Degree project

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Prescribed Ego-Death: The Therapeutic Effects Found in the Psychedelic-Induced Absence of Self

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Abstract

Depression and anxiety are two of the world's most common neuropsychiatric conditions. There has been some success in treating depression and anxiety by using classic psychedelic drugs to cause positive changes in psychological well-being. Depression and anxiety are often correlated to self-rumination and a heightened sense of self, making sufferers unable to withdraw from repetitive negative self-referenced thought patterns. Some researchers hypothesize that the therapeutic effects of psychedelics come from their acute subjective effects, specifically ego-dissolution. This systematic review aimed to investigate what clinical studies can support this hypothesis. By reviewing five studies that examined this correlation, this review found that the majority of the studies could present a moderate correlation. This suggests a negative correlation between the degree of ego-dissolution and the therapeutic improvements in disorders with a heightened sense of self.

Keywords: ego-dissolution, psychedelics, anxiety, depression

Prescribed Ego-Death: The Therapeutic Effects Found in the Psychedelic-Induced Absence of Self

What is the *self?* The experience of having a self is central to human consciousness but continually defies all attempts at easy definitions. Modern science describes self-consciousness as multilayered and dynamic, but its nature has throughout history been one of the most prominent questions in philosophy, religion, and various fields of science (Lebedev et al., 2015). The discussion has not only centred between dualism and materialism but has sprung on an abundance of theories and self-concepts. Descartes (1596-1650) famously described the self (or the soul) as a substance in itself, completely separate from the body. He asked the questions: "Am I identical with my body? If not, can I exist without having a body?" (Cassam, 2011, p. 5), and answered yes to both. There are non-dualist philosophers who would also agree with Descartes on this point (Cassam, 2011). However, Locke (1689/1997) was against the cartesian (dualistic) idea, meaning instead that the self is a psychological continuity dependent on our brain's ability to remember our past. Hume (1739-40) presented the *bundle theory* where the self (defined as a substance with identity and simplicity) only is a "bundle" of ever-changing perceptions with no connection to introspection.

In the late 19th century, James (1890) suggested different aspects of the self, which has become the generally accepted approach today. It proposes that the self consists of a broad range of aspects which can include the social self, emotional self, embodied self, and narrative self, among others (Gallagher, 2000). This is revealed in the modern approach to Hume's bundle theory: Gallagher's (2013) *pattern theory* of self. The latter considers the fact that what we define as the self consists of a number of complex contributors which cannot be considered necessary to any self on their own. Instead, these characteristic features of self make up a pattern, adding up to a cluster we can call self.

Studies investigating the self in cognitive neuroscience mostly focus on contrasting self-related stimuli with non-self-related stimuli. The studies aimed at revealing different aspects of the self and their neural correlates using functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) techniques. However, the list of neural correlates grows as long as the different focuses of these studies, focusing on everything between recognizing one's own face and assessing one's own emotions or identity. Nonetheless, by reviewing the literature it can be found that both self and others' mind representation shares activity in mainly the medial prefrontal cortex and precuneus. Furthermore, cortical midline structures are

considered to be specific for the self and self-processing (Qin & Northoff, 2011). In self versus non-self stimuli, a difference in activation could be seen mainly in the temporoparietal junction, temporal pole, precuneus/posterior cingulate gyrus, and medial prefrontal cortex (Legrand & Ruby, 2009).

Modern research of the self is focusing its efforts on studying different aspects of the self. The target of this literature review will be the experiential aspects of self.

Self-Experience

Girn and Christoff (2019) described self-experience as a "multifaceted construct that can be divided into reflective (the 'me') and non-reflective aspects (the 'I'), and can encompass multiple components" (p. 132). Self-experience includes both bodily self-consciousness as well as mental self-consciousness. It also includes a first-person perspective: the awareness of one's body as one's own, which is the anchoring point from which everything is experienced (Legrand, 2007).

For the reflective aspects of self-experience, Gallagher (2000) distinguished a *narrative self* (also known as the autobiographical self) which consists of the stories we, and others, tell us about ourselves. It is through the narrative self we think about our future and past, creating the continuum of our self-identity. At a more fundamental, non-reflective level the *minimal self* considers the minimal necessary conditions for self-consciousness; creating the foundation for consciousness itself. It includes the phenomenological experience of ourselves as immediate subjects to the stream of stimuli and events of the world when we are awake and conscious. With the minimal self, the assumption is made that all experiences have a "mineness" to them, making them a part of the self. When I drink coffee, listen to music or look at art, there is no doubt about *who* is experiencing these things (Gallagher, 2000). Sebastián (2020) argued that the minimal self should be understood as the first-person perspective.

The experiential dimension of self can be described from a perspective-approach, describing our phenomenology from a first or third-person perspective. The first-person perspective is a part of pre-reflective self-consciousness and minimal consciousness. As the name suggests, it is simply our own experiences from a first-person perspective and the "mineness" of those experiences. It considers the self as a subject that holds a perspective, and a world on which the perspective is held. In contrast, the third-person perspective is when one considers the experience of oneself and others, still having the first-person perspective in the background of those reflections (Legrand, 2007).

