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The Influence of Psychedelic Drugs on the 'Sense of Self'

Literature Review

Potent psychedelic drugs such as LSD and psilocybin are implicated in a multitude of cognitive and perceptual alterations. Through the mediation of serotonergic 5-HT₂ receptors, distortion of the self is a common effect of these drugs. The self is usually referred to as an entity comprising physical and psychological attributes that are coherent with our self-concept. This so-called binding process can be affected through psychedelic experiences and can oftentimes lead to the phenomenon of ego-dissolution. Given this, ego-dissolving experiences lead to the elimination of a bound self-model which eventually results in the perception of distorted self-boundaries. There have been improvements conceptualizing and assessing ego-dissolution. The Ego-Dissolution Inventory is the first questionnaire dealing with the assessment of this phenomenon. In addition, a variety of neural studies associate this common psychedelia-induced phenomenon with different brain regions. The Default Mode Network and the Salience Network, two large-scale networks associated with distinct components of the self, show

altered activity and disintegration, leading to an enhanced global connectivity within the brain. Additionally, decoupling of the Medial Temporal Lobe, alterations in parahippocampal activity and reduced interhemispheric communication show the same correlations. These findings are first attempts to conceptualize the self and the concept of ego-dissolution in terms of large-scale networks within the brain.

Keywords: sense of self, psychedelics, self-binding, ego-dissolution, neural correlates, brain networks

INTRODUCTION

Despite their different chemical structure, these psychedelic effects are mediated by serotonin 2A receptor (5-HT₂) agonism (Nichols, 2016). People under the influence of psychedelics experience visual alterations, such as color enhancement and color shifting. Common physical responses comprise increased heart rate, pupil dilation and tactile enhancement. Commonly referred to as hallucinogens, they increase a vivid perception of the outer world and generate strong visual, auditory and tactile hallucinations.

Arguably, a unique side effect of psychedelic drugs is the capacity to generate distorted thoughts, delusions and spiritual experiences. In this regard, being under the influence of psychedelics can lead to remarkably distorted ego perceptions, a phenomenon called ego-dissolution (ED) (Dittrich, 1998). This phenomenon can be explained by a disruption of the subjective experience of the 'sense of self' (James, 1882, Carhart-Harris et al., 2014), which oftentimes leads to the perception of blurred self-boundaries. For instance, during the activity of these mind-altering drugs the self-concept can experience a breakdown within its subjective and coherent psychological attributes. Subjects under psychedelic intoxication report a sense of alienation with the outer world, obtrusive internalized thought or an abolished feeling of connection with one's body and self (Milliere, 2017). Therefore, typical experiences under psychedelic drugs comprise an altered state of the sense of self, known as ego-dissolution as well as self-oriented mental activities (Palhano-Fontes et al., 2015).

It is necessary to precede with a short theoretical framework of the sense of self in order to understand the mechanisms of a self-disruptive phenomenon such as ego-dissolution. On the one hand, the self can be explained as a three-folded concept including a conjoint construct of experience, self-awareness and selfhood (Zahavi, 2008). On the other hand, the psychoanalytic approach defined by Freudian devotees, explains the ego as an intermediary unit between the unsocialized and selfish impulse-driven identity and the superego, which keeps internalized societal norms in check (Hogg & Vaughan, 1995).

To emphasize the importance of a cohesive or dissolved ego, clinical samples present major scientific insights. Disturbances of the self are one of the main symptoms in patients suffering from schizophrenia. Commonly, schizophrenic patients often show symptoms like hallucinations, delusions, avolition and affective/cognitive disruptions (Andreasen, 1995). Furthermore, people suffering from schizophrenia report in progressing stages of their illness a passivity phenomenon, which is characterized by a disturbance of the self which is no longer perceived as part of the human. In addition to the absence of a coherent self-image, patients become detached, show feelings of alienation and have a sense of estrangement concerning their own experiences (Northoff, 2014). It is therefore that in schizophrenia self-models are blurred, non-stationary and unpredictable by the perceiver.

