Degree project

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Understanding Ego Dissolution: A Gateway to Psychedelic Therapy

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Abstract

The investigation into the therapeutic potential of psychedelics has marked a paradigm shift in mental health research, with potential outcomes for disorders such as depression. Amidst the diverse varieties of psychedelic effects, one phenomenon that has captured the researcher's attention is the term ego dissolution: a state characterized by the dissolution and reduction of one's ego. Yet, within this phenomenon, a gap exists, one that links the dissolution of an individual's ego to the potential treatment of depression.

The study aims to understand the connection between ego dissolution and depression. Neural processes will be discussed to provide further insight into the relationship between brain activity and subjective experiences during ego dissolution. The present study reveals a negative correlation between ego dissolution and depression, indicating decreased depression levels. The collective findings highlight ego dissolution as a possible component in psychedelic therapy, associated with improved mental health outcomes.

Keywords: ego dissolution, psychedelics, therapy, depression.

Understanding Ego Dissolution: A Gateway to Psychedelic Therapy

The 'Self'

Within the exploration of the 'self', lies an intricate and elusive concept defying a singular, clear-cut definition. Lebedev et al. (2015) describe the term as an umbrella, encompassing a diverse spectrum of mental phenomena, notably the profound elements of agency and ownership. Amidst this exploration, the sense of agency emerges as a fundamental aspect, involving the subjective awareness of being the initiator or actor behind intentional actions (Lebedev et al., 2015). It establishes a critical link between the individual and their innate capacity to influence and control their behaviors, thereby enhancing the intricate layers of self-awareness.

Throughout this study the term 'self' in apostrophes is used to refer to an individual's subjective sense of personal identity and existence, This distinction is important because it highlights the focus on the subjective experience of being. The 'self' interlaces components such as self-identity, theory of mind, and the nuanced interplay between subject and object (Lebedev et al., 2015). Delving into philosophical nuances, a distinction surfaces between "being a self" which pertains to existing as a subject of conscious experience, and "being, reflectively, self-aware" which refers to the ability to contemplate oneself as the subject of experience (Millière, 2017).

Gallagher's perspective on the self underscores a relationship between cognitive neuroscience and philosophy, emphasizing a two-way collaboration, particularly in relation to the "narrative self" and the "minimal self" (Gallagher, 2000). The narrative self is a coherent sense of self that encompasses past experiences and future intentions, formed through stories about oneself and by others about one's life. Conversely, the minimal self refers to the immediate and present experience of being a subject of experience, without consideration of the past or future. This sense of self is phenomenological and relies on brain processes and the body's interaction with its environment (Gallagher, 2000).

According to Nagel (1980), a mental state is considered phenomenally conscious if there is a subjective experience associated with it, including the specific qualities or sensations we experience. However, this statement has been recently debated, suggesting that while the qualitative character of the experience certainly is a part of phenomenal consciousness, there might be additional aspects to consciousness, beyond the subjective character (Millière, 2017). While qualia focuses on the specific qualities or sensations of an experience, such as the experience of "bluishness" when seeing the sky (Nagel, 1980), subjective character pertains to the understanding that there is a subjective experience associated with being in a certain state. The subjective character differs from qualia by addressing the personal aspect of consciousness, highlighting an individual's subjective experience within a mental state (Millière, 2017). This implies that the relationship between consciousness and self-awareness might be more complex than previously thought, challenging the idea that self-awareness and consciousness are separable.

What separates the 'self' from the ego? The ego, as described by Freud, is referred to as "the I" (Freud, 1927), referring to the feelings of having an unchanging sense of 'self'. It suggests that an individual perceives their identity as consistent over time, without alterations. Essentially, the ego complements the concept of the 'self' (Carhart-Harris et al., 2014), making the ego and 'self' synonyms.

In essence, Freud's concept of the ego and Gallagher's narrative self work together: the narrative self provides context for the ego's function and together they construct a consistent and enduring sense of identity. However, the minimal self is not concerned with the past or future, but with the direct moment of awareness (Gallagher, 2000).

Studying the 'self' and consciousness involves diving into the essence of our existence, focusing not on objective realities but on the subjective realm of human consciousness (Revonsuo, 2009). This subjective existence is what animates individuals, allowing them to perceive, feel, and comprehend their own being. It encompasses subjective experiences that define one's sense of 'self'.

This study aims to delve into the intricate concept of the 'self', focusing particularly on the notion of the ego. Previous research by Lebedev et al. (2015) and Millière (2017) underscores the complexity of self-referential processing, emphasizing the subjective sense of agency and ownership as fundamental components of the ‘self’. Throughout this study, the term ‘self’ will be used to refer to an individual’s subjective sense of personal identity and existence, distinguishing it from objective realities and highlighting the focus on subjective experience. Drawing on Gallagher's theories (2000), the narrative self is understood as a coherent sense of identity formed through personal and shared stories, encompassing past experiences and future intentions.

Psychedelics

Serotonergic psychedelics such as lysergic acid diethylamide (LSD), psilocybin, and ayahuasca have emerged as potential therapeutic agents for a range of psychiatric and neurological conditions including, anxiety, and depressive disorders (Kałużna et al., 2022).