Neurologically, the Default Mode Network (DMN) is most commonly associated with the narrative self. The main functions of this network are self-referential processing, theory of mind, mental time travel, and moral decision-making. Meanwhile, the minimal self is suggested to be correlated to the function of the saliency network (Lebedev et al., 2015). A correlation has been found between the first-person perspective with higher activation in somatosensory-related cortices (insula or postcentral gyrus), in comparison to the third-person perspective (Legrand & Ruby, 2009).

Empirically, the self-reflective parts of the self have been studied extensively compared to the non-reflective parts of self-experience. This can be linked to methodological difficulties of isolating the non-reflective aspects. A suggested solution is to induce altered reflective and non-reflective aspects of self-experience through the administration of psychedelics (see *Psychedelics*) (Girn & Christoff, 2019).

Ego-Dissolution

Ego-dissolution is a main aspect of the psychedelic experience and has been described as "an ecstatic state, characterized by the loss of boundaries between the subject and objective world, with ensuing feelings of unity with other people, nature, the entire Universe, and God" (Deane, 2020, p. 2).

Even if one's sense of self may feel permanent, it is easily affected. A distortion of one's experience of self is one of the main aspects of the psychedelic experience. Commonly referred to as ego-dissolution, ego-death, or ego-disintegration, the phenomenon is caused by a reduction in self-referential awareness that is normally present in baseline waking consciousness (Deane, 2020). It diminishes one's sense of self, and the boundaries between the self and the rest of the world break down. This is closely connected to *mystical experiences,* which are described as feelings of unity with the world and other people (Nour & Carhart-Harris, 2017). Both the reflective (narrative) and non-reflective aspects (thought ownership/first-person perspective) of self-experience are affected and reduced in ego-dissolution. Ego-dissolution may stop individuals from feeling the "mineness" of their thoughts, creating an estrangement from them. However, primarily ego-dissolution affects one's feeling of an individual, temporally extended autobiographical identity (Girn & Christoff, 2019).

All classic psychedelic drugs have the ability to induce ego-dissolution, including lysergic acid diethylamide (LSD), psilocybin, and dimethyltryptamine (DMT) (Nour et al., 2016). A disintegration of the self can also be achieved through deep meditation (Millière et al., 2018).

Mystical experiences, along with ego-dissolution, are key features of the psychedelic experience that some scientists believe are responsible for the outcome of psychedelically-assisted therapies (Nour & Carhart-Harris, 2017; Deane, 2020). This belief is due to the discovery that the long-lasting positive effects of psychedelics are linked to their ability to cause mystical-type experiences and profound insights. The positive therapeutic effects seemingly rise along with mystical experiences or a psychedelic "peak" (Deane, 2020).

Integration of the whole brain and disintegration of the DMN has been shown after an intake of psychedelics correlated with subjects' ratings of ego-dissolution (Nour & Carhart-Harris, 2017). However, in one study by Lebedev and colleagues (2015), they could not find a correlation between psilocybin-induced ego-dissolution and disintegration of the DMN. Instead, their study showed a disrupted interplay between the neocortex and the medial temporal lobe (MTL) as well as decreased saliency network integrity.

Measurements of Ego-Dissolution

To measure the subjective experience of ego-dissolution in a reliable and easy way, The Ego Dissolution Inventory (EDI) was developed and validated in 2016 by Nour and colleagues (2016). EDI is a self-report questionnaire that consists of eight items related to altered self-consciousness. A strong positive correlation was found between ego-dissolution and an increase in well-being by measuring EDI after a psychedelic experience (Nour et al., 2016). Furthermore, the results from the EDI were consistent with earlier findings of the positive correlation between the intensity of a psychedelic experience and the degree of mystical experiences, feelings of *oceanic boundlessness*, and *dread of ego-dissolution*.

Nevertheless, there have been arguments against the validity of the EDI. Firstly, Girn & Christoff (2019) expressed concerns about how some of the questions are related to self-experience and its specific components. Sebastián (2020) agreed with the former and argues that the questionnaire is unable to show the disintegration of the first-person perspective.

Mystical experiences are measured by the Mystical Experiences Questionnaire (MEQ) which consists of four parts. The first part measures the "mystical" parts of the experience, asking questions about feelings of unity with the world and a releasing of a personal self, as well as gaining intuitive knowledge, and having spiritual and "holy" experiences (Trippingly, 2020).

Disturbances of Self-Experience

There are several psychiatric conditions affected by an altered state of self-experience, such as psychosis, depression, and anxiety (Deane, 2020; Girn & Christoff, 2019). Psychosis is characterized by the loss of boundaries between the self and the environment. Ego disturbances have been a central focus of research and diagnostics of schizophrenia since its earliest clinical description (Lebedev et al., 2015). Depression and anxiety are, on the other hand, associated with an increase in self-focus and being unable to disengage from self-referential ruminative thoughts (Nour & Carhart-Harris, 2017). Self-rumination is when individuals engage in repetitive self-focused evaluative thinking as a form of experiential avoidance. As a result, negative emotions cannot be processed correctly which can lead to depressive symptoms. Self-compassion on the other hand allows for effective processing of negative emotions, which can combat variables affecting poor mental health, such as anxiety, depression, shame, and self-rumination. Therapy that focuses on self-compassion has been shown to efficiently decrease depression, anxiety, and stress (Fauvel et al., 2021). Hence, there is a suggested correlation between depression and anxiety and the narrative/autobiographical self (Girn & Christoff, 2019).