Scientific investigations of the underlying mechanisms shaping the dynamic character of the self, remains a challenge. However, since psychedelics are known to induce a self-distortive ego-dissolution, it could be used as a tool to explore its underlying behavioral and neurobiological

mechanisms. So far, recent neuroscientific research shows little insight into the neurological grounds of ego-dissolution phenomena outside of the clinical context. Promoting a thorough neurobiological understanding of ego-disturbances under the influence of psychedelia would serve two purposes. First, the experimental use of psychedelic-induced ego-dissolution may provide us with new tools to investigate the neural correlates of the self, increasing the valence of research on self-models. Second, the understanding of neurological agents in ego-dissolution may emphasize beneficial effects of psychedelia-induced ego-dissolution which may inform novel treatment strategies.

In the latter scenario, recent studies have already given insight into positively experienced ego-dissolution and spiritual phenomena during the psychedelic experience. One work by Uthaug et al. (2018) studied the long-term impact of an Ayahuasca ceremony on affective and cognitive capacities as well as attitudes towards life. Moreover, this research attempted to shed light on positive ego-dissolution experience and according changes in life satisfaction, affective alterations and mindfulness. The results showed that all three aspects were significantly correlated with experienced ego-dissolution during Ayahuasca intake, therefore affirming useful long-lasting changes (Uthaug et al., 2018). This finding is consistent with other research on treatment-resistant depression, where an experimentally induced psilocybin dose predicted positive therapy outcome. In this context, an enhanced mystical experience termed oceanic boundlessness and low fear for ego-dissolution were main predictors of this effect (Roseman, Nutt & Carhart-Harris, 2018). In summary, ego-

dissolution plays an integral part in positive psychedelic experiences and can be associated with schizophrenic or depressive symptoms.

In spite of these promising findings, ego-dissolution remains a vague concept which requires further clarification. It remains unknown how to conceptualize distinct ego-dissolving experiences or which neurobiological processes take place. It is therefore crucial to shed light on to the psychological aspects of the self, the neurobiological structures of psychedelic ego-dissolution, and to quantify the construct through validated measures. This literature review seeks to elaborate on the question of how psychedelics influence the sense of self in terms of neurobiological and behavioral findings. First, binding as a mechanism of a coherent sense of self and the process of ego-dissolution will be investigated. Second, the novel Ego-Dissolution Inventory will be presented with its robust internal and construct validity. Lastly, the review concludes with findings on neural correlates underlying ego-dissolution. In order to study the mechanisms of ED, the online databases PubMed and Google Scholar were searched for publications containing the following key words: sense of self, psychedelics and self-binding, psychedelia induced ego-dissolution, ego-dissolution inventory, neural correlates of drug induced ego-dissolution, ego-dissolution and brain networks.

The self-concept and the process of binding

When trying to conceptualize the self or the self-concept, one comes across a wide range of defining features. Baumeister (1997) characterizes it as “The individual's belief about himself or herself, including the person's attributes on who and what the self is” (Baumeister, 1999). Another view stems from

Carhart-Harris and Friston (2010) who refer to the self as an umbrella term. Here they state that the concepts of self-awareness, self-monitoring, self-recognition and self-control/agency constitute the bases of the self. Furthermore, Letheby & Gerrans (2017) explain the self as an entity which is guided by higher-level processes in order to bind or integrate information and attributes which matter to oneself. Binding is therefore a process in which physical and psychological attributes are linked to one's self-model in a coherent and persistent way. Within this framework, a prediction processing model has been postulated, dating back to early developments of Helmholtz and Kant (Helmholtz, 1925; Swanson, 2016). Generally, the process of binding relies on an error signal detection mechanism, finding discrepancies between predicted and actual inputs. In other words, information bound to our self-model is facilitated via a probabilistic model weighing relevant in- and outputs (Letheby & Gerrans, 2017). Therefore, binding is phenomenally or cognitively described as the unity of self-experience and the coherence or integration of existing ideas of the self-model (Revonsuo, 1999). Given this, the self-model represents a persisting object in order to make sense of, to unify and predict patterns of egocentric and salient autobiographical experience.