Psychedelic substances have been recognized for causing alterations in the way individuals perceive their sense of ‘self’ or “ego” (Nour et al., 2016; Kałużna et al., 2022). These substances are acknowledged for inducing various subjective phenomena, with a specific focus on ego dissolution (Kałużna et al., 2022). Serotonin 2A receptors (5-HT2AR), are receptors in the brain that play a role in the effects of psychedelics, representing a class of psychoactive substances that significantly alter perception and impact cognitive processes. Consequently, psychedelic substances are recognized for inducing significant alterations in consciousness (Millière, 2017). These hallucinogens not only influence mood but are also believed to expand consciousness (Kałużna et al., 2022), potentially leading to experiences where individuals feel united or merged with other beings, objects, and/or the universe itself (Girn & Christoff, 2018).

Substances such as LSD, psilocybin, and dimethyltryptamine (DMT), share a commonality; they influence the central nervous system. Despite their diverse chemical origins, these psychedelics induce similar subjective effects. As per Millière’s (2017) findings, experienced users frequently encounter challenges in discerning between these substances during blind experiments. Notably, psychedelics stand out for their ability to produce vivid visual effects, including both simple and complex hallucinations, a feature less pronounced in other types of psychoactive substances.

Ego Dissolution

Ego dissolution, also known as ego death, refers to an altered perception of 'self' marked by the dissolution of boundaries between the individual and the external world. This phenomenon describes the sensation of the 'self' undergoing a psychedelic experience, signifying a reduction in one's ego (Stoliker et al., 2022; Nour & Carhart-Harris, 2017). It involves ecstatic feelings and the loss of distinctions between the external world and one's perception. Ego dissolution is characterized as an emergent shift in the individual, akin to the mystery of consciousness (Stoliker et al., 2022). This suggests that individuals who are using psychedelics and undergoing ego dissolution feel a sense of unity with others, the universe, nature, and even a higher power or God.

Research has shown that classical drugs, including DMT, LSD, and psilocybin, possess the ability to reduce one's ego (Nour et al., 2016). The authors suggest that the previous psychological state of the individual, as well as the environmental setting in which the drugs are consumed, likely play a significant role in determining whether the experience is perceived as pleasant and positive or frightening and uncomfortable. The experience bears a resemblance to a mystical encounter, drawing parallels with spirituality and religion. Hence evoking a sense of unity with the universe and perhaps even a connection to a higher metaphysical entity.

Non-classical psychedelic drugs, such as ketamine and 3,4-methylenedioxymethamphetamine (MDMA), can also induce ego dissolution (Lynn et al., 2023). In their study, Lynn et al. (2023) indicate that ketamine increases ego dissolution in subjective measurements, with higher scores aligning with increased activity in various subregions associated with self-experience.

Measurements of Ego Dissolution

How do researchers measure ego dissolution, and what methodologies have been employed in prior studies to comprehend the effects of this phenomenon? Nour et al. (2016), who assert that ego dissolution is a prominent aspect of the psychedelic experience, have developed a self-report scale, named the Ego Dissolution Inventory (EDI), specifically made to measure ego dissolution. The EDI contains sixteen statements, with individuals providing ratings on a scale from 0 to 100. Among these, eight of the statements were designed to understand the feelings of unity with one's surroundings, while the remaining eight reflect the level of elevated confidence and self-assurance.

However, Girn and Christoff (2018), contend that while the EDI serves as a tool for evaluating and quantifying the phenomenon, it lacks specificity in delineating the particular aspects of the self-experience and which ones are implicated. The EDI fails to address this aspect, leaving ambiguity regarding the relationship between the reported ego dissolution and specific components of the 'self'.

Another measurement method to be explored in this study is the Altered States of Consciousness (ASC) (Studerus et al., 2010). ASC typically signifies changes in an individual's cognitive processes or the subjective perception from their typical state of wakefulness (Studerus et al., 2010). The APZ (Abnormal Mental States) questionnaire developed by Dittrich (1998) is widely utilized for evaluating subjective experiences of ASC. One of the revised versions is the 5-Dimensional Altered States of Consciousness Rating Scale (5D-ASC), which is typically used as a measurement in cases involving psychedelic substances. It encompasses five dimensions in its assessment (Studerus et al., 2010): oceanic boundlessness (OBN), indicating a loss of ego boundaries; anxious ego-disintegration, meaning a loss of self-control; visual hallucinations, acoustic alterations, as well as altered vigilance. The report contains eleven different subscales including experience of unity, spiritual experience, blissful state, insightfulness, disembodiment, impaired control, and others (Uthaug et al., 2019).

The OBN scale measures positive depersonalization, derealization, strong positive mood, and feelings of unity (Studerus et al., 2010). Elevated scores on the OBN scale may indicate similar experiences akin to mystical experiences, which ego dissolution has also been closely associated with (Nour et al., 2016). Consequently, it evaluates somewhat similar experiences, allowing for comparison.

While EDI delves into the unity and confidence aspects, the ASC self-reports provide a broader assessment, using multiple dimensions of altered states of consciousness experiences. Nonetheless, both instruments assess ASC, as ego dissolution is a component of ASC.