Both depression and schizophrenia exhibit abnormal resting-state activity in the DMN. Depressed individuals have also shown abnormal activity in the perigenual anterior cingulate cortex, which has been observed to exhibit increased activity for self-specific stimuli (Nour & Carhart-Harris, 2017). There has been some success in treating depression and anxiety using classic psychedelic drugs (see *Psychedelics)* to cause positive changes in psychological well-being and reduce symptoms of anxiety, stress, and depression. Psilocybin specifically has been shown to cause persisting positive changes in areas such as attitude, mood, behavior, trait openness, as well as higher life satisfaction (Schmid & Lechti, 2018). Some scientists suggest that these therapeutic successes are caused by ego-dissolution (Nour & Carhart-Harris, 2017). Generalized Anxiety Disorder (GAD) is defined by DSM-5 (2013) as excessive anxiety and worry followed by cognitive or physical symptoms such as difficulty sleeping, aching muscles, impaired concentration, increased irritability, and restlessness. For a depression diagnosis, there are nine criteria from which the patient must experience five. The individual must either experience a depressed mood every day or experience diminished pleasure in almost all activities. Further symptoms include significant weight loss, lack of energy, diminished ability to think, and recurrent thoughts of death.

Psychedelics

The psychoactive substances known as *psychedelics* (5-HT2A receptor agonists)

have the ability to cause powerful alterations in phenomenology, affecting cognition, sensory and time perception, emotion, and self-consciousness. Self-experience has been successfully altered in a dose-dependent, reversible and transient way by the use of psychedelic drugs. The drugs make it possible to study their transformative therapeutic abilities (Nour & Carhart-Harris, 2017; Deane, 2020). Psychedelics have in recent years caused a wave of research on their therapeutic properties (see *Ego-dissolution)* (Deane, 2020). Classical psychedelics include LSD, psilocybin, DMT, and mescaline which can fall into one of two categories of general structure. Either they have the structure of the amino acid tryptamine (e.g. LSD, psilocybin, and DMT) or phenethylamine (e.g. mescaline) (Johnson et al., 2019). Studies have shown that psychedelics affect the segregation between resting-state brain networks important for the sense of self (e.g. the DMN) as well as the integrity of these networks. This results in a globally unified mode of brain function, compared to baseline (Nour & Carhart-Harris, 2017). Furthermore, psychedelic substances affect the neurogenesis of the hippocampus, which have been shown to alleviate depression and conditioned fear (Catlow et al., 2016).

Psychedelics affect both bodily and mental self-experience: The bodily aspects include the body's awareness, boundaries, representation, ownership, and location; the mental aspects are the autobiographical (narrative/self-reflective) self and thought ownership (minimal self/first-person perspective/pre-reflective self). The bodily effects are more easily found in the psychedelic experience, while the mental aspects are more often correlated with higher doses. The ability of psychedelics to elicit a broad variety of altered states of self-experience makes them an important tool for both theoretical and empirical research. Psychedelics may therefore be indispensable to the scientific study of self, as well as the research on the possible therapeutic treatments of disorders of self-experience (Girn & Christoff, 2019).

Objectives

Neuropsychiatric disorders such as depression and anxiety are among the greatest contributors to disability and mental illness around the world (Steel et al., 2014). Traditional treatments are often unsuccessful, pushing science to find new ones (Olson, 2021). So far there is no conclusive evidence that ego-dissolution is the cause of the mental health benefits seen after psychedelic treatments. Investigating the neural correlates of self-experience is of interest for the field of consciousness, as well as for implementing new treatments of psychiatric conditions. Further knowledge of distorted

self-experience, and how it is modulated by psychedelic treatments, could potentially give new insights into the nature of the self and our consciousness.

In this literature review, I will gather the studies done on the therapeutic effects of ego-dissolution and mystical experiences (induced by the classic psychedelics LSD, psilocybin, mescaline, and DMT) on the psychiatric disorders depression and anxiety. The aim is to use both new (EDI) and old (MEQ) measurements of ego-dissolution to find what evidence supports the idea that ego-dissolution is responsible for the therapeutic effects seen in depression and anxiety after the use of psychedelics.