Ego-dissolution

In some subjects, the intake of psychedelics can generate a powerfully altered perception of the self, named ego-dissolution. Distortions in subjective experiences of one's self or ego are central to the psychedelic experience (Carhart-Harris et al., 2014; James, 1882). From a psychoanalytical perspective, it is the disruption of ego-boundaries, which

results in a blurring of the distinction between self-representation and object-representation. This leads to an unstable synthesis of self-representations into a coherent whole (Federn, 1926; Fischman, 1983; Savage, 1955). Therefore, the dissolution of the self within the psychedelic experience leads to cognitions that are not bound to our self-models any longer. Moreover, the lack of reliable flow of information about the body and one's self-perception as well as the loss of the sense of ownership (Letheby & Gerrans, 2017) particularly contribute to this ego-loss.

As we continue our discussion it will become clear that converging, yet sparse evidence of underlying neurobiological evidence in ego-dissolution phenomena exist. So far, neuroscientific evidence of psychedelic ego-dissolution has been correlated to aspects of separate self-representations such as the embodied and narrative self. The embodied self relates to a persisting entity of the self and the narrative representation to that of goals and attributes important to the self-model (Letheby & Gerrans, 2017). Although this hypothesis remains a challenge to test, both self-modules seemingly seated in different brain networks (Craig & Craig, 2009; Davey & Harrison, 2018; Seth, 2013) compromise the integrity of a functioning binding process. Therefore, it is assumed that psychedelic ego-dissolution represents the collapse of a well-functioning self-binding process. However, evidence that psychedelic ego-dissolution directly abolishes a naturally functioning binding process is currently lacking. Nonetheless, research starts making assumptions about affected entities of self-models based on differential findings on psychedelia-influenced brain activation, as will be discussed in the course of this review.

All in all, diverse aspects and dimensions of the self-model during the psychedelic experience are disturbed, resulting in a decoupling of self-representations. On one hand, this stark feeling can evoke strong emotional reactivity (Soler et al., 2015), but, on the other hand, one can see own dysfunctional emotional and behavioral patterns and can act upon those (Shanon, 2002). Given different conditions, the disruption can lead to a wide range of reactions and can be linked to distinct neural networks related to the self. Therefore, fine-grained psychometric instruments are needed to distinguish between different aspects of the self.

The Ego-Dissolution Inventory

So far, the concept of the self has been discussed, as well as aberrations that can occur during the psychedelic experience. The understanding of this particular phenomenon should be further researched, because self-disturbances and disturbed ego-boundaries are a core phenomenological aspect of psychosis and schizophrenia (Northoff, 2014; Nour and Barrera, 2015). Additionally, experiencing the loss of ego-boundaries is a primary feature of the mystical experience (James, 1985) and leads commonly to cathartic maturity (Shannon, 2002). Conceptualizing the ego is a crucial step to understand pathologies in which the self is disrupted, in order to elaborate on therapeutic interventions. Accordingly, psychedelic drugs may bring a beneficial thoroughfare for upcoming research into neural correlates of normal and abnormal self-awareness (Nour et al. 2016). In order to clear this path, the construction of validated assessments for the concept of psychedelia-induced ego-dissolution is needed.

Currently, there is a considerable number of surveys assessing states of drug-induced self- distortion. The widely used standardized ASC (Altered States of Consciousness) and its revised 5D-ASC scale measure positively and negatively experienced ego dissolving phenomena. Indices of positive depersonalization experiences are captured by the dimension of ‘oceanic boundlessness’, whereas negative and unpleasant experiences are related to the ‘dread of ego dissolution’ dimension. In addition, the ‘visionary restructuralization’ and ‘auditory alterations’ captures hallucinations or illusions frequently reported by psychedelic drug users. A latter secondary index entails a general measure of consciousness alteration (Dittrich, 1998; Studerus, Gamma & Vollweider, 2010). Although this validated scale offers a comprehensive evaluation of drug-induced experiences, it is not satisfactory to efficiently gauge the single dimension of ego dissolution (Nour et al. (2016)). However, if the field of ego-disturbances through psychedelic drugs is to prevail in future, it necessitates a simple and quick measure of the ego-dissolution dimension.