The 'Self' in Neuroscience

The 'self' is not only a feeling or an intangible sensation but also, through neuroimaging techniques such as functional magnetic resonance imaging (fMRI), its neural mechanisms and correlates have been demonstrated (Nour & Carhart-Harris., 2017). This was evident in a meta-analysis conducted by Qin and Nortoff (2011), which investigated the neural mechanisms involved in self-experience, gathering data from nearly 1500 participants. The results indicated that a substantial amount of activity associated with self-experience primarily occurred within the cortical midline brain regions, particularly the pregenual anterior cingulate cortex (pACC). This specific region was found to be involved in processing stimuli that are 'self'-specific, distinguishing them from stimuli that are not 'self'-specific. The pACC is thought to play a role in processing positive emotions and experiences (Palomero-Gallagher et al., 2019), which aligns with its involvement in self-referential thinking. This finding is not surprising, as the pACC has been consistently implicated in emotional regulation and self-related processes. However, it underscores the significance of this region in distinguishing self-specific stimuli, which may have broader implications for understanding self-perception and emotional well-being. Additionally, in an fMRI study (Wagner et al., 2013) with 34 healthy participants, the researchers presented self-referential stimuli and a Stroop task in an event-related design. The authors observed that the activity in the rostral anterior cingulate cortex (rACC) during the processing of negative self-referential information, varied depending on the emotional content of the self-referential stimuli. Specifically, there was an increased interaction between the rACC when participants were exposed to negative self-referential information compared to neutral information.

The default mode network (DMN) emerges as an important region concerning the 'self' (Nour & Carhart-Harris., 2017). Comprising predominantly cortical brain regions, this network has demonstrated involvement in various functions, such as emotional processing, recollection of previous experiences, as well as self-referential mental activity (Raichle, 2015). Specifically, self-referential mental activity is associated with the dorsal medial prefrontal cortex (DMPC) (Gusnard et al., 2001). According to Raichle (2015), these functions are distinguishable through task performance, which helps identify the DMPC's involvement in self-referential activity.

Previous research examining the neural correlates of the 'self' has indicated that self-referential processing results in increased activation of the DMN (Lebedev et al., 2015). A study by Carhart-Harris et al. (2014), using neuroimaging, revealed that during a psychedelic experience with psilocybin, there is a decrease in cerebral blood flow (CBF) within the DMN. This was demonstrated using fMRI, where 15 healthy participants exhibited decreased CBF without any observed increases. The study also indicated reductions in both alpha power and functional connectivity. Functional connectivity refers to the synchronized activity between different brain regions, measured using seed-based resting-state functional connectivity (RSFC). In the study, three regions of interest were selected for RSFC analysis: the medial prefrontal cortex (mPFC), the right middle frontal gyrus (mFG), and the bilateral hippocampus. These effects were observed in regions known for their high metabolic activity and typical DMN regions, such as the posterior cingulate cortex (PCC), which is a key part of the DMN. The decrease in alpha waves, referring to the brain's electrical activity, was strongly linked to the feeling of ego dissolution. Essentially, these findings suggest that psilocybin reduces cerebral blood flow, functional connectivity, and oscillatory power in brain regions that are typically highly active and well-connected.

Carhart-Harris and colleagues (2012) conducted a study to investigate the effects of psychedelics on the brain using fMRI. The study was specifically designed to observe the transition from normal waking consciousness to a psychedelic state through imaging techniques. Overall, psilocybin notably led to decreased CBF in specifically anterior and posterior cingulate cortex. To investigate whether there was a relationship between these CBF changes and the subjective effects of the drug, the researchers graphed each individual's change in CBF in specific brain regions against their ratings of drug effects intensity. The results showed a clear pattern: the greater the decrease in CBF in each region, the more intense the subjective effects experienced by the participants. The decrease was most significant in the ACC and PCC. Furthermore, another decrease was revealed in the functional connectivity between the medial prefrontal cortex (mPFC) and the PCC, suggesting disrupted connectivity between these two regions, indicating an effect on the DMN.

Depression

Melancholia, a term not commonly used today but profoundly relevant, was defined during the time of Hippocrates by affective dimensions, specifically feelings of fear and sadness (Telles-Correia & Marques, 2015). Over time, psychiatric terms have evolved, undergoing various interpretations. Melancholia's meaning has shifted over time, with modern usage now commonly referring to what we recognize as depression (Paykel, 2008). At present time, the diagnosis of depression follows the guidelines of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (American Psychiatric Association, 2013).

The term “depression” emerged in the 19th century, initially describing a lowering of spirits (Paykel, 2008). Depression is recognized as a multifactorial disorder that is influenced by a combination of factors, with no single theory being able to fully explain its full variance nor is there any universal treatment proving its effectiveness (De Jonge et al., 2015). Over the last decade, depression has been increasing and according to the World Health Organization (2023), there are an estimated 280 million people who suffer from the disorder.

The core symptoms of depression, as defined by the DSM-IV include depressed mood, loss of interest, reduced pleasure, and even decreased energy or fatigability (Paykel, 2008). Additional symptoms include gain or loss in weight, difficulty concentrating, loss of appetite, and even suicidal thoughts (Schechter et al., 2005).

Clinically, depression is assessed by utilizing a 21-item self-report scale named Depression and Anxiety Stress Scales (DASS-21). Within the DASS-21, there are three scales (depression, anxiety, and stress) that consist of 7 items each. Participants rate their responses on a scale ranging from 0-3 and a maximum score of 42 on the DASS-21 scale indicates elevated levels of depression, anxiety, or stress (Ronk et al., 2013). Alongside DASS-21, another widely used tool to clinically measure depression is the Beck Depression Inventory (BDI). The BDI is designed to assess the severity of depression by using a 21-item self-report instrument that presents four statements that describe different levels of severity for specific depressive symptoms (Beck et al., 1987).