Methods

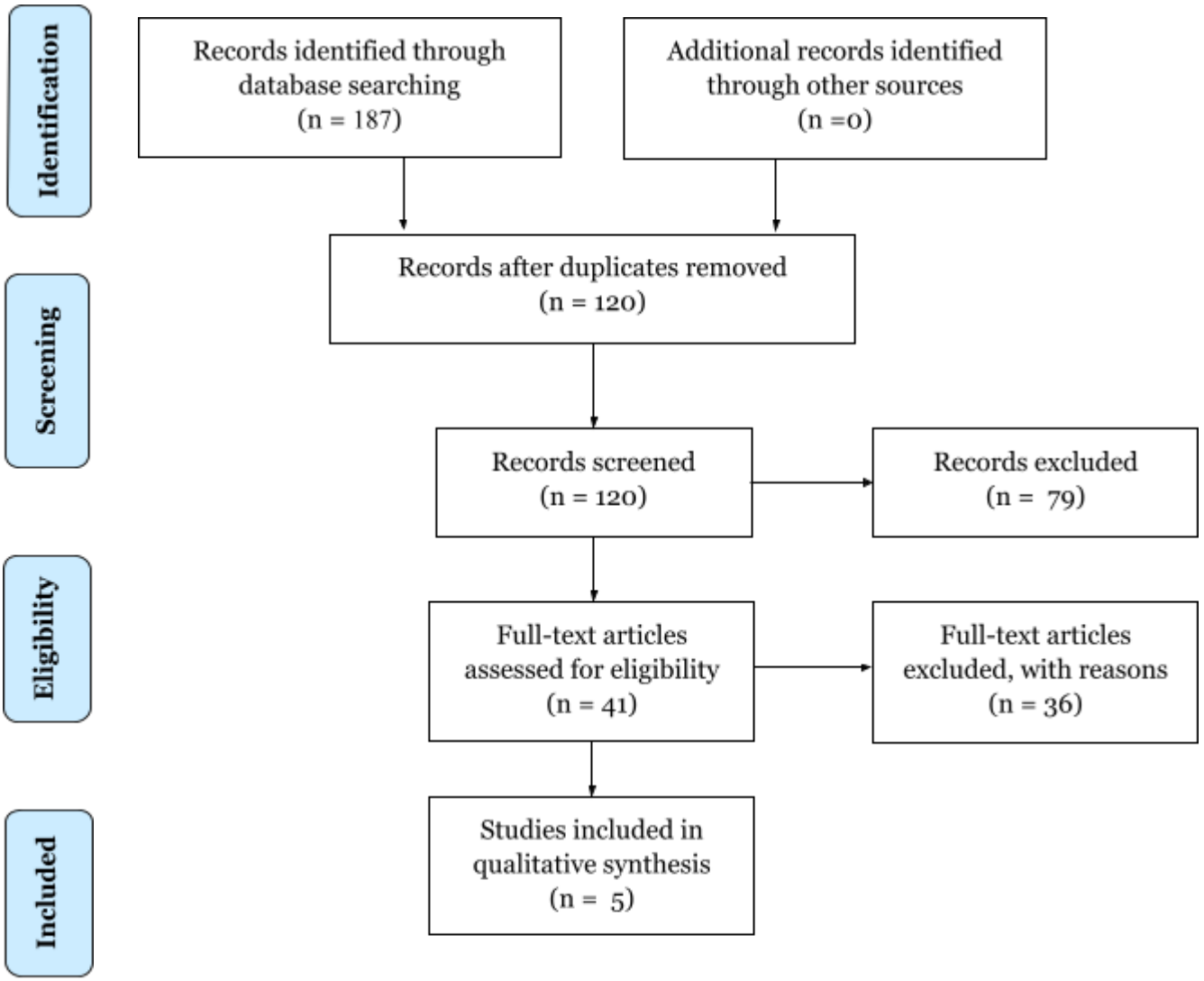
Search Strategy

The literature search was carried out on the 28th of February, 2022, using the databases Scopus and Web of Science. The search string was: *(*"ego dissolution" OR "mystical experience") AND (psychedelic* OR LSD OR psilocybin OR DMT OR mescaline) AND (therapeutic OR therapy OR depression OR anxiety OR "mental health").

The search string resulted in 187 articles (Scopus n = 100, Web of Science n = 87). After removing duplicates, 120 articles were screened. 79 articles were then removed based on title and abstract, leaving 41 full-text articles to be evaluated based on the inclusion/exclusion criteria (see below). The remaining 5 articles were used for the systematic review (see Figure 1 for an illustration of the literature search process).

Figure 1

Flow Chart of Article Selection Process.



Note. The standard flow diagram is used to document the literature search process (Moher et al., 2009)

Inclusion and Exclusion Criteria

To be included, the studies had to measure the effects of ego-dissolution induced by classic psychedelics (LSD, psilocybin, DMT, or mescaline) on the neuropsychiatric conditions anxiety and depression. The articles need to use the measurements *Ego-dissolution inventory* (EDI) and/or *Mystical Experience Questionnaire* (MEQ) to measure ego-dissolution. Furthermore, the articles had to measure levels of anxiety and/or depression in participants before and after a psychedelic experience. The articles need to be published between 2000 and 2022 in peer-reviewed journals and be written in English.

Exclusion criteria included: the use of other measurements of ego-dissolution than EDI and MEQ; if the study did not discuss a correlation between the effect of ego-dissolution on depression and/or anxiety; if the article type was a meta-analysis, book/book chapter, editorial, or systematic review.

Data Extraction

The following data were extracted from the articles: Measurements of MEQ or EDI, and measurements of anxiety and/or depression before and after a psychedelic experience. The PICO criteria are:

P: Healthy participants (to see how the baseline is affected) AND/OR participants suffering from depression or anxiety (to see how psychedelics affect an altered baseline)

I: Psychedelic treatment

C: Placebo / No treatment

O: Symptoms of depression and/or anxiety

Table 1

Criterion for articles of interest for this systematic review.

