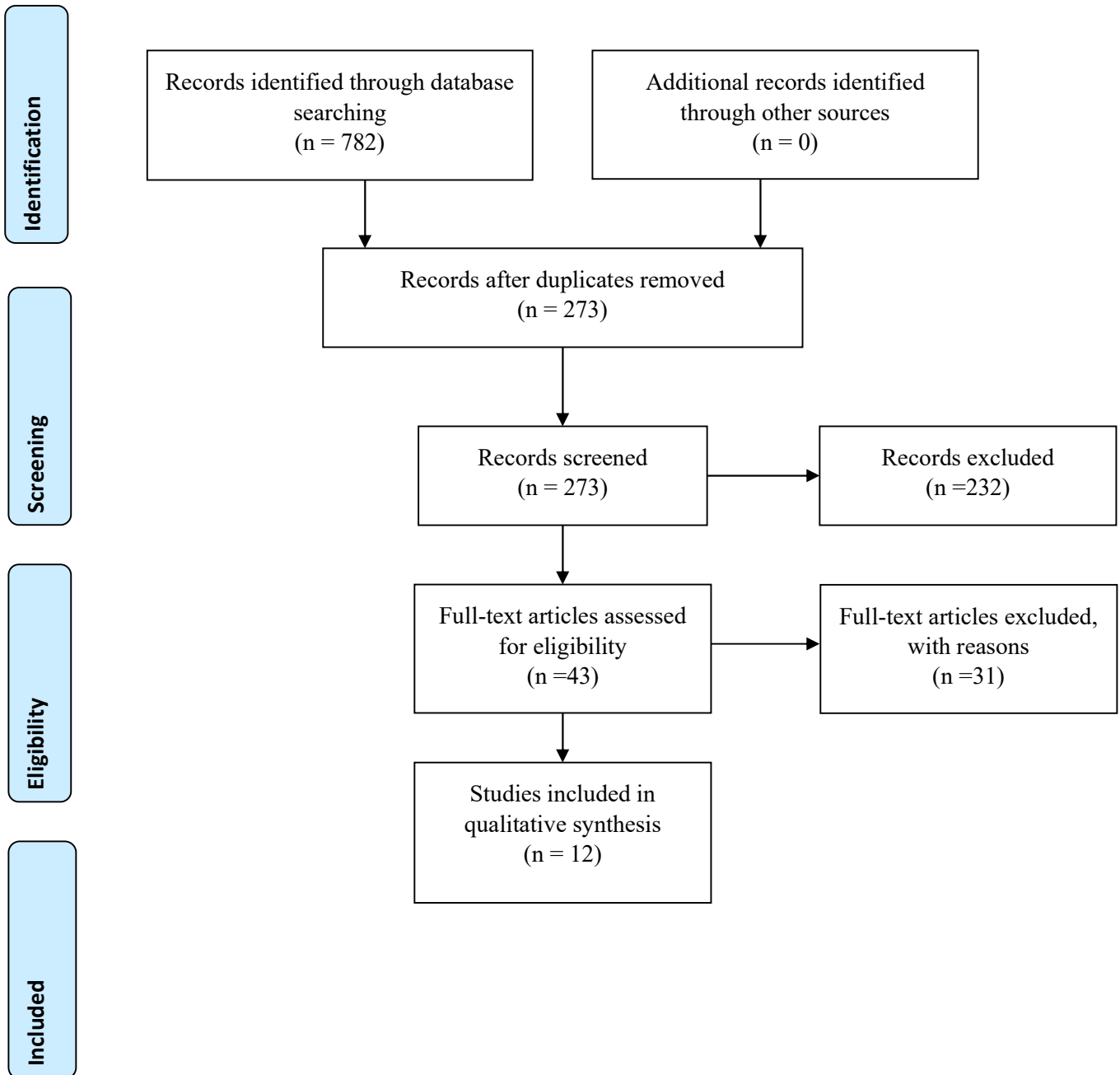


Table 1*Summary of Studies That Investigate The Effect of Psilocybin in Healthy Individuals and Entail Well-Being Outcome Measures*

Reference	Study Design	Study Objectives and Sample Size (N)	WB Concepts	Procedure, WB-related outcome measures, measurement timing	Dosage	Outcomes
Barrett et al., 2020	Open-label, within-subjects, longitudinal pilot study	Long-term enduring impact of psilocybin on affect and associated brain function (<i>N</i> = 12)	Positive emotions (joy, contentment, pride, amusement)	One individual session DPES One day before, one week after, and one month later	25 mg of psilocybin per 70 kg of bodyweight	One month post-psilocybin, positive emotions remained elevated
Carbonaro et al., 2016	Cross-sectional survey study	An online survey about individuals' single most psychologically difficult or challenging experience after consuming psilocybin mushrooms (<i>N</i> = 1993)	WB and life satisfaction	Questionnaire with one item retrieved from the PEQ, asking if psilocybin use affected participants' current sense of WB or life satisfaction, in regards to their single most difficult psilocybin experience, answered on a 7-point Likert scale	Median reported weight of dried psilocybin mushrooms = 4 g (<i>N</i> = 1203), median weight of fresh mushrooms = 21–30 g (<i>N</i> = 148)	76% of the participants reported an increase and 8% reported a decrease in WB due to their most psychologically difficult or challenging psilocybin experience