Studies have identified connections between depression and neurodegenerative processes, including structural changes in brain regions such as the hippocampus and prefrontal cortex (Schechter et al., 2005). However, the exact relationship between neurodegenerative processes and depression is still not fully understood since it is unclear whether depression causes these structural changes in the brain or if these changes lead individuals to develop depression. Furthermore, the anterior cingulate cortex (ACC) is activated during the self-referential processing of emotional information, causing individuals with major depressive disorder to struggle with the inability to deactivate the rACC during cognitive processing (Wagner et al., 2006).

The Effects of Psychedelics on Mental Health

Psychedelics have received attention for their potential to positively impact mental health, particularly in the domain of depression. Beyond easing the symptoms, psychedelics have been described as providing profound and significant spiritual experiences for individuals, leading to an overall improvement in well-being and quality of life (Andersen et al., 2021). The underlying idea of using psychedelics to treat individuals with depression is the intensity of the immediate substance experience can exert long-term effects on our mental health (Roseman et al., 2018). Furthermore, the authors found that the experiences characterized by high levels of OBN (reminiscent of mystical-type experiences) and low levels of Dread of Ego Dissolution (related to anxiety and impaired cognition) have resulted in positive long-term outcomes, in individuals with Treatment-Resistant Depression (TRD).

Thus, substances such as ayahuasca, psilocybin, and LSD exhibit significant antidepressant and anxiolytic effects (Spriggs et al., 2021). They also provide quicker relief from the symptoms of depression and anxiety, compared to traditional antidepressants which may take up to weeks to demonstrate such an effect. Moreover, the benefits of the substances, as indicated by Spriggs et al. (2021) appear to be sustained for several months, which suggests the reduced requirement for frequent dosing, compared to standard treatments.

In a systematic review conducted by Ko and colleagues (2023), 14 studies examining the therapeutic use of psychedelics were analyzed. The results revealed a significant short-term reduction in depressive symptoms when participants used psychedelics alongside psychological support.

Aim

Existing research has indicated that psychedelics can influence mental health, particularly having therapeutic effects for disorders such as anxiety and depression (Andersen et al., 2021; Roseman et al., 2018; Spriggs et al., 2021; Ko et al., 2023). Psychedelics are recognized for inducing the phenomena of ego dissolution, a state characterized by the dissolution and reduction of one's ego mediated by their effects on their underlying brain structures and mechanisms. This leads us to our hypothesis: ego dissolution as an experience plays a role in the therapeutic effects of psychedelics. By examining the intersection of these aspects, this study aims to investigate the therapeutic effects of ego dissolution. Subsequently, the results will be examined within a broader context to explore the neural aspects, specifically evaluating whether there are underlying neural mechanisms that can elucidate this phenomenon. The question remains, does the dissolution of oneself lead to therapeutic outcomes?

Methods

Search Strategy

The literature search utilized the Web of Science and PubMed databases. The search string included the following keywords: "Ego Dissolution" AND Psychedelic* AND (Depression OR Therapeutic OR Therapy OR "Mental Health").

On May 20th 2024, the search string yielded 69 results on Web of Science and 52 on PubMed. Duplicates were removed by using the software tool Zotero, resulting in 71 searches in total. Following the screening of titles and abstracts, there were 13 articles remaining. Full texts were retrieved successfully from all 13 articles. 9 articles were excluded due to six different reasons: 1. Failure to assess depression; 2. Use of irrelevant measurements for ego dissolution assessment; 4. Focus on unrelated subjective experiences; 5. Review article; 6: fails to address the correlation between the effect of ego dissolution on depression. This resulted in the further investigation of four articles (Fig. 1, PRISMA Flow Chart of the selection process).

Inclusion and Exclusion Criteria

Studies were required to incorporate any type of psychedelic drug administered to either healthy or depressed participants, without limitations on the specific psychedelic used. Additionally, the studies needed to incorporate self-report questionnaires assessing ego dissolution through EDI and/or 5D-ASC. The studies must also incorporate assessments measuring depression ratings to evaluate the impact of psychedelics on depression. Only peer-reviewed articles will be included. The articles have to be published after the year 2000 up until the present time.

Exclusion criteria will include the exclusion of meta-analyses, books, review articles and/or articles using languages other than English. Furthermore, experiments involving participants with severe psychiatric conditions other than depression (such as schizophrenia and bipolar disorder) will be excluded to minimize confounds. Studies that fail to address the correlation between the effect of ego dissolution on depression will be excluded.

Data Extraction

Our data extraction will include measurements of EDI and 5D-ASC, and measurements of depression before and after a psychedelic experience (see Table 1).

This present study aims to include healthy participants and/or individuals with depression. Healthy participants will also be assessed for depressive symptoms and will complete depression rating scales. No specific restrictions regarding age, gender, or other demographic factors. It aims to examine the psychedelic experience by assessing subjective measurements like ego dissolution and altered states of consciousness. A comparison will be made between those undergoing a psychedelic experience and individuals at baseline, with a focus on analyzing the effects of depression and ego dissolution. The objective is to explore the therapeutic effects of depression resulting from ego dissolution during a psychedelic experience.