Outcome measure	**Type of measure**	**Intervention**
Experience of depressive/anxious symptoms	Self-report	A psychedelic dose
Experience of ego-dissolution	Self-report in EDI and/or MEQ	A psychedelic dose

Results

Five articles were eligible for this literature review that investigates the relationship between ego-dissolution/mystical experiences and improvements in depression and anxiety (Uthaug et al., 2019; Gukasyan et al., 2022; Reckweg et al., 2021; Davis et al., 2020; Fauvel et al., 2021). Two of the studies were questionnaires that asked participants questions about a memorable experience they had with psychedelics (Fauvel et al., 2021; Davis et al., 2020). The remaining three studies admissioned the drug on location to consenting participants (Uthaug et al., 2019; Gukasyan et al., 2022; Reckweg et al., 2021). A majority of the studies found a moderate negative correlation between the degree of mystical experiences/ego-dissolution during the psychedelic experience and the level of anxiety and depression afterward. The one study that could not find any correlation insists that their results do not invalidate other findings because of their participants' general low levels of anxiety and depression at baseline (Reckweg et al., 2021).

Efficacy and Safety of Psilocybin-Assisted Treatment for Major Depressive Disorder

Gukasyan et al. (2022) aimed to examine the safety and efficacy of psilocybin in participants with moderate to severe unipolar depression (MDD) through four follow-up time points (4 weeks, 3, 6, 12 months). 27 participants (age 21-75) were enrolled who were medically stable and met the criteria for moderate to severe MDD by receiving a score of ⩾17 on the GRID-Hamilton Depression Rating Scale (GRID-HAMD). The participants received two doses of psilocybin with supporting psychotherapy approximately two weeks apart. 24 participants completed both sessions of psilocybin and completed the follow-up 12 months after their last dose. The ratings of mystical experiences significantly correlated with ratings of well-being at all follow-ups. However, only ratings of personal meaning and spiritual significance were correlated with improvements in depression, and only at the first follow-up session (4 weeks). The results from the MEQ30 were not reported anywhere in the study, only the correlation. The correlation between MEQ30 and GRID-HAMD was at its highest four weeks after the session ($r = 0.38$; $p=.066$) but was substantially lower at later time points ($r = 0.17$, 0.05, and 0.19 at 3, 6, and 12 months). Hence, MEQ30 is suggested by the authors to not be a reliable predictor of psilocybin's enduring antidepressant effects. MEQ30 could be a reliable predictor, but psilocybin ii itself may not have an antidepressant effect.

Investigation of the Use and Effects of 5-MeO-DMT in a Naturalistic Setting

The primary aim of Uthaug et al. (2019) was to examine whether the vapor from the 5-MeO-DMT-rich toad secretion produced long-lasting and/or acute improvements in cognition and affects. A secondary aim was to investigate if certain aspects of the psychedelic experience (such as ego-dissolution) were related to mental health measures. The participants went through a baseline assessment before inhaling vapor 5-MeO-DMT (from dried toad secretion), a follow-up assessment within 24 hours of the session, and then again 4 weeks post-session. 42 participants completed the first two assessments, and 24 participants completed all three. The test battery for the assessment consisted of EDI, the Satisfaction with Life Scale (SWL), the 5-Dimensional Altered States of Consciousness Rating Scale (5D-ASC), the Five Facets Mindfulness Questionnaire (FFMQ-15), the Brief Symptom Inventory-18 (BSI-18), and the Depression, Anxiety, Stress Scale-21 (DASS-21). Pearson's correlation was carried out to investigate the correlation between ego-dissolution and their outcome measures. For EDI, the mean (SE) was 74.24 (3.99). Around 80% of the sample reached higher levels of ego-dissolution (between 60-100), while 20% reported their ego-dissolution in the lower range (0-60).

Correlational analysis showed that ratings of ego dissolution was negatively correlated with stress (DASS-21: $r = -0.46$; $p = 0.003$) and depression (BSI-18: $r = -0.378$, $p = 0.016$), and positively correlated with the ratings of satisfaction with life ($r = 0.357$, $p = 0.026$),. The results showed a reduction in DASS-21 ratings immediately after the session; observing a decrease in the participants' scores on feelings of stress (27%), depression (18%), and anxiety (39%) compared to pre-treatment. The scores decreased after four weeks to 48%, 68%, and 39%, respectively. The measurement of BSI-18 showed similar results. At 4 weeks, however, EDI did not correlate with any changes.

Assessing Safety and Psychoactive Effects of 5-MeO-DMT in Different Doses

The study (Reckweg et al., 2021) was conducted in preparation for a study assessing the effects of four different levels of dosage of vaporized 5-MeO-DMT in patients with depression. The phenomenality was assessed through the EDI, MEQ30, Peak Experience Scale (PES), 5D-ASC, and the Challenging Experience Questionnaire (CEQ). Furthermore, subjective well-being was measured through DASS-21, the Brief Psychiatric Rating Scale (BPRS), the FFMQ, and the Satisfaction with Life Scale (SWL).

The study consisted of two single-arm parts. The first part was a single ascending dose study, while the second part was an individualized dose escalation

(IDE) regimen. Results showed no significant correlation between MEQ30/EDI and improvements in DASS-21 scores. However, the participants were selected because of their minimal BPRS ratings. Therefore, Reckweg et al. (2021) conclude that their results do not contradict results from other studies where results have shown significant therapeutic improvements, since the former did not expect a change in mental health in their sample.