Carhart-Harris & Nutt, 2010	Cross-sectional survey study	User perceptions of the benefits and harms of hallucinogenic drug use (<i>N</i> = 503)	WB, self-acceptance	Questionnaire with open-ended questions about perceived health benefits and risks of psilocybin use One item asking whether lifetime psilocybin use has had a long-term effect on participants' WB, answered on a 5-point Likert scale	Not specified	In the open-ended answers, 35% of psilocybin users commented on perceived benefits (e.g. improved self acceptance) and 12% commented on perceived risks of psilocybin use (e.g. increased anxiety) 2.4% of psilocybin users attributed a negative effect to the use of psilocybin on WB, and 0.2% a very negative effect. 87% of psilocybin users attributed a positive or very positive effect to the use of psilocybin on WB
Griffiths et al., 2018	Double-blind, randomized, active placebo, planned comparison between and within group	Changes in psychological functioning resulting from psilocybin use in combination with meditation and other spiritual practices (<i>N</i> = 75)	Positive emotions (joy, contentment, pride, amusement), WB, life satisfaction, positive mood, attitude about life, attitude about self, positive social	Two groups with two individual sessions of high-dose psilocybin, whereas one group received high support for spiritual practices One group with two individual low-dose psilocybin session (active placebo)	Low-dose group (active placebo): 1mg/70kg psilocybin High-dose groups: 20mg/70kg on session one and 30mg/70kg on session two	Positive significant changes on all well-being-related measures in both high-dose groups compared to the low-dose group except for positive emotions as measured with the DPES 72% of the high-dose standard support and 92% of the high-dose high support group attributed a moderate to very high increase in WB or life satisfaction to the use of psilocybin. No decrease of WB or life satisfaction

			effects, meaning/purpose in life	PEQ, DPES, PIL		Baseline and 6 months later	Positive outcomes were predicted by the intensity of psilocybin-occasioned mystical experience and rates of engagement with meditation and other spiritual practices
Griffiths et al., 2011	Double-blind, quasi-random, placebo-controlled	Evaluation of the psychological effects of different psilocybin doses (N = 18)	WB, life satisfaction, positive mood, attitude about life, attitude about self, positive social effects	Five individual sessions, with four active doses in either ascending or descending order PEQ, written comments	0, 5, 10, 20, 30 mg/70 kg	One month after each session, 14 months later	94% of the participants attributed a moderately or very high increase in WB or life satisfaction to the use of psilocybin. Positive significant changes on all well-being-related measures, which were sustained at the 14-month follow-up 89% rated moderate or higher changes in positive behavior at the 14-month follow-up, such as better social relationships, increased physical and psychological self-care and increased spiritual practice No decrease of WB or life satisfaction Persisting positive effects increased with increasing dose

Griffiths et al., 2008	Follow-up	Persistence of positive changes in psychological functioning following psilocybin administration (<i>N</i> = 36)	WB, life satisfaction, positive mood, attitude about life, attitude about self, positive social effects	Psilocbin administered on one of two or three individual sessions PEQ, 14-16 months later	30 mg/70 kg	Positive changes on all well-being-related measures were sustained 64% of the participants attributed a moderately or very high increase in WB or life satisfaction to the use of psilocybin. No decrease of WB or life satisfaction
Griffiths et al., 2006	Double-blind, counterbalanced comparison	Acute and long-term psychological effects of a high dose of psilocybin (<i>N</i> = 36)	WB, life satisfaction, positive mood, attitude about life, attitude about self, positive social effects	Psilocybin on one of two or three individual sessions, placebo during the other sessions PEQ, PANAS-X, two months later	30 mg/70 kg Placebo: methylphenidate hydrochloride (40 mg/70 kg)	Participants rated their psilocybin experiences as having substantial personal meaning Positive significant changes on all PEQ well-being-related measures (WB or life satisfaction, positive mood, attitude about life, attitude about self, positive social effects) 79% of the participants attributed a moderately or very high increase in WB or life satisfaction to the use of psilocybin. No difference in positive affect as measured with the PANAS-X between the two conditions.
Lutkajtis, 2021	Qualitative phenomenol	Four individuals' experiences during and following a	WB, positive emotion, self-acceptance,	One session in a group retreat setting	30-40 grams of psilocybin truffles	Personally significant changes to health and wellbeing due to behavioural lifestyle changes, an increased sense of self-love, self-acceptance,

