A Dose of Creativity: An Integrative Review of the Effects of Serotonergic Psychedelics on Creativity

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Abstract

This integrative review was conducted to summarize the knowledge pertaining to the effects that serotonergic psychedelics can have on creativity, a multi-dimensional construct referring to the ability to produce original and valuable artefacts. Psychedelics, which have long been hailed as substances that can enhance the creative process in their users, have experienced a recent resurgence in research, allowing the opportunity to better understand this relationship. To this end, I reviewed the extant literature which attempted to study the effects of serotonergic psychedelics on creativity through psychometric methods. A total of eleven studies were reviewed, with four psychedelic compounds represented. Every study assessed components and subcomponents of divergent and convergent thinking, with only one instance of product assessment. Results suggest that convergent thinking may increase during the post-acute phases of the drugs' intake, fostering the capacity for development of previously generated ideas. However, this evidence may be circumstantial based on the low number of studies available, small sample sizes, overall lack of randomized controlled trials, and significant methodological limitations throughout most studies. Potential mechanisms underlying these effects are discussed, along with the current state of the research and implications for future studies.

Keywords*:* convergent thinking, creativity, divergent thinking, hallucinogens, psychedelics

Introduction

Creativity is a distinctive human cognitive ability which, while traditionally difficult to define, can be understood as the ability to come up with ideas or artefacts that are new, surprising, and valuable, requiring both originality and effectiveness (Boden 2007; Gabora 2013; Runco and Jaeger, 2012). The creative process is considered to be a product of two mutualistic abilities in divergent thinking (DT) and convergent thinking (CT) (Cropley 2006). The former is defined as the production of multiple answers to an open problem and the latter as finding a single correct solution to a well-established problem (Razoumnikova 2013). DT itself is associated with four core dimensions: fluency, flexibility, elaboration, and originality (Guilford 1967). Both types of thinking play a role in different stages of the creative process, with DT prevalent in the early stages of idea finding, while CT is needed to convert an idea into a useful product (Kim and Pierce 2013).

Several different definitions of creativity have been synthesized to conceptualize this construct into four categories: **persons**, encompassing individual traits such as personality types or attitudes associated with creativity; **process**, pertaining to the mental processes that operate in creative thinking; **press**, referring to the influence of the environment on the individual; and **products**, referring to an idea made into a tangible form (Rhodes 1961). These categories are reflected in psychometric methods of creativity research (Plucker, Makel, and Qian 2019).

Since time immemorial, use of substances known as psychedelics has been associated with artistic creativity from cultures all around the world, alongside recent anecdotal evidence of their capacity to enhance the creative process (Sessa 2008). These psychedelic substances, namely serotonergic psychedelics (SPs), are psychoactive drugs

which share a common agonist action on 5-HT_{2A} receptors in the brain (e.g.: lysergic acid diethylamide [LSD] and psilocybin; Nichols 2016). This link between SPs and creativity has been a topic of interest ever since these substances started capturing the curiosity of the scientific community (Fadiman 2011). Notably, Nobel Prize winning chemist Dr. Kary Mullis has famously attributed his invention of polymerase chain reaction to the use of LSD (Sessa 2008). Moreover, reports that SPs can induce long lasting changes in the creative process or result in more original productions can be found throughout the literature (e.g.: Jones 2007; Berlin et al. 1955; Janiger and de Rios 1989). Likewise, observational studies have verified that SP users score higher on measures of creativity (Sweat, Bates, and Hendricks 2016; Anderson et al. 2019; Kangaslampi, Hausen, and Rauteenmaa 2020).

Despite research done on the relationship between SPs and creativity, how, or if, SPs can improve creativity in the individual is yet poorly understood. According to Girn et al. (2020), the capacity of these drugs to elicit effects such as an unconstrained and hyperassociative mode of cognition featuring changes in affect and meaning-attribution may underlie its potential effects on creativity. Additionally, these authors postulate that the psychedelic state can be conducive of creative generation associated with DT, with evaluation of the usefulness of generated ideas taking place post-acutely, which could mean that CT is fostered in later stages.

Following the recent resurgence in psychedelic research (Sessa 2012), interest in the study of a possible association between SPs and creativity concurrently followed. Considering this, alongside the plethora of anecdotal reports and observational studies that pair the use of these drugs with enhanced creativity, a review of existing studies on this matter is warranted, which, to my knowledge, has yet to be performed. As such, the

present review aims to analyze all existing human studies on the effects of SPs on creativity to clarify whether a relationship between both truly exists.

Methods

This review was conducted according to the guidelines established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher et al. 2009).