A Survey Investigating Improvements in Mental Health After Use of 5-MeO-DMT in a Naturalistic Group Setting

This study (Davis et al., 2019) used an anonymous web-based survey to investigate self-reported improvements in anxiety and depression among participants who have used 5-MeO-DMT. The participants were recruited from a group that uses the hallucinogen in a group setting with structured procedures which are similar to those of clinical trials of administration. A secondary aim was to examine whether or not acute subjective effects in the form of mystical or challenging experiences were correlated to these mental health improvements. The survey consisted of extensive questions about the epidemiology, as well as if the respondents had the psychiatric conditions depression and/or depression and if it had changed after 5-MeO-DMT consumption. The acute subjective effects were assessed through MEQ30, CEQ, and PEQ and their subscales. For the analysis, the sample was divided into two groups based on if they reported having anxiety or depression. A series of chi-squares and t-tests were used to compare the variables between the groups, and the effect size was calculated with Cohen's *d*.

362 (Mean age = 47.7; Male = 55%) completed the survey. Most of those who reported having been diagnosed with anxiety (48%; n = 173), depression (41%; n=149), or both (34%; n=117), reported an improvement in these conditions after the use of 5-MeO-DMT. Out of the diagnosed participants (within each condition), 79% of participants with anxiety and 80% of the participants with depression described an improvement in their condition. Those who reported improvements in anxiety and/or depression scored higher on the MEQ30 (Depression group: MEQ30 total score and positive mood subscale; Anxiety group: MEQ30 total score, and all MEQ30 subscales) than those who did not report an improvement in these conditions. The t-statistics for the means and standard deviations for the total MEQ score between the two groups of participants with self-reported depression (Group 1: Participants who reported improvements; Group 2: Participants whose condition worsened/reported no difference): t-stat = -2.5, $p<.05$. For the total MEQ30 score between the two groups in

anxiety (Group 1: Participants who reported improvements; Group 2: Participants whose condition worsened/reported no difference): t-stat= -3.3, $p<.01$. Both t-stat values are significant.

Furthermore, those who improved in both groups received higher scores of spiritual significance and personal meaning, which they reported contributed to heightened life satisfaction/sense of well-being. In both the depression and anxiety groups, those who reported improvements in those conditions were significantly younger than those who had reported that their condition remained the same or worsened.

A Survey Investigating the Shift from Self-Rumination to Self-Compassion Under the Influence of Psychedelics

Fauvel et al. (2021) focused on how mystical experiences and psychological insights have been indicated to shift the mind from self-rumination to self-compassion, which improves symptoms of depression, anxiety, and stress (DAS).

Fauvel et al. (2021) conducted an internet-based survey where the participants reported having had a subjectively significant psychedelic experience. The measurements used in the survey were MEQ30, Psychological Insight Questionnaire (PIQ), DASS-21, The Self-Compassion Scale-Short Form (SCS-SF), and Rumination Response Scale (RRS). A regression analysis was conducted to test if mystical experiences and psychological insight can predict improvements in DAS.

164 participants completed the full survey (female = 34). They concluded that the decrease in stress, anxiety, and depression (Mean (SD): −10.7 (11.6)) is to some degree mediated by mystical experiences (Mean (SD): 3.6 (1); $r = -.28$). However, psychological insight (Mean (SD): 3.1 (1)) was significantly associated with decreases in DAS ($r = -.33$) and self-rumination ($r = -.34$), as well as increases in self-compassion ($r = .35$). The researchers suggest that increases in self-compassion and decreases in self-rumination could be partial mediators of the effects that psychedelics have on DAS. They conclude that their result supports the use of contextual behavioral science to get the best effects from psychedelic-assisted therapy.

Table 3

Results from the selected articles.

Study	Psychedelic intervention	Ego-dissolution, Mean	Depression/anxiety, Mean	Correlation
Gukasyan et al. (2022)	Psilocybin; 2 doses	MEQ30: Not reported	GRID-HAMD: Baseline: 22.8 (3.9) 12 months post-treatment: 7.7 (7.9)	Moderate correlation
Uthaug et al. (2019)	5-MeO-DMT; 1 supervised dose	EDI: 74.24	DASS-21 (pre-session): Depression: 7; Anxiety: 4.5 DASS-21 (31 days post-session): Depression: 3; Anxiety: 1 BSI-18 (pre-session): Depression: 3; Anxiety: 3 BSI-18 (31 days post-session): Depression: 1; Anxiety: 1	Moderate correlation
Reckweg et al. (2021)	5-MeO-DMT; one session IDE until PE was reached	EDI: 70 MEQ: 3.5	DASS-21 (baseline): Depression: 1,5; Anxiety: 3 DASS-21 (IDE, 7 days post-dose): Depression: 2; Anxiety: 1	No correlation
Davis et al. (2019)	5-MeO-DMT; web-based survey on the participants general usage	MEQ30: 4.3	Depression and Anxiety self-report, Improvement after psychedelic dose: Anxiety =79%; Depression=80%	Moderate correlation
Fauvel et al. (2021)	Classic psychedelics; a memorable experience with psychedelics	MEQ30: 3.6	DASS-21: Decrease in depression, anxiety, and stress −10.7	Weak correlation

Note: GRID-HAMD = GRID-Hamilton Depression Rating Scale, DASS-21 = The Depression, Anxiety and Stress Scale - 21 Items , IDE = Individualized Dose Escalation, MEQ30 = The 30-item revised Mystical Experience Questionnaire, BSI-18 = Brief Symptom Inventor

Discussion

The aim of this systematic review was to assess what evidence can be presented for the therapeutic impact of psychedelic-induced ego-dissolution on the neuropsychiatric conditions of depression and anxiety. Both disorders are affected by a heightened sense of self.