	ological approach	psilocybin truffle retreat in the Netherlands (<i>N</i> = 4)	positive relationships, personal growth, environmental mastery	Semi-structured interview questions, asking participants to describe their journey since the retreat, including any significant after-effects and changes			self-confidence, positive emotions, an increased interest in spirituality and improved interpersonal connection
				Eight to twelve months later			
Madsen et al., 2020	Open label, within-subject study	Long-term changes in mindfulness, neocortical 5-HT2A receptor binding and psychological functioning (<i>N</i> = 10)	Positive mood, attitude about life, attitude about self, positive social effects	One individual session PEQ Three months later	14 mg/70 kg (<i>N</i> = 4) and 21 mg/70kg (<i>N</i> = 6)		Positive changes on all well-being-related measures
Mason et al., 2019	Open label, within subject study	Assessment of the sub-acute effects of psilocybin on creative thinking, empathy, and well-being in a psilocybin retreat (<i>N</i> = 22)	Life satisfaction	One guided session in a group retreat setting SWLS Baseline, one day later, seven days later	An average (SD) of 34.2 g (8.9) of psilocybin truffles Final (average) psilocin consumption of 27.1 mg		Persistent significant increase in life satisfaction after one week

Nicholas et al., 2018	Open-label within-subject study	Positive subjective effects of high dose psilocybin in healthy volunteers (<i>N</i> = 12)	WB/life satisfaction, positive mood, attitude about life, attitude about self, positive social effects	Three individual sessions with escalating doses PEQ One month later	21mg/70kg;31.5 mg/70kg; 42mg/70kg)	Positive changes on all well-being-related measures 83.3% of the participants attributed a moderately or very high increase in WB or life satisfaction to the use of psilocybin. Moderate decrease of WB or life satisfaction for one participant
Smigielski et al., 2019	Double-blind randomized, placebo controlled	Characterization and prediction of acute and sustained response to psychedelic psilocybin in a mindfulness group retreat (<i>N</i> = 39)	Self-acceptance, meaning/purpose in life	One guided session in a group retreat setting LCI-R Four months later	22.05mg/70kg Placebo: lactose	Increased appreciation for life, self acceptance and quest for meaning/sense of purpose significantly different to the placebo group The extent of self-dissolution contributed to the global change in attitude and behaviour, the experience of unity predicted self-acceptance, and sacredness and ineffability contributed to the change in appreciation of life

Note. DPES = Dispositional Positive Emotion Scale. LCI-R = Life Changes Inventory, Revised. PANAS-X = Positive and Negative Affect Scale – X. PEQ = Persisting

Effects Questionnaire. PIL = Purpose in Life Test. RCT = Randomised Controlled Trial. SWLS = Satisfaction with Life Scale. WB = well-being.

Objectives of the Studies, Conceptualization and Measurement of Well-being

All of the studies contained data about well-being-related effects of psilocybin use in healthy individuals. Only one study was conducted with the primary aim of examining the effect of psilocybin on well-being specifically (Mason et al., 2019). In some studies, the primary objective was to investigate constructs such as mindfulness, creativity, or empathy, but well-being measures were nevertheless included as a secondary outcome measure. In none of the studies well-being was explicitly conceptualized but a variety of measurement instruments were employed that can be related to the well-being conceptualization of this paper.

Six of the studies employed the Persistent Effects Questionnaire (PEQ) as the main outcome measure related to well-being (Griffiths et al., 2018; Griffiths et al., 2011; Griffiths et al., 2008, Griffiths et al., 2006; Madsen et al., 2020; Nicholas et al., 2018). This instrument entails subscales dealing with positive changes in mood, social effects, attitudes about life and oneself. From these subscales of the questionnaire, inferences to the well-being conceptualization of this paper can be made since they are closely linked conceptually. The subscale *positive attitude about life* from the PEQ includes items related to the concept of meaning/purpose in life (e.g., “your life has more meaning”), *positive attitude about self* includes questions related to self-acceptance (e.g., “your self-confidence/self-assurance has increased”), and *positive social effects* include questions related to positive relationships (e.g., “you have a more positive relationship with others”). The PEQ also entails a final item that asks participants on a 7-point Likert scale whether they believe that the experience of using psilocybin and the contemplation about the experience led to changes in their current sense of personal well-being or life satisfaction. In one study using the PEQ, this item was not reported (Madsen et al., 2020).