In this context, Nour et al. (2016) introduced the Ego-Dissolution Inventory (EDI) based on individuals’ subjective experiences under psychedelic drugs (Nour et al., 2016). The EDI includes a total of 16 items which capture ego-dissolution and the opposing construct called ego-inflation also titled as self-assuredness. Within the factor of ego-dissolution, items pose statements such as ‘I experienced a dissolution of my ‘self’ or ‘ego” in which individuals have to respond on a visual analog scale (VAS) with 0 defined as ‘No, not more than usually’ and 100 defined as ‘Yes, entirely or completely’. Further, 8 items of ego-inflation such as ‘My ego felt inflated’ on the same VAS are included. The scores are calculated

as the sum across items for both factors separately and as a total sum across all items. The statistical analyses show internal consistency and construct validity of the EDI and convergent validity with the well-established Mystical Experiences Questionnaire (MEQ) (Barrett, Johnsons & Griffiths, 2015; MacLean, Leoutsakos, Johnson & Griffiths, 2012). Moreover, it exhibits a significant positive correlation with drug dose and experience intensity for the ego-dissolution and -inflation subscale for psychedelics and cocaine respectively (Nour et al. 2016). These findings argue for a dose-response and intensity-response relationship in psychedelic drug use. Arguably, a higher dose and higher subjective intensity correlates with stronger ego-dissolving experiences. On the contrary, larger cocaine drug doses are associated with increasing ego-inflation, whereas alcohol does not show such trends. Lastly, both cocaine and alcohol seem to be positively associated with subjective intensity and ego-inflation. All in all, ego-dissolution is significantly explained by experience intensity and drug class (Nour et al., 2016).

To sum up, the EDI captures the construct of ego-inflation as an antithetical concept of ego-dissolution. In contrast, the ASC refers to positively ego-dissolution experiences as oceanic boundlessness reported by drug users as pleasant mystical experience. Therefore, these two concepts are related to ego-dissolution in different ways: ego-inflation as an antagonistic factor and oceanic boundlessness diverging in the subjective level of valence.

Interestingly, the conceptual dissociation between positive (oceanic boundlessness) and negative ego-dissolution can be demonstrated by looking into recent neurophysiological findings. Neurobiological studies

using multimodal brain imaging after a dose of psilocybin revealed different anatomical and functional patterns depending on a positively or negatively experienced ego-dissolution. According to studies, glutamate release within 5-HT₂ receptors plays a central role in stimulating and maintaining primary effects of psychedelics. It is hypothesized that prefrontal cortex cell activation depends on the level of glutamate release through 5-HT₂ receptors, fostering the psychedelic experience (Aghajanian & Marek, 1997; Aghajanian & Marek 1999; Mason et al., 2020; Vollenweider & Kometer, 2010). To be more precise, a study by Mason et al. (2020), suggests that glutamate levels in brain regions such as the medial prefrontal cortex (mPFC) and the hippocampus play a key role in initiating subjective experiences of positive and negative ego-dissolution. Both of these regions overlap with the large-scale brain network called the Default Mode Network (DMN), which is implicated in self-referential mental tasks and thought to show heightened activation during psychedelic experiences. The findings demonstrate that negatively experienced ego-dissolution correlates strongly with an increase in glutamate within the mPFC, whereas a positively experienced ego-dissolution termed oceanic boundlessness suggests a diminution of glutamate in hippocampal regions. The questionnaires used to assess different aspects of the psychedelic experience were the ASC and EDI. Besides the fact that these preliminary findings show regional dissociation of subjective experiences of psychedelic drugs, they also emphasize the importance and need for standardized, validated scales for different types of ego-dissolution. Taken together, the ED-inventories serve as a primary tool to investigate the subjective,

phenomenological and behavioral effects that accompany neurobiological changes in the brain during psychedelic states.

Ego-dissolution and the brain

So far, the paper sought to examine the conceptual influence of psychedelia on disrupted self-binding and the relationship of distinct ego-dissolution phenomena such as oceanic boundlessness. In this context, the EDI as a standardized survey has been explored. However, it remains ambiguous which neural correlates are linked to these processes and how brain regions behave in reaction to psychedelics. Therefore, it is crucial to associate brain regions with the experience of a dissolved ego under psychedelics.