Five articles were reviewed. Three of the articles presented in this review showed a moderate negative correlation between psychedelic-induced ego-dissolution/mystical experiences and depression and/or anxiety (Gukasyan et al., 2022; Davis et al., 2019; Uthaug et al., 2019). One study showed a weak correlation (Fauvel et al., 2021), and one study could not show any correlation (Reckweg et al., 2021). These findings suggest that there could be a correlation between ego-dissolution and improvements in depression and anxiety, which is in line with other philosophical and clinical studies (Deane, 2020; Nour & Carhart-Harris, 2017; Roseman et al., 2018; Griffiths et al., 2011).

However, there could be other variables of acute subjective effects that have the same, if not a more significant, impact. Davis et al. (2019) received high ratings of spiritual significance and personal meaning in the groups with improvements in depression or anxiety. In the study by Fauvel et al. (2021), psychological insights were correlated with decreases in DAS and seemed to mediate the shift between self-rumination and self-compassion. An earlier study by Davis et al. (2020) found that acute psychological insights during a psychedelic session better predicted improvements in anxiety and depression than mystical-type experiences. Psychological insight is considered an important element of psychotherapy and is one aspect of quantum change phenomena, which describes a sudden and enduring transformation that affects behavior, cognition, and emotions (Johnson et al., 2019; Miller, 2004). Additionally, results from Fauvel et al. (2021) support the view that psychedelic experiences trigger psychological insights. Psychological insights can induce long-term shifts in perspective and deconstruct old negative thinking patterns. This is the shift from self-rumination to self-compassion, from experiential avoidance to acceptance, which has been argued to be a reason why psychedelic-assisted therapy works (Wolff et al., 2020). Furthermore, the results from Fauvel et al. (2021) are in line with previous studies that have shown that experiential avoidance and psychological flexibility are key features of the therapeutic outcome of psychedelics (Zeifman et al., 2020; Davis et al., 2021).

The second aim of this literature review was to investigate if research in this

area could give insights into the nature of the self. Ego-dissolution can cause disruptions in the feeling of “mineness” in the experiential dimension of the self, also referred to as the minimal self and the first-person perspective. However, to a larger extent ego-dissolution is the disruption of the self-referential activity that defines the third-person perspective and the narrative/autobiographical self. Self-referential activity is the foundation of self-rumination which in higher degrees can cause anxiety and depression (Nour & Carhart-Harris, 2017). The results from these studies suggest that ego-dissolution possibly can cause a shift in the narrative self, allowing the mind to turn from self-rumination to self-compassion (Fauvel et al., 2021; Girn & Christoff, 2019). Nevertheless, since none of the present studies used brain imaging techniques, the neural correlates of their results become speculative.

Some indications emerge from an earlier understanding of the role of the DMN in the narrative self, anxiety, depression, and the psychedelic experience. Abnormal resting state activity in the DMN, as well as activity in the perigenual anterior cingulate cortex, had been found in patients with depression (Nour & Carhart-Harris, 2017). However, there is no conclusive evidence for this. A previous study found that increased functional connectivity between the DMN and the subgenual prefrontal cortex (sgPFC) often could predict the levels of depressive rumination (Hamilton et al., 2015). Depressive self-ruminative thoughts often accompany depression and anxiety (Nour & Carhart-Harris, 2017). These studies, and more, suggest that DMN is a main variable in both psychiatric disorders (Posner et al., 2016; Whitton et al., 2018). The DMN is connected to the narrative self which becomes overactive in depression and anxiety with higher levels of self-rumination (Davey & Harrison, 2018; Girn & Christoff, 2019). The narrative self is affected by higher-level prior beliefs, controlling how we experience the world and ourselves.

Psychedelics cause a reduction in DMN activity and disrupt self-referential activity. The Relaxed Beliefs under Psychedelics (REBUS) model proposes that psychedelics “relax” high-level priors or beliefs by increasing the sensitization to bottom-up signaling, causing the priors to be revised and discarded if outweighed (Carhart-Harris & Friston, 2019). Furthermore, psychedelic substances have been shown to increase neurogenesis in the hippocampus, which has effects on learning and memory. Drug-induced altered neurogenesis has also been found to alleviate depression (Catlow et al., 2016). It is possible that psychedelics affect depression and anxiety positively by relaxing the higher-level prior beliefs, increasing neurogenesis, and altering the patients' learning and memory abilities (Gallagher, 2000). Then the

patient is able to re-evaluate their prior beliefs and shed those who no longer are in tune with reality (Deane, 2020). An example of a higher-level prior belief is the view of oneself as having a particular personality, characteristics, and opinions (the narrative self; Carhart-Harris & Friston, 2019). Consequently, this process might make it possible for the patient to look at themselves and the world with new eyes and absorb information more objectively. Ego-dissolution, psychological insights, oceanic boundlessness, or another acute subjective effect of psychedelics could be the cause of this shift from self-rumination to self-compassion (Griffiths et al., 2011; Roseman et al., 2018; Fauvel et al., 2021). Or these subjective effects might just be biomarkers for the 5-HT2A receptor activation, and not critical for the therapeutic outcome at all (Olson, 2021).