Three other studies also examined life satisfaction. One of them used the final item of the PEQ, asking about changes in well-being/life satisfaction (Carbonaro et al., 2016). Carhart-Harris and Nutt (2010) used a similar ad-hoc item, asking whether lifetime psilocybin use has had a long-term effect on participants’ well-being, answered on a 5-point Likert scale. The last study used the Satisfaction with Life Scale (Mason et al., 2019).

Besides the PEQ, the Positive and Negative Affect Scale – X (PANAS-X) and the Dispositional Positive Emotion Scale (DPES) were used as additional questionnaires that also examined positive emotions (Barrett et al., 2020; Griffiths et al., 2018, Griffiths et al., 2006).

Furthermore, in one study, the purpose in life test (PIL) was employed, which is related to the well-being sub-concepts of meaning/purpose in life (Griffiths et al., 2018). In another

study, the Life Changes Inventory (LCI) was used, which entails a subscale related to self-acceptance and a subscale related to meaning/purpose in life (Smigielski et al., 2019).

In the study by Lutkajtis (2021), a qualitative phenomenological approach was chosen. In a semi-structured interview, participants were questioned about the long-lasting effects of their psilocybin experience. Hence, no formal well-being measures were employed, but the author provided descriptions of the interviews and identified key themes, which entailed information related to improvements in well-being and several sub-concept (i.e., self-acceptance, positive relationships, personal growth, environmental mastery).

Study Design and Sample Size

Regarding the study design, the twelve studies were rather heterogenous. There were eight experimental studies, of which four were open-label and double-blind studies, respectively, one study with follow-up data, two cross-sectional survey studies, and one qualitative interview study. All studies in which psilocybin was administered in a controlled setting included a sample size in the double-digit range, with a total of 228 participants. Two cross-sectional survey studies assessed experiences with psilocybin in a non-experimental, uncontrolled setting, and entailed a total of 2496 participants (Carbonaro et al., 2016; Carhart-Harris & Nutt, 2010).

Study Procedure and Dosage

Studies varied in setting, amount of dosing sessions, form of psilocybin administration and dosage. In most of the studies, psilocybin was administered in individual sessions. Three studies were conducted in a group retreat setting (Lutkajtis, 2021; Mason et al., 2019; Smigielski et al., 2019). The two survey studies asked about psilocybin use in an uncontrolled setting (Carbonaro et al., 2016; Carhart-Harris & Nutt, 2010).

Also, most studies dealt with one single psilocybin dosing session (Barrett et al., 2020; Carbonaro et al., 2006; Griffiths et al., 2008; Griffiths et al., 2006; Lutkajtis, 2021; Madsen et al., 2020; Mason et al., 2019; Smigielski et al., 2019), three studies employed multiple dosing sessions (Griffiths et al., 2018; Griffiths et al., 2011; Nicholas et al., 2018), and one asked for lifetime use of psilocybin (Carhart-Harris & Nutt, 2010).

In most studies, the researchers administered synthetic psilocybin in the form of a capsule. Dosage ranged from a low dose of 5mg of psilocybin per 70 kg of bodyweight (Griffiths et al., 2011) to 42mg/70kg (Nicholas et al., 2018), which marks the highest administered dosage of all studies in this review. Most studies involved dosing session that can be considered a high dose of psilocybin (≥ 25 mg psilocybin; Johnson, Richards, & Griffiths,

2008) Four studies did not use synthetic psilocybin. They varied in dose and form of administration. In one study, dose and form of administration was not specified (Carhart-Harris & Nutt, 2010), in the second study participants reported having taken an average of 4 grams of dried psilocybin mushrooms and 21 to 30 grams of fresh mushrooms (Carbonaro et al., 2016) and in the two remaining studies, participants took similar doses of psilocybin truffles (around 30 to 40 grams; Lutkajtis, 2021; Mason et al., 2019).

The four studies that had a control group all used different placebos, either methylphenidate hydrochloride (40 mg/70 kg), lactose, or capsules with either no dosage or a very low dosage of psilocybin (1mg/70kg).