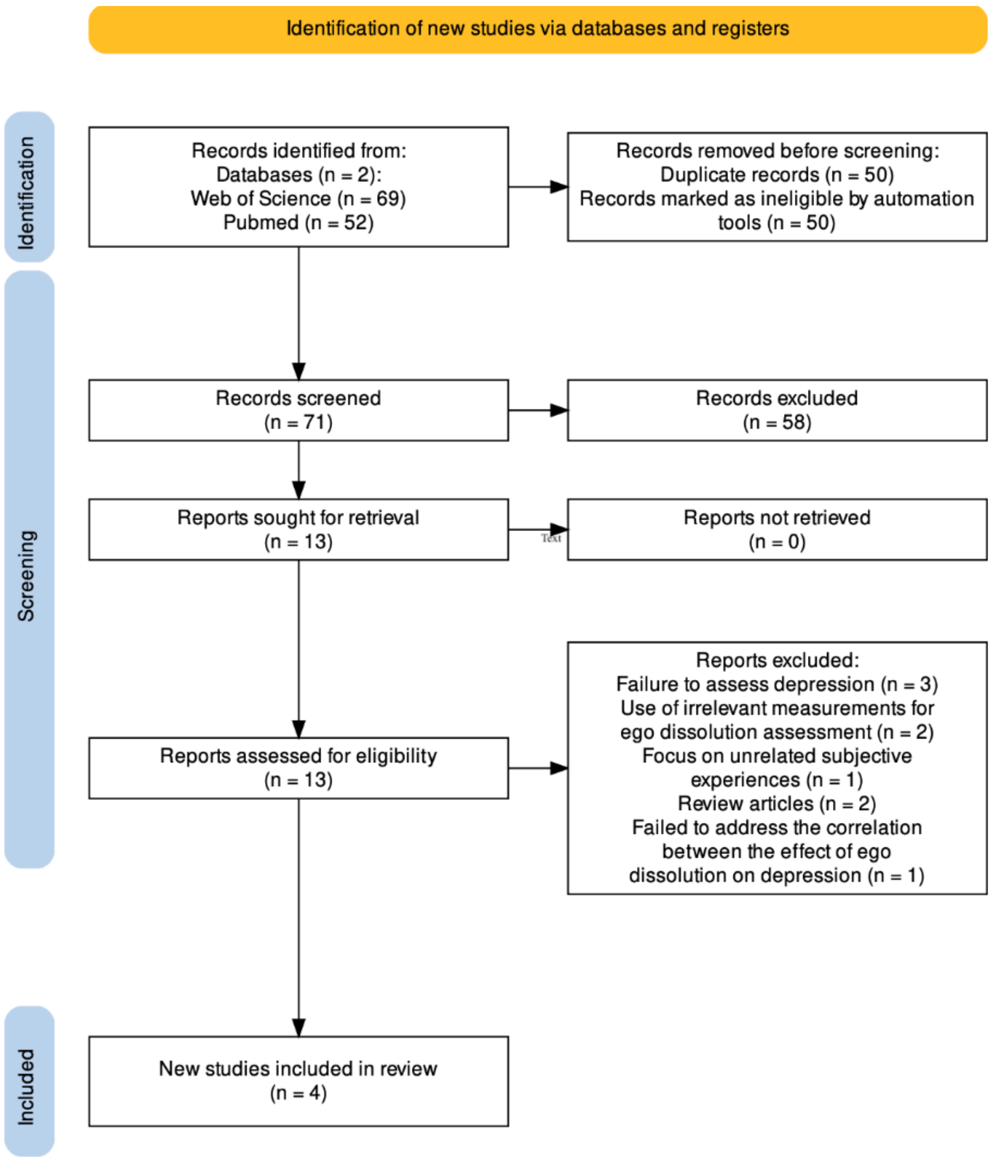
Table 1

Data Extraction Criterion

Outcome measure	Type of measure	Intervention
Depressive symptoms	Self-report	Psychedelic dose
Ego dissolution experience	Self-report in EDI and/or 5D-ASC	Psychedelic dose

Figure 1

PRISMA Flow Chart of the Selection Process



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

Results

The combined findings from four different studies that investigate the effects of psychedelic substances reveal evidence of their potential therapeutic benefits for mental health and well-being. Among these articles, they investigated the therapeutic effects of psychedelics on mental health by examining the subjective experience and correlations between ego dissolution and depression (Uthaug et al., 2019; Reckweg et al., 2021; Van Oorsouw et al., 2021; Van Oorsouw et al., 2022), further explaining if such correlations exist and how they influence mental health (see Table 2).

In the following section, we will look at the selection of four articles that provide evidence regarding the use of psychedelics in treating depression, as measured by self-reports such as DASS-21 and BDI, by exploring the correlation between depression and ego dissolution.

Effects of 5-MeO-DMT Inhalation on Life Satisfaction and Mindfulness: Naturalistic Setting (Uthaug et al., 2019)

Uthaug and colleagues (2019) initially aimed to investigate the sub-acute and long-term effects on cognition and affect from inhaling vapor from dried toad secretion, containing 5-methoxy-N, N-dimethyltryptamine (5-MeO-DMT). The second objective was to assess if the changes were due to the psychedelics. This study lacked precise dosing controls of 5-MeO-DMT and the reported doses varied between 20-120 mg. The research included 42 participants who conducted various psychological assessments including, DASS-21, EDI, and the 5D-ASC scale.