In regard to psychedelic induced ego-dissolution, two large-scale brain networks have been investigated: The Salience Network (SN) and the Default Mode Network (DMN). Identifying coherent and salient information fitting into the self-model is associated with the SN of the brain, which is anchored in the anterior insula and dorsal anterior cingulate cortex (Menon, 2015). Moreover, it is involved in directing and binding emotionally salient information and is often referred to as the seat of the embodied self (Letheby & Gerrans, 2017). In contrast, the DMN which is rooted in the posterior cingulate cortex and the medial prefrontal cortex, is suggested to be responsible for the narrative, egocentric self. Besides a heightened activation during self-referential tasks, it is also implicated in self- and other-judgements (Lou et al., 2004; van Buuren, Gladwin, Zandbelt, Kahn, & Vink, 2010). Because of their distinct association with self-perceptive processes, these brain networks are currently under investigation in relation to psychedelic ego-dissolving experiences.

First attempts have been made to study the self-concept via advanced brain imaging. A study by Tagliazucchi et al. (2016) investigated the communication between large scale networks after an LSD administration through fMRI. This neuroimaging measure captures the oxygenated blood of the brain (BOLD). The results show an enhancing effect of LSD on the global and between-module communication within the brain, while ceasing the integrity of individual modules. This means that single large-scale networks are more interconnected compared to a sober state of the brain. This is a coherent finding with earlier studies on global brain communication under psychedelics (Carhart-Harris et al., 2014; Muthukumaraswamy et al., 2013). This research utilized the overall functional connectivity density (FCD), a measure of average correlation between fluctuating BOLD signals of regions in relation to others. Herein, high values in a region coincide with a strong connectivity with the rest of the brain. Generally, under the influence of LSD the resting state networks such as the DMN and SN were identified as major hubs using this analysis. Also, the high FCD value corresponded and overlapped with an enlarged distribution of 5-HT₂ receptors in these regions. The modulatory role of the 5-HT₂ receptors leads back to the effect psychedelics have on the self-perception and to the findings of positively and negatively experienced ego-dissolution (Mason et al., 2020). This study revealed that the bilateral temporo-parietal junction (angular gyrus), which is a part of the DMN and the bilateral insular cortex corresponding to a subpart of the SN, correlated with intensity of subjective ego-dissolution (Tagliazucchi et al., 2016). It has been further suggested that the angular gyrus is typically involved in out-of-body experiences which occur during ego-dissolution (Blanke et al.,

2002). In addition, the insular cortex is commonly referred to as the seat of self-awareness and the main processor of emotional information. Both of these findings are significantly associated with ego-dissolution (Tagliazucchi et al., 2016). Lastly, the study hypothesized that the increase in global connectivity of higher-level regions such as the DMN and SN particularly involve sensory areas. This enhanced communication of association and sensory cortices might represent a collapse of the hierarchical organization compared to a normal state of the brain. Accordingly, such collapse leads to the experience of blurred ego-boundaries and ultimately to an ego-dissolution. Taken together, this study informs our understanding on brain mechanisms of psychedelic ego-dissolution.

Further, converging evidence from Carhart-Harris et al. (2016) support the relationship of the DMN integrity and profound ego-dissolution experiences. Results show a replication of a disintegrated DMN which correlated with acute ratings of LSD-induced ego-dissolution by means of FCD. However, the study also found a relationship between decoupled parahippocampal gyrus resting state activity (PH-RSC) and psychedelic ego-dissolution assessed by the ASC, revealing another possible neurobiological correlate of psychedelic-induced ego-dissolution (Carhart-Harris et al., 2016). Taken together, the preservation of the DMN and PH-RSC integrity may contribute significantly to the perception of the self and its abolishment shaping deep psychedelic experiences.