Most studies involved screening procedures to assess the eligibility of participants (Griffiths et al., 2018; Griffiths et al., 2011; Griffiths et al., 2008, Griffiths et al., 2006; Lutkajtis, 2021; Madsen et al., 2020; Mason et al., 2019; Nicholas et al., 2018; Smigielski et al., 2019). They were required to be medically and psychiatrically healthy, and without personal or family histories of psychotic disorders or bipolar I or II disorder. For that purpose, interviews were conducted and multiple health indicators such as medical history, physical examination, blood analysis, electrocardiography, and urine tests for drug abuse and pregnancy were examined. The seven experimental studies that involved individual dosing sessions followed research protocols similar to each other (Barrett et al., 2020; Griffiths et al., 2018; Griffiths et al., 2011; Griffiths et al., 2008, Griffiths et al., 2006; Madsen et al., 2020; Nicholas et al., 2018), in line with safety guidelines for human hallucinogen research (Johnson et al., 2008). Before the dosing sessions, multiple preparatory meetings with the monitoring staff were conducted, with the purpose of building rapport and trust, explaining safety precautions and reviewing life history and current life circumstances of participants. In all studies, music was played during the session and two monitors of the research staff were present to offer support and reassurance in case of anxiety. Except for Madsen et al. (2020), it was furthermore described that sessions took place in an aesthetic living-room-like environment, whereby participants were instructed to lay down on a couch, using an eye mask to block external visual distraction. After the psilocybin session, participants were offered further meetings to discuss and reflect upon their experience. The three experimental studies that were conducted in group retreat settings, followed different schedules and procedures regarding the duration of stay, and activities before and after the sessions, but they all shared common features as well. In all studies, preparatory activities such as meditation exercises and meetings with facilitators and other participants took place, psilocybin was consumed under supervision in a comfortable

surrounding accompanied by music, and after the experience, participants had the opportunity to discuss their experience with the facilitators and other participants.

Well-being-related Outcomes

In all studies, the majority of participants reported that psilocybin use had positive psychological implications. In more than half of the studies, the percentage of participants that felt a sense of increased wellbeing or life satisfaction following the use of psilocybin was reported. Most participants indicated a moderate to very high increase in their sense of wellbeing, ranging from 64% (Griffiths et al., 2008) to 94% (Griffiths et al., 2011).

In the experimental studies, the most commonly identified well-being-related outcomes were related to the PEQ: an increased sense of well-being or life satisfaction, heightened mood, more positive attitudes about life (related to meaning/purpose in life), positive attitudes about oneself (related to self-acceptance) and positive social effects (related to positive relationships). In all studies that employed the PEQ, these concepts were elevated after the use of psilocybin, up to 14 months after the ingestion (Griffiths et al., 2011; Griffiths et al., 2008). Those studies employing a control condition found these effects to be significantly higher than for the control group (Griffiths et al., 2018; Griffiths et al., 2011; Griffiths et al., 2008; Griffiths et al., 2006). Positive effects were found to be augmented with increasing dosage (Griffiths et al., 2011).

Other questionnaires also revealed that psilocybin use led to an increase in a variety of well-being (sub-)concepts. Smigielski et al. (2019) reported significant improvements for all well-being-related concepts that were assessed with the LCI-R, namely appreciation of life, self-acceptance, and quest for meaning/purpose in life. Similarly, meaning/purpose in life as measured with the PIL was also significantly increased in the study by Griffiths et al. (2018).

Three studies provided qualitative data that also indicate improvements for a number of well-being-related concepts. In Griffiths et al. (2011), written comments pointed towards an increase particularly in spiritual practices and in positive relationships (i.e., feeling closer to family and friends, being more empathetic, accepting, loving, open, forgiving, comfortable, and less judgmental with other people). In Lutkajtis (2021), participants reported an increased ability to handle challenges in life, which can be related to the concept of environmental mastery, an increased sense of self-confidence, self-love and self-acceptance, health improvements due to weight loss and other lifestyle changes, more warm and loving relationships, an increased sense of interpersonal connection, greater sense of ease around other people, more tolerance, acceptance and empathy towards others and new interests to learn about and drive towards, which can be related to the concept of personal growth. In the open

comments section of the survey by Carhart-Harris and Nutt (2010), improved insight, perspective, wellbeing, optimism, self-acceptance and self-realization, a sense of inner peace, a greater appreciation of nature, and an increased sense of spirituality was reported.

Regarding long-term effects of psilocybin on positive emotion, study results were somewhat ambiguous. In all studies that employed the PEQ, the questionnaire indicated improvements in positive mood (Griffiths et al., 2018; Griffiths et al., 2011; Griffiths et al., 2008; Griffiths et al., 2006; Madsen et al., 2020; Nicholas et al., 2018). In Griffiths et al. (2006), however, positive affect as measured with the PANAS-X did not significantly increase. Positive emotions, as measured with the DPES were not significantly elevated in the study by Griffiths et al. (2018) either. However, they were significantly increased one month after the administration of psilocybin in the study by Barrett et al. (2020).

Summarizing, the most frequently reported well-being outcomes related to Seligman's PERMA Model of Well-being and Ryff's Six-Factor Model of Psychological Well-Being were self-acceptance, positive relationships, positive emotion and meaning/purpose in life. Only one study yielded results that can be interpreted as being related to the well-being facets of personal growth and environmental mastery (Lutkajtis, 2021). The well-being facets autonomy and engagement were not addressed in the studies.