Limitations

Apart from the methodological limitations in the reviewed studies, this literature review has a number of limitations. This review looked at measurements of mystical experiences as a measurement of ego-dissolution. Even though both phenomena are similar, mystical experiences encompass several acute subjective effects that differ from ego-dissolution. Therefore, having MEQ30 as a measurement does not isolate ego-dissolution as a variable, instead involving other factors (such as “positive mood” and “ineffability”) that could have affected the result. Moreover, oceanic boundlessness could, alongside mystical experiences, have been used as a measurement of ego-dissolution. The definitions are related, oceanic boundlessness being defined as a feeling of infinity and being one with the external world as a whole. However, as to not stray too far from the main variable of interest (ego-dissolution), feelings of oceanic boundlessness alone was not a variable of interest. Furthermore, the EDI has been criticized for not being able to properly capture the breakdown of the first-person perspective. This is of importance when measuring ego-dissolution which affects both the first and third-person perspectives. Therefore, this measurement is also not a perfect candidate for measuring ego-dissolution.

Reckweg et al. (2021), who did not find a correlation, present the possibility that MEQ and EDI may capture a wider array of aspects surrounding the phenomenology of the psychedelic experience that does not translate well to the short and intense experiences of 5-MeO-DMT in a clinical setting. In their study, only a few reached the threshold for a mystical experience (n = 3, MEQ rating >3), and EDI ratings over 60% of the total score (n = 4). Instead, EDI and MEQ might be preferable for spiritual or self-exploratory contexts.

Limitations included the studies' varying methods of presenting their results. Even though they used MEQ30 and/or EDI, and often DASS-21, not every study reported the exact numbers. Instead, Reckweg et al. (2021) presented their DASS-21, MEQ30, and EDI results in hard-to-read diagrams from which the numbers had to be estimated. Two of the studies (Reckweg et al., 2021; Gukusyan et al., 2022) were limited by their small sample size (n = 22, 24, respectively). Also, Davis et al. (2019)'s participants reported to a large extent the use of alcohol, cannabis, and other psychedelic substances such as LSD and psilocybin. This resulted in an inability to conclude that the results came singlehandedly from the use of 5-Meo-DMT. Furthermore, it might have skewed the results since the participants may have had a higher probability of reporting the psychedelics more favorably in their answers. Uthaug et al. (2019) were limited by their lack of a control group, as well as 54 participants not completing the measurements after the dosage. This might have skewed the data if the participants dropped out because of disappointment that the experience did not fulfill reported motivations, which included self-development and spiritual healing.

According to the authors, selection bias could have affected the studies that used web-based surveys. The participants might have been drawn to the studies because of positive experiences with psychedelics, hence skewing the data (Davis et al., 2019; Fauvel et al., 2021).

Future Research

Further clinical research is needed to replicate and investigate the implications of current findings. There is a need for randomized, placebo-controlled clinical trials with larger sample groups and clearly defined measurements of acute subjective effects. Additionally, the research needs to continue to study the efficacy and safety of psychedelic substances to be able to investigate their therapeutic properties and medicinal potential. Psychological insights and psychological flexibility seem to positively affect the outcome of psychedelic-assisted therapy. A future research area of interest would be to combine psychedelics with therapies targeting psychological flexibility.

Future research especially needs to investigate how psychedelics affect the experiential self both psychologically and neurologically in regard to neuropsychiatric disorders. Deeper knowledge about how the self affects and is affected could lay the foundation for future treatments for disorders of the self, such as anxiety, depression, schizophrenia, and psychosis.

Ethical and social aspects

The ethical and social aspects are important when it comes to researching psychedelics because of western culture's outlook on drugs as well as the strict laws surrounding them. It is important when working with participants, especially those diagnosed with illnesses, that they remain full autonomy and are well-informed about possible outcomes. Also, being strict with exclusion criteria to exclude those who are too ill to fully consent to the treatment.

Conclusion

The aim of this systematic review was to investigate what evidence supports the hypothesis that ego-dissolution is responsible for the positive therapeutic effects of classic psychedelic substances on anxiety and depression. Three of the studies found a moderate correlation between measurements of mystical experiences and ego-dissolution and improvements in anxiety and depression. One of the studies found a weak correlation, and one study found no correlation. These results indicate that there might be a correlation between the absence of self and improvements in disorders of a heightened sense of self. Further research is needed, with larger sample groups, properly defined measurements of ego-dissolution, and tracking the changes with brain-imaging methods as well. Research on the impact of psychedelics on the self could give insight into neuropsychiatric disorders of the self and new treatment methods, as well as catapult the philosophical and clinical research of self into a new era.

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