Another recent work by Lebedev et al. (2015) investigates the effect of psilocybin-induced ego-dissolution on the Salience Network and the Medial Temporal Lobe (MTL). The MTL with its key PHC area is implicated

in contextual processing, associative memory and is commonly referred to as the mediating link between the DMN and the SN (Aminoff et al., 2013). The study identifies a disruption of the MTL communication with neocortical areas such as the SN, associated with the drug-induced ego-dissolving phenomenon. In addition, Lebedev et al. (2015) observed a decreased SN integrity under psilocybin, which was significantly related to the ego-dissolution phenomenon. Furthermore, the study displayed a disconnected crosstalk between PHC regions and the DMN which was strongly associated with the experience of ego-dissolution and consistent with previous work (Carhart-Harris, 2016; Carhart-Harris & Friston, 2010). Above all, this research reports results about the aberrant role of interhemispheric communication found during ego-dissolution. Incoherent functioning between the two hemispheres contributes to the maintenance of an aberrant sense of self, especially in regions such as the medial temporal lobe under a psilocybin dose (Lebedev et al., 2015). These results highlight the role of the PHC, the DMN and SN in the neurobiological framework of psychedelic ego-dissolution. The PHC is thought to play a key role in the communication with the DMN and research in which stimulation of the MTL circuitry has been performed, lead to dreamy states and depersonalization-like experiences (Bancaud, Brunet-Bourgin, Chauvel & Halgren, 1994; Bartolomei et al., 2012; Lee & Axmacher, 2013) In addition, altered states of self-awareness as it is experienced in patients suffering from psychosis, has been linked to the aberrant function of the MTL (Lambert et al., 2002; Lemche et al., 2013). Further, the SN and related components represent neural correlates of self-awareness and are thought to be the seed of the embodied self (Craig &

Craig, 2009; Seth, 2013). In summary, this research affirms ceased SN integrity, decreased inter-hemispheric communication and MTL-neocortex disintegration under psilocybin promoting a state of ego-disturbance.

At last, a study by Carhart-Harris et al. (2013) analyzed the role of orthogonality (inverse coupling) between resting-state networks such as the DMN and the task-positive network (TPN). In this experiment, subjects under psilocybin exhibited an abolishment of orthogonal DMN-TPN functional connectivity which is thought to be characteristic of the psychedelic state (Carhart-Harris et al., 2013). Interestingly, along with a reduced DMN-TPN inverse coupling, results exhibited a preservation of thalamocortical connectivity. This is especially indicative of a confused state of consciousness, since this was not found in a study using a propofol sedative (Boveroux et al., 2010). The DMN as previously stated is implicated in introspection and exploratory thoughts, whereas the TPN is associated with focused attention. Usually, both DMN and TPN show a dissociated activity pattern especially during task performance (Fox et al., 2005). If, however, these fundamental processes are unified, a confusion of consciousness states may result. Such an increase in coupling is seen in experienced meditators and introduces a disturbed state of cognitions observed in high-risk schizophrenia patients (Brewer et al., 2011; Shim et al., 2010). Therefore, suppressed orthogonality by means of the DMN-TPN coupling and preserved thalamocortical connectivity are indicative of psychedelic induced consciousness alterations. This model is a neurobiological hallmark for psychedelics and ego-dissolution experiences.

All in all, the integrative role of the DMN/DMN-TPN connectivity and the SN as well as cortical decoupling of the MTL, enhanced interhemispheric and global network communication are crucial contributors in the experience of ego-dissolution. Further, ongoing brain research with regards to psychedelia-induced ego-dissolution shed light onto a novel stream of research, which will be helpful in treating self-distorted mental disorders. Under the assumption that positive ego-dissolution in mystical practices is closely associated with self-distortions in psychopathologies, treatments may target ego-dissolution. These first neurological correlation studies are a tentative draft to define the neurobiological basis of ego-dissolution exploratively. In the future, controlled studies should involve investigations of the specific functionality of large-scale brain networks. In the context of psychedelia these networks could be inspected closely, hereby defining regions implicated in positive and negative ego-dissolving experiences. In these cases, studies will be able to determine long-term effects of psychedelic treatments in depression or psychosis. This potential notwithstanding, the studies used are primarily correlational studies, therefore no causality should be drawn between the investigated regions and experiencing ego-dissolution.