Regarding the correlational analysis, the scores from the EDI showed a negative correlation[1] with depression ratings from the DASS-21. The day after the session, scores of ego dissolution ratings continued to show a negative correlation with depression. However, no correlation with any changes was observed on the four-week follow-up.

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[1] A negative correlation between subjective experiences and depression means that as subjective experiences increase, such as experiencing more ego dissolution, depression decreases. Negative correlation indicates that higher levels of EDI or 5D-ASC result in reduced depression.

Dose-Ranging Study of Vaporized 5-MeO-DMT in Healthy Volunteers (Reckweg et al., 2021)

Reckweg et al. (2021) conducted a study including a vaporized formulation of 5-MeO-DMT, examining its effects across four dosage levels: 2, 6, 12, and 18 mg on 22 healthy participants. The study aimed to evaluate the safety of the drugs and determine the dosage that produces peak experiences, as well as understand how consciousness is altered during the process through subjective self-reports. Subjective experiences with the psychedelic were evaluated through various self-report questionnaires, including the EDI and 5D-ASC. Additionally, the DASS-21 was used to measure mood and well-being, where one focused on depression.

Results of this study showed that higher doses of 5-MeO-DMT exhibited significant increases in the average intensity of the psychedelic experience compared to the lowest 2 mg dose. The results indicated a significant impact of 5-MeO-DMT dose on EDI ratings, suggesting that varying doses influenced the extent of ego dissolution experienced by participants.

Regarding the correlational analysis examining the relationship between EDI and 5D-ASC with depression, no significant correlation was found.

Effects of Ayahuasca on Mental Health and Well-Being in Healthy Ceremony Attendants (Van Oorsouw et al., 2021)

Van Oorsouw et al. (2021) primarily aimed to assess the sub-acute and long-term effects of ayahuasca on mental health and well-being in both first-time and experienced users. The second aim was to extend the evaluation of altered states of consciousness induced by ayahuasca and further investigate how these altered states related to changes in mental health. In the study, 73 participants were assessed with various measures to evaluate their mental health and well-being before, the day after, and four weeks after they attended the ayahuasca ceremonies. The different assessments included DASS-21, 5D-ASC, and EDI, among others. The ceremony was overseen by a skilled shaman who administered two rounds of ayahuasca (approximately 50 ml) liquid to each participant.

The correlational analysis revealed that the EDI was negatively correlated with the post-ceremony depression ratings, whereas the 5D-ASC (OBN) displayed a significant negative correlation with depression during the sub-acute phase. The findings show that greater levels of ego dissolution were associated with improvements in depression ratings and higher levels of OBN were linked to lower depression ratings following the ceremony.

Therapeutic Effect of an Ayahuasca Analogue in Clinically Depressed Patients (Van Oorsouw et al., 2022)

In a study conducted by Van Oorsouw and colleagues (2022), the therapeutic effects of ayahuasca on 20 clinically depressed patients were investigated after one ceremony. They hypothesized that individuals would demonstrate enhancements in all mental health factors, while also anticipating that changes in mental health would correlate with levels of ASC, particularly focusing on ego dissolution and OBN. This observational study involved two drinking rounds of ayahuasca in one night, during which changes in mood, affect, and subjective experiences were measured. The drinks consisted of 50-60 ml of liquid, with varying amounts of ayahuasca dosage diluted into each one. Depression and ego dissolution were assessed using various self-report measures, including EDI, 5D-ASC, and BDI. These assessments were conducted initially at baseline and followed up one day, one month, and one year after the intake of ayahuasca.

Significant negative correlations were found between 5D-ASC (OBN) scores and BDI depression scores, as well as a negative correlation between EDI scores and BDI scores. The results suggest that higher levels of ego dissolution are associated with a greater decrease in depression. These correlations persisted at the 1-month follow-up but were no longer evident at the 1-year post-ceremony follow-up for either variable.

Table 2

Summary of Selected Articles

Study	Psychedelic intervention	Subjective rating(s)	Correlation between subjective ratings and depression
Uthaug et al. (2019)	5-MeO-DMT	EDI 5D-ASC	Significant correlation
Reckweg et al. (2021)	5-MeO-DMT	EDI 5D-ASC	No correlation
Van Oorsouw et al. (2021)	Ayahuasca	EDI 5D-ASC	Significant correlation
Van Oorsouw et al. (2022)	Ayahuasca	EDI 5D-ASC	Significant correlation

Note. 5-MeO-DMT = 5-methoxy-N, N-dimethyltryptamine, EDI = Ego dissolution inventory, 5D-ASC = 5-dimensional altered states of consciousness rating scale.

Discussion

This review aimed at examining the impact of psychedelics on depression, specifically focusing on the phenomenon of ego dissolution and its potential effects on mental health. Previous research has consistently demonstrated the positive effects of psychedelics on mental health and well-being (Andersen et al., 2021; Roseman et al., 2018; Spriggs et al., 2021; Ko et al., 2023). Ego dissolution is a well-known experience associated with psychedelics (Nour et al., 2016), however, it remains unclear if the phenomenon of ego dissolution contributes to alleviating depression symptoms.