Action Mechanisms

Underlying mechanisms that constitute the positive effects of psilocybin on well-being were only scarcely investigated. In multiple studies however, positive outcomes were linked to the substances ability to evoke mystical-type experiences. In Griffiths et al. (2008), correlation analyses between measures of mystical experience and ratings of personal meaning and spiritual significance were performed with subsequent regression analysis, controlling for the intensity of drug effects. Scores for mystical experience were significantly related to high ratings of personal meaning and spiritual significance at follow-up. From these results, the authors inferred that having a mystical experience can be considered an underlying action mechanism for positive outcomes of psilocybin use. In another study, hierarchical regression analysis revealed that the intensity of the psilocybin-occasioned mystical experience was predictive of various long-term positive outcomes (Griffiths et al., 2018). Finally, in the study by Smigielski et al. (2019), regression analysis revealed that various concepts related to mystical-type experiences were predictive of the long-term positive outcomes. The extent of self-dissolution contributed to the global change in attitude and behaviour, the experience of

unity predicted self-acceptance, and sacredness and ineffability contributed to the change in appreciation of life.

Adverse Effects

Generally speaking, serious adverse events (e.g., physical discomfort, disorientation, severe anxiety, panic, or psychotic-like reactions) did not occur in the experimental studies. Only one participant attributed a moderate decrease in well-being to the use of psilocybin (Nicholas et al., 2018). In multiple studies, minor adverse effects such as acute distress, anxiety and dysphoria were reported, but these effects were of short duration, well managed by the study staff or were described as cathartic (Griffiths et al., 2018, Griffiths et al., 2011; Griffiths et al., 2006; Lutkajtis, 2021). In most studies taking place in a controlled environment, no adverse effects whatsoever were reported (Barrett et al., 2020; Griffiths, 2008; Madsen et al., 2020; Mason et al., 2019; Smigielski et al., 2019). In contrast to that, adverse effects were reported in the two cross-sectional survey studies. In Carhart-Harris and Nutt (2010), 2.6% of psilocybin users attributed a negative effect on well-being to the use of the drug and 13% of psilocybin users reported that the use was associated with physical or mental health problems (i.e., persistent psychotic symptoms, worsened depressive symptoms, gastrointestinal problems, lasting visual or perceptual distortions, feeling generally negatively affected). In the survey study on participants' worst "bad trip" by Carbonaro et al. (2016), 11% percent of participants put themselves or others at risk of physical harm after using psilocybin, with 2.6% exhibiting physically aggressive or violent behaviour towards themselves or others, and 2.7% requiring medical help at a hospital or emergency department. Three individuals reported enduring psychotic symptoms and three individuals reported a subsequent suicide attempt.

Limitations

A limitation that applied to most studies and might restrict the generalizability of study results lies in the sample homogeneity in regard to socioeconomic status and ethnicity. In most studies, a large majority of participants were predominantly white, well-educated individuals. Additionally, samples of experimental studies might be unrepresentative due to exclusion of participants that are subject to risk factors such as history of drug abuse or psychiatric illness. Moreover, in both survey studies, a convenience sample was employed which may have facilitated a selection bias, as participants were mainly recruited on websites with a relatively favorable view of psychedelic drug use. Similarly, individuals with positive attitudes towards psychedelic drugs might have been more inclined to take part in the experimental studies. Furthermore, limitations that apply to web-based questionnaires more generally were high rates

of non-completion, difficulty in assessing truthfulness of respondents, the subjective nature of data and the lack of a control group. Several experimental studies also lacked control groups, or had difficulties to maintain the blinding procedures due to the perceptible effects of psilocybin (Smigielski et al., 2019), which also could have led to expectancy effects. Lastly, small sample sizes of experimental studies potentially limited statistical power.

Discussion

In this scoping review, the current literature on the use of psilocybin and its effect on well-being in healthy individuals was investigated, employing a rigorous, multifaceted conceptualization of well-being. The aim was to examine well-being-related outcomes of psilocybin use and identify factors that contribute to such outcomes. Additionally, this study explored what research protocols have therefore been employed, what underlying action mechanisms have been proposed in literature, and which facets of well-being are influenced by psilocybin use in healthy individuals.

The data revealed subsequent improvements in a wide range of well-being (sub-) concepts after the use of psilocybin in all studies included in this review. These findings lend support to the view that a low number of high-dose psilocybin administration sessions can have broad and sustained positive implications for well-being in healthy individuals. This is in line with previous research that finds broad increases for a variety of well-being-related measures sustained two years after psychedelic experiences (Mans et al., 2021).