The electronic search was performed on the following databases: MEDLINE, Web of Science, and PsycINFO. The following search terms were used: (psychedelics OR hallucinogens) AND (creativity OR creative OR divergent thinking OR convergent thinking OR problem-solving OR originality). In addition, studies not identified through the aforementioned databases were searched for on references from relevant articles. Two *post hoc* searches were performed for any new studies.

The following inclusion criteria were used: human studies with no restriction of sex or age; studies involving intake of a serotonergic psychedelic; studies that measured creativity through psychometric measures; articles in English, Portuguese, or Spanish; all studies published until 17 November 2020.

After excluding duplicates, the titles and abstracts of all articles were reviewed considering the selection criteria. The selected articles were further reviewed before inclusion in the final list. The selection process was performed solely by one reviewer. **Table 1 [at end of manuscript]** shows an overview of all studies included.

The following variables from each study were registered: authors; year of publication; type of study; sample population and size; type of drug and dose; phase

(acute, subacute, and/or long-term); creativity test used; task approach (process, person, product, or press); and outcomes.

Results

Figure 1 [at end of manuscript] shows a diagram representing the different phases of the integrative review. The initial search yielded a total of 401 articles. An additional study was identified in a review article (Baggot, 2015) and two additional studies through *post hoc* searches. After excluding duplicates, 316 studies remained for title and abstract screening, of which nineteen were selected according to the criteria established. Full-text analyses of these studies were then performed, after which a further eight were excluded: one was removed because it assessed creativity through subjective measures, one because it was not found to adequately assess creativity, three because they did not assess creativity, one because there was no direct administration of SPs, one because it involved administration of an SP alongside other psychoactive drugs, and one because it did not involve administration of an SP. Thus, a total of eleven studies were selected for qualitative synthesis.

All three different phases of the drugs (acute, sub-acute, long-term) are represented and four different SPs are studied, which are reviewed together due to their similar mechanism of action. Studies ranged from 1964 to 2021. Two studies were randomized controlled trials (RCTs), while five studies were quasi-experiments, and five studies were observational in naturalistic settings. Sample size varied from eighteen to seventy-two, most of which were healthy subjects. Assessment of creativity was mostly done through measurements of DT and CT, with only one instance of product assessment.

This information can be found in **Table 2 [at end of manuscript]**. Each study is reviewed in detail below, grouped in terms of substance used.

LSD

McGlothlin, Cohen, and McGlothlin (1964)

This quasi-experimental study aimed to assess the effects of LSD on normal subjects with no previous experience with LSD or similar agents. A test battery, which was not given to all participants, was administered to an experimental (n=15) and comparison group (n=14) pre- and one-week post LSD administration.

The experimental group received 200 μg of LSD orally in sessions of about 8 hours. Subjects were initially tested on the day preceding the LSD experience and again one week after. Alternate forms of the same tests were given in a counterbalanced order. The comparison group took the same tests with a one-week interval. The authors stressed that this was not a placebo condition group. A distinct practice effect was evident in the comparison group, which was considered identical to the gains shown by the experimental group in the post-LSD tests. Pre- and post-LSD results did not differ significantly after practice effects were considered.

McGlothlin, Cohen, and McGlothlin (1967)

This RCT aimed to assess long-term personality, attitude, value, interest, and performance changes after LSD administration in normative individuals. Seventy-two male subjects participated in the experiment. Subjects were assigned to either an

experimental group or one of two control groups of twenty-four subjects each based on six matching variables: knowledge of hallucinogens, expectations, experience with marijuana, hypnotic susceptibility, sensing-intuition, and judgment-perception.

The experiment was double-blind during preparation of subjects, where a one-hour interview with a clinical psychologist attending the drug session was undertaken by each subject, up until the point where drug effects became noticeable. Drugs were administered in three separate sessions. The experimental group received 200 μg of LSD, while each control group received 20 mg of amphetamine and 25 μg of LSD respectively as active placebo. Nine subjects dropped out from the study.

Assessments were taken prior to drug intake and again at intervals of two weeks and six months following the third session. The creativity tests administered assessed DT and CT. Three tests of aesthetic sensitivity were also administered, a construct which, while related to creativity, comprises its own distinct ability (Corradi et al. 2019). The individuals administering the tests did not participate in other parts of the experiment.

One in each of the control groups did not complete the six-month testing. Both control groups were combined into a single group due to no systematic differences between them.

At the six-month testing, 25% of the experimental group felt that the drug experience had resulted in enhanced creativity in their work, as compared to 9% and 0% for the amphetamine and 25 μg group, respectively. However, all measures of creativity failed to reveal any significant changes at the two week and six-month testing.