The results of the selected articles indicate a correlation between ego dissolution and depression, demonstrating that this phenomenon does indeed impact depression. Studies (Uthaug et al., 2019; Van Oorsouw et al., 2021; Van Oorsouw et al., 2022) revealed a negative correlation between ego dissolution and depression, indicating that participants reported decreased levels of depression after experiencing ego dissolution. However, the long-term sustainability of therapeutic effects remains unclear, as the correlation between ego dissolution and depression was no longer evident at the 1-year post-ceremony follow-up (Van Oorsouw et al., 2022). While some studies have demonstrated sustained improvements in mental health following psychedelic experiences, others have found that these effects may diminish over time. Factors such as lifestyle changes, ongoing mental health treatments, and individual differences (Van Oorsouw et al., 2021) in response to psychedelics may influence the longevity of therapeutic effects. This information corresponds with the findings of Ko et al. (2023), who reported a significant short-term reduction in depressive symptoms across 14 studies. However, they suggested that maintaining long-term results may require ongoing maintenance, indicating weaknesses in the long-term follow-up outcomes.

One article did not demonstrate any correlations (Reckweg et al., 2021), however, the author noted that such outcomes were not unexpected in their study, as the healthy volunteers selected had minimal baseline scores on the Brief Psychiatric Rating Score (BPRS). It was explained that this absence of correlation was anticipated due to the baseline scores of participants claiming that the lack of alterations in mental health outcomes in their study does not contradict previous research supporting such findings. It is important to note that the relationship between ego dissolution and depression is likely complex and may involve additional psychological and neurobiological factors. For instance, individual differences in personality traits, such as openness to experience and trait mindfulness, may moderate the impact of ego dissolution on depression (Nour et al., 2016).

Ego dissolution, characterized by a temporary loss of the sense of 'self', may lead to a shift in perspective and a reevaluation of one's life circumstances and priorities. According to Letheby (2021), the positive effects of psychedelic therapy often arise from changes in the individual's sense of 'self', particularly brought about by ego dissolution. This altered state of consciousness could promote psychological flexibility to new perspectives (Roseman et al., 2018), helping to resolve depressive symptoms by reducing negative thought patterns.

Beyond the individual studies, and by analyzing the combined results, it is evident that there are central themes or key patterns that become apparent when an individual experiences ego dissolution. When we look at the collective findings, we see that ego dissolution emerges as a mechanism in the field of psychedelic therapy. Given this information, understanding how ego dissolution contributes to mental health improvements necessitates consideration of the neural mechanisms responsible for the therapeutic effects.

There are fMRI findings that provide a further understanding of the relationship between neural activity and subjective experiences. Specifically, Carhart-Harris et al. (2012) found that greater decreases in CBF in specific brain regions, such as ACC and PCC, were associated with more intense subjective effects reported by participants. This suggests a direct link between alterations in brain function and the intensity of psychedelic experiences. Notably, subjective experiences such as feelings of unity, bliss, and spirituality are associated with higher levels of ego dissolution and lower levels of depression, as observed in studies by Uthaug et al. (2019) and Van Oorsouw et al. (2021).

Overall, it appears that the cingulate cortex, which includes regions such as the ACC, rACC, pACC, and PCC, appears to play a significant role in both depression, self-referential processing, and the effects of psychedelics (Qin & Northoff, 2011; Wagner et al., 2013;

Carhart-Harris et al., 2012; Wagner et al., 2006). The ACC, in particular, becomes active during self-referential tasks and shows heightened activity in patients with major depressive disorder (Nejad et al., 2013; Wagner et al., 2006). This suggests that the reduction in ACC activity induced by psychedelics (Carhart-Harris et al., 2012) could result in lower depression ratings. Additionally, the rACC, associated with self-referential information, shows heightened activity when processing negative stimuli. This persistent hyperactivity may contribute to the difficulty depressive patients have in disengaging from negative thoughts. Psychedelics' ability to reduce rACC activity suggests a pathway through which these substances may alleviate symptoms by promoting a more flexible and positive self-concept. This could potentially enhance receptivity to new perspectives, contributing to a form of psychological flexibility as stated by Roseman et al. (2018).

These discoveries suggest the cingulate cortex is an important aspect in this context, suggesting further investigation into its role, given its apparent centrality. The evidence suggests that psychedelics' therapeutic effects on depression are mediated by modulating activity in the cingulate cortex and DMN, leading to decreased self-referential processing and a more adaptive sense of self. The alteration observed in the DMN and regions in the cingulate cortex could initiate a reset of the neural networks implicated in depression, thus explaining the psychological changes reported by patients after ego dissolution.

The evidence reviewed indicated that ego dissolution, induced by psychedelics, has therapeutic effects on depression. Studies consistently show a negative correlation between ego dissolution and depression, with participants reporting decreased depression levels during ego dissolution experiences in both healthy individuals and those with depression. This suggests that psychedelic therapy may not only benefit diagnosed individuals but may also be valuable for those seeking to enhance their overall well-being, even if not medically required. However, the long-term sustainability of these effects remains uncertain, as some studies note a dissipation of benefits over time. The reduction in activity within key regions of the cingulate cortex aligns with the decreased depressive symptoms, suggesting that the neural changes associated with ego dissolution contribute to its therapeutic effects.

Therefore, while ego dissolution appears to offer substantial short-term relief from depressive symptoms, further research is needed to understand and enhance its long-term efficacy.