Following the conceptualization of well-being in this review, self-acceptance, positive relationships, and meaning/purpose in life were facets of well-being that stood out to consistently show significant improvements in multiple studies. These results are consistent with data obtained in a qualitative study dealing with treatment-resistant depression patients that underwent psilocybin-assisted therapy (Watts et al., 2017). Patients in the study reported an improved connection to the self and a boosted sense of self-worth and self-compassion. They reported strengthened bonds with loved ones (friends, children, parents, colleagues, and spouses), and an improved a sense of meaning, purpose, and hope. Furthermore, in another qualitative study on participants' experiences in psilocybin-assisted psychotherapy, all participants described significant insights or positive changes concerning close personal relationships (Belser et al., 2017). They also reported "new feelings of empowerment and personal agency to live meaningful lives, and a sense of belonging within their communities and the larger universe" (Belser et al., 2017, p. 369).

The well-being facets of autonomy, accomplishment, engagement, and personal growth were only implicitly mentioned or not reported at all as well-being-related outcomes of psilocybin use. Hereby, it is important to consider that none of these concepts were explicitly assessed by the well-being-related measurement instruments employed in the reviewed studies. Thus, it remains unclear whether these well-being facets do not occur due to the lack of adequate measurement instruments or because they are not as relevant for positive well-being-related outcomes of psilocybin use.

Action Mechanisms

Most studies did not elaborate on underlying action mechanisms explaining positive outcomes of psilocybin use. However, as described in the Results section, a central role was attributed to the occurrence of mystical-type experiences in multiple articles. This finding is frequently reported in the scientific literature on psilocybin (e.g., Doblin, 1991; Garcia-Romeu et al., 2014; Haijen et al., 2018; Kangaslampi et al., 2020; Ross et al., 2016; Russ et al., 2019). Other concepts that have been linked to the mystical-type experiences and to positive outcomes of psilocybin use are *feelings of unity, connectedness, and ego dissolution*. According to Stace (1960), a central part that lies at the core of the mystical-type experience is a feeling of unity, which involves an experience of the complete dissolution of the self, a loss of the sense of a personal identity. Therefore mystical-type experiences have been conceptually closely tied to the concept of ego dissolution which is supported by literature that finds a unitive experience to correlate highly with scores of ego dissolution (Nour et al. 2016). It has been put forward that through this blurring of lines between self and others, and an inclusion of others in the construct of the self, an increased sense of connectedness with external objects or entities is achieved (Forstmann, Yudkin, Prosser, Megan Heller, & Crockett, 2020). In line with this, the concept of “connectedness” has been commonly theorized to be a central mechanism leading to positive outcomes of psilocybin use (Aday, Mitzkovitz, Bloesch, Davoli, & Davis, 2020; Carhart-Harris, Erritzoe, Haijen, Kaelen, & Watts, 2018; Watts et al., 2017). Watts et al. (2017), for example, found that an increased connection towards oneself, others and the world was a central theme in patient reports of psilocybin experiences. Similarly, in the study by Smigielski et al. (2019), regression analysis showed feelings of unity to be linked to increased self-acceptance and ego-dissolution generally predicted positive outcomes. The authors argued that self-referential and egocentric processing is diminished as a result of psilocybin use, which can reshape one’s perspective towards oneself, others, and the environment.

These proposed mechanisms might hint at possible explanations why self-acceptance, positive relationships and meaning/purpose in life seem to be well-being facets affected by psilocybin use. Feelings of unity, ego dissolution and a sense of connectedness as part of the mystical experience might facilitate a sense of belonging and an altered perspective towards oneself, others, and the world that is more benevolent and accepting.

Adverse Effects

Concerning studies conducted in a controlled setting, either few minor adverse effects such as acute distress and anxiety or no adverse effects at all were evident. Carbonaro et al. (2016) concluded that risks of dangerous behavior or prolonged psychological problems are extremely low in laboratory studies of psilocybin with carefully screened, well-prepared and supported participants. This underpins the relative safety of administering psilocybin under conducive conditions and is consistent with previous research. In a pooled analysis of 110 healthy psilocybin research participants, for example, the authors found low rates of sustained negative psychological symptoms, and no subsequent drug abuse, persisting perception disorders, prolonged psychosis, or other long-term impairment of functioning (Studerus et al., 2011). Psilocybin has low physiological toxicity, is not associated with compulsive drug craving or withdrawal symptoms, and is considered to be non-addictive (Johnson et al., 2008; Teixeira et al., 2021). Moreover, two independent studies in the United States found no evidence for a link between psychedelic use and mental health concerns or suicidality (Johansen & Krebs, 2015; Krebs & Johansen, 2013). In fact, an additional study found that lifetime use of psilocybin is associated with decreased likelihood of psychological distress and suicidality (Hendricks, Johnson, & Griffiths, 2015).