DISCUSSION

In this literature review, the research question of how psychedelics influence the sense of self has been addressed. The paper sought to explore current scientific findings on brain correlates of ED and psychometric properties of a standardized ED questionnaire. The theoretical ideas of the

self with its psychedelic ego-dissolution, as well as the EDI and the neural correlates, revealed mixed results. From a theoretical standpoint, the self can be defined according to Letheby & Gerrans (2017) with the help of the binding process, whereas ego-dissolution is a course where the coherent self is distorted, and loss of ego-boundaries are experienced. People generally seek for information that is salient and coherent with their self-model. This binding process is presumably mediated via two large-scale networks: the DMN and the SN. FMRI research suggested this mediating role, showing that disintegration and alterations of the activity in these networks are a crucial contributor in ego-loss (Tagliazucchi et al., 2016). Furthermore, global communication and interhemispheric connection give additional proof that neural processes influence the experience of ego-dissolution. To conclude, the changes in diverse brain regions and processes lead to a breakdown of the normal hierarchical organization of the mind with regard to psychedelic experiences such as altered perception of the self (Lebedev et al., 2015).

This research is an essential step towards a more detailed comprehension of the self and its related concepts. The investigations are first attempts to conceptualize the self and its components. In future upcoming studies, subjects who suffer from self-concept disturbances, e.g. psychosis, should be included in order to compare such conditions and its related brain areas. Negatively experienced ego-distortions should be researched in near future, because ego-dissolutions are not necessarily unpleasant experiences but can lead to the suspension of dysfunctional self-patterns. Hereby, existing therapeutic interventions in psychosis and depression, where patients suffer from aberrant self-representations, will

profit from future lines of ED research. Also, the examination of large-scale networks such as the DMN could reveal more implicated features of these regions, which fosters the understanding of brain-self-concept interactions. Besides the already known functions of the DMN in self-referential activities, the network is correlated with the experience of a dispersed self, demonstrating additional roles of such networks. For instance, studies showed that an induction of dexamphetamine reduced connectivity of large resting state networks such as the DMN and SN, establishing convergent validity ongoing drug research (Schrantee et al., 2016). In the following years, neurobiological research should examine the specifics of psychedelia-induced ego-dissolution. Furthermore, studies should comprise scientific comparisons with other drugs, for instance cocaine, in order to disentangle the opposite of a dissolved ego, namely ego-inflation. This could help to yield a clearer and more concise overview of the diverse elements of the self. For this reason, the concept of ego-dissolution necessitates assessments through accurate inventories. The EDI is a comprehensive inventory addressing this concept and future investigations should implement and use this detailed questionnaire, therewith facilitating analyses.

Nonetheless, some limitations need to be mentioned. First, the self-model proved to be a complicated intertwined concept with different constituents connected to it. In this context, processes like binding and predictive processing are elaborated components of the model, but other additional concepts need to be mentioned. It also incorporates self-knowledge and identity, as well as cultural differences that can be found when comparing individuals. These points should be taken into

consideration; therefore, these studies give only limited information about the self as a whole. Second, current research showed only correlational results, so nothing can be stated about causal relations between ego-dissolution and the brain areas. To establish stronger correlations in the future and to obtain insights into brain areas, a variety of brain imaging technologies and questionnaires have to be used interchangeably. Third, several psychedelics should be used for the purpose of settling differences between the ego-effects. Knowing the action mechanisms of psychedelics in combination with a hazard-free ego-dissolution experience can lead to the solving of pathological self-models. This should be helpful for integrating psychedelics in future therapeutic contexts.

Conclusion

The research question *'How do psychedelic drugs influence the sense of self'* has been interpreted by looking conceptually at the various effect mainly psilocybin and LSD have on the bound self-concept, by means of indicative neural evidence underlying this process. All in all, this review dealt with the conceptualization of the self and elaborated on the process of ego-dissolution. By investigating large-scale networks via brain imaging studies essential neural underpinnings of self-distortions can be found, occurring under influence of psychedelic drugs. However, future research should include patients suffering from disorders related to the self, as well as comparisons to other drugs in order to yield a sophisticated view on the concept of the self.

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