Limitations

While various studies use similar measurements to evaluate ego dissolution, it is crucial to observe and examine the reliability and bias inherent in subjective self-report measures. The consistent use of terms such as "ego" and "unity" in the items, prompts us to question whether these tools truly encapsulate the full spectrum of the ego dissolution experience. Examples include statements like "My 'self' or ego dissolves into nothingness" and "I feel at one with the universe." (Nour et al., 2016).

A compilation of research reports investigating the therapeutic use of LSD, involving nearly 5000 individuals, revealed that subjects encountered effects such as delusions, dissociations, fears, and sympathetic nervous system responses (Barrett et al., 2016), essentially, undergoing a bad trip. In the scientific realm, ego dissolution has been a focal point when studying psychedelics. Given these findings, the inquiry arises as to whether the individuals participating in studies aimed to research ego dissolution, would express different sentiments about their experiences had they not been informed that the drug's purpose was to induce a distinct alternation in terms of the ego. This raises reflection on whether ego dissolution is genuinely the most prominent aspect of psychedelic experiences. If the notion of ego dissolution was not explicitly introduced to individuals undergoing a psychedelic experience, would they naturally consider it, or would their primary focus be elsewhere? As noted by Girn and Christoff (2018), the EDI fails to fully articulate the nature of the experience, allowing potential misinterpretations regarding self-experience and the actual nature of the phenomenon.

Examining the methodology used to assess ego dissolution, a common thread emerges in the measurement approaches used across previous studies. The use of subjective self-report measures raises questions about their adequacy and reliability in capturing the true effects of ego dissolution. Are these established methods sufficiently reliable and unbiased, or might there be alternative measures that could potentially reshape our comprehension of ego dissolution? For instance, Reckweg and colleagues (2021) informed participants about the potential subjective effects of the drug to prevent potential biases from pre-study internet searches. However, this approach may introduce bias by influencing participants' expectations of what to expect during the study.

Future Research

For future research in the field of psychedelic substances, it is important to emphasize several important areas. First and foremost, it is essential for extensive clinical trials to confirm and further elaborate the demonstrated therapeutic effects shown. Secondly, considering the observed correlations between psychedelic experiences and psychological outcomes such as ego dissolution, future research should aim to identify the underlying mechanisms that drive these effects, such as more advanced neuroimaging techniques that examine the alteration in brain function and connectivity during ego dissolutions therapeutic effects. Using resting-state functional connectivity fMRI, for example, can provide insights into the brain's functional organization by measuring spontaneous BOLD signals and identifying networks of brain regions that are functionally connected during rest. This method helps elucidate the brain's intrinsic connectivity patterns and their alterations in different states. Furthermore, it would be valuable to conduct a study that examines the fMRI findings of the therapeutic effects of ego dissolution. Currently, there seems to be limited research that integrates behavioral interventions with their corresponding neural mechanisms, highlighting a gap in the understanding of how these interventions work on a neural level. Thirdly, developing an understanding of the neural correlates of the 'self' related to ego dissolution could further encourage more established research, specifically aiming to form intervention therapies, targeting neuronal structures involved in the experience of ego dissolution. In addition, gaining an improved clarification of how neural activity generates subjective experiences, such as the sense of 'self', provides insight into fundamental philosophical questions regarding consciousness and the essence of the 'self'. Furthermore, it is of great importance for future studies to personalize the psychedelic dosages for each individual to minimize potential risks. This personalized approach could be important due to individual differences in psychological factors and past experiences. Including control groups in future studies would help navigate and enhance understanding by enabling researchers to isolate pharmacological effects more effectively.

Future research may consider integrating psychotherapy into studies examining the therapeutic effects of psychedelics. Combining traditional psychotherapy with psychedelic drugs could potentially prolong the therapeutic effects (Reiff et al., 2020), extending their duration for several months.

Social and Ethical Aspects

Despite potential therapeutic effects, societal stigma and negative historical associations can impede progress. Issues like limited access to psychedelic therapy due to cost and legal barriers worsen inequalities in mental healthcare. Moreover, the cultural significance of psychedelics in indigenous communities raises ethical questions about respecting cultural knowledge and practices. However, by integrating indigenous knowledge and modern scientific approaches, it can validate and honor traditional practices while also advancing mental healthcare. This can rather be seen as respect for the cultural heritage of indigenous communities.

Ensuring participants are fully aware of risks, benefits, and their rights is vital for ethical practice. Implementing safety measures, including thorough monitoring, is essential to address potential risks associated with psychedelic therapy, especially because it is relatively new to the field.

Conclusion

Combining the understanding of ego dissolution, the underlying neural mechanisms associated with it, and its relationship to depression may provide a foundation for developing an alternative approach to treating individuals. Subjective experiences and altered states of consciousness remain complex areas of study, requiring further research. However, the findings gathered in this review suggest a potential positive impact on mental health through experiences of ego dissolution. The findings from the selected articles collectively point towards a correlation between ego dissolution and depression, suggesting that this phenomenon indeed influences mental health outcomes. Ultimately, while ego dissolution holds a promising therapeutic outcome regarding depression, future research is required to further understand the process underlying these effects and to develop reliable and enduring methods of treatments that offer sustainable benefits for individuals in need.

Word count: 6624

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