Rates and severity of both acute and enduring adverse effects were comparatively higher in the cross-sectional survey studies in comparison to studies conducted in controlled laboratory settings. Such differences are argued to arise due to factors such as lack of psychological screening and preparation, absence of physical comfort and social support during the session, and inappropriate dosage (Carbonaro et al., 2016). It has been acknowledged that unsupervised use of psilocybin can be potentially harmful. The most likely risk is overwhelming distress or anxiety, which can escalate to dangerous behaviors such as self-harm or violence (Johnson et al., 2008). In rare cases, even for seemingly healthy individuals, psilocybin might prompt or exacerbate psychotic disorders among those predisposed to such disorders (Johnson et al., 2008).

Promoting Positive Results – The Importance of Set and Setting

Such potential adverse effects highlight the importance of non-pharmacological factors for shaping the outcome of psychedelic experiences. Adequate *set* and *setting* are crucial determinants for positive outcomes of a psychedelic experience (Elsey, 2017; Haijen et al., 2018; Pahnke, 1969). *Set* refers to characteristics of the person taking the drug and *setting* refers to characteristics of the environment. To account for this, modern day clinical trials adhere to safety guidelines for human hallucinogen research (Johnson et al., 2008).

This way, a proper *set* of participants in clinical trials is ensured by employing a screening process that excludes individuals with cardiovascular conditions and with history of psychotic disorders (Aday et al., 2020). Additionally, preparation sessions are recommended to take place, with the aim to build rapport, to foster the ability to be emotionally open to the psychedelic experience and to enhance psychological flexibility (Johnson et al., 2008). In order to provide a pleasant *setting*, psilocybin studies usually take place in a comfortable environment with psychological support available (Andersen et al., 2021; Roseman et al., 2018). In conclusion, adequate screening and preparation procedures, a supportive setting, appropriate dosage, psychological support and proper integration of the experience promote positive outcomes and minimize adverse effects.

Limitations

This review should be viewed in light of its limitations. The primary aim of this scoping review was to provide an initial and broad overview of the available evidence in the field, irrespective of study quality. Therefore, studies were included independently of methodological rigor or quality, which is considered a common limitation of the scoping review methodology (Arksey & O'Malley, 2005; Hanneke, Asada, Lieberman, Neubauer, & Fagen, 2017). As described in the Results section, several studies featured small and homogenous samples, were potentially subject to self-selection or expectancy biases, and lacked adequate control conditions.

Moreover, only a small number of studies were included in this review. Although there is a recent renewed interest in psychedelic research (Chi & Gold, 2020), current drug laws restrict the use of psilocybin for research in healthy individuals. Permission to investigate psychedelic drugs is granted to a very limited number of research labs only and is associated with high administrative and financial burdens (Nutt, King, & Nichols, 2013).

Furthermore, this scoping review focused on outcomes related to a predefined conceptualization of well-being. Several factors external to Ryff's and Seligman's well-being

models such as *nature-relatedness* (Forstmann & Sagioglou, 2017; Nour, Evans, & Carhart-Harris, 2017), *mindfulness* (Madsen et al., 2020; Smigielski et al., 2019), *empathy* (Mans et al., 2021), *optimism* (Mans et al., 2021), *resilience* (Lutkajtis, 2021; Mans et al., 2021) and *lifestyle changes* (e.g., exercise and dietary changes, weight loss, reduced alcohol consumption; Lutkajtis, 2021; Teixeira et al., 2021; Watts et al., 2017) have also been related to the positive effect of psilocybin on well-being.

Future Research

Future research should focus on increasing the representativeness and generalizability of results, to assess whether psilocybin use can effectively and safely improve well-being for healthy individuals in the general public. Larger, more diverse samples with varying socioeconomic status, ethnicity, and attitude towards psychedelic drugs are therefore needed. Additionally, more comprehensive well-being measures should be used in future studies. Such data would allow to make more meaningful claims about the efficacy of psilocybin to improve well-being. Moreover, rigorous double-blind, placebo-controlled, crossover experimental designs with standardized dosages should be employed, to minimize blinding and expectancy effects, and increase reliability of results.

Conclusion

This scoping review provided preliminary evidence regarding psilocybin use in healthy individuals and its effect on well-being. To the authors knowledge, this study was the first to employ a rigorous well-being conceptualization in the context of psilocybin use, which revealed more precisely how and which well-being (sub-)concepts are affected by psilocybin. Following Ryff's and Seligman's conceptualization, self-acceptance, positive relationships and meaning/purpose in life were well-being sub-concepts consistently reported to be improved by psilocybin use. Ego-dissolution, unity, connectedness, and mystical-type experiences are interrelated concepts that seem to be crucial for explaining such positive well-being-related effects of psilocybin. Under conducive conditions, the use of psilocybin can contribute to healthy human functioning, through broad and sustained improvements in a variety of well-being concepts.

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