Zegans, Pollard, and Brown (1967)

This quasi-experimental study aimed to investigate whether administration of LSD would acutely enhance potential for creative performance. Thirty male volunteers with no psychological and physical contraindications were recruited. Of these, twenty subjects were randomly assigned to the experimental group, while the remaining eleven comprised the control group.

During selection, a statement was read to all subjects concerning the purpose of the experiment and some of the effects of the drug, but the possibility of hallucinogenic experiences was not stressed. A battery of projective tests was then administered based on which subjects were classified as predicted to improve or not to improve their performance after drug intake. Subjects predicted to improve (D1) displayed an integrated mixture of affect, intelligence, and abstract skill, while those predicted not to improve (DN1) were rigid, stereotypical, and inflexible. In addition, subjects performed a fifteen-minute period of free association before and after drug intake. Easiness in this process was considered a predictive factor for improving creative performance.

In each session, each subject completed the first battery of tests. These included measures of CT, originality, and products. In addition, the Gottschalk Figure-Perception Test and the Tachistoscopic Stimulation task were also administered; however, since these tests respectively measured perceptual ability and latency time of visual stimuli recognition, for the purpose of this review they were not considered measures of creativity. The experimental group then ingested an LSD dose equal to 0.5 μg/kg body weight, while controls took none. Following ingestion, subjects could read or relax while waiting for two hours to elapse, after which they were again tested. Parallel versions of the tests were administered at both time points.

Positive mean changes were verified for all outcomes except CT when comparing pre- and post-drug creativity assessments in the LSD group, whereas in the control group

negative mean changes were verified in all outcomes but product. Originality was significantly higher for the LSD group compared to control, but product ratings were lower. There were no significant differences between DN1 subjects and controls. Based on projective criteria, originality ratings were significantly higher for D1 subjects compared to controls. The same was verified based on free-associate criteria, while product ratings were also lower. Using projective criteria, originality and CT scores were higher for D1 subjects compared to DN1, while using free-associate criteria D1 subjects had only significantly higher CT scores.

Psilocybin

Prochazkova et al. (2018)

This quasi-experimental open-label study aimed to assess DT and CT after administration of sub-perceptual doses (microdoses) of truffles containing psilocybin. Thirty-eight healthy individuals were recruited during a microdosing event in the Netherlands. All but two had previous experience with psychedelics.

The truffles consisted of three possible dose sizes: 0.22 g, 0.33 g, and 0.44 g, administered according to self-reported body weight. Average psilocybin content of the truffles was 1595 μg/g ± 3.75.

Participants were assessed with three creativity tasks at baseline before ingestion of truffles and after while under their acute influence. After finishing the tasks in the first session, participants consumed their dose and, approximately ninety minutes after, were again assessed with the same tasks. Two different versions of each task were used with a counterbalanced order. Thirteen participants dropped out.

Results show that microdosing of truffles significantly improved CT and DT. Specifically for DT, fluency, flexibility, and originality scores increased significantly, whereas elaboration did not.

Mason et al. (2019)

This naturalistic study aimed to assess the sub-acute effects of psilocybin on creative thinking, empathy, and subjective well-being during a psilocybin retreat in the Netherlands. Fifty-five volunteers were initially recruited. About half had previously taken psychedelics.

Assessments were taken on three separate occasions: at baseline, the morning after ingesting psilocybin, and seven days after. Pre- and post-psilocybin assessments were completed at the retreat, while the third assessment was completed online.

Fifty-five participants completed parts of the test battery at baseline, fifty participants the morning after, and twenty-two participants seven days after. Participants ingested truffles containing psilocybin in a tea form. An average of 34.2 g of truffles was ingested by participants throughout the day. A 15 g truffle sample was analyzed for psilocybin content, yielding 1.9 mg.

CT remained unchanged when assessed the morning after taking psilocybin, while increasing significantly compared to baseline when assessed seven days after. Fluency and originality were found to be significantly higher the morning after compared to baseline, while the ratio of both did not differ. There were no significant effects of psilocybin on any DT parameter seven days after. No significant differences were found between subjects experienced with psilocybin and unexperienced subjects.

Mason et al. (2021)

This RCT aimed to assess the acute and persisting effect of psilocybin on DT and CT and to assess acute biological predictors of changes in these constructs. Sixty healthy participants, with previous experience with psychedelics, were randomly allocated to either a treatment condition (0.17 mg/kg psilocybin) or control group (placebo).

Parallel versions of creativity tasks were administered on the first day at baseline, the following day (under the effect of either psilocybin or placebo), and seven days after the acute testing day (follow-up). All responses were scored afterwards by two independent raters who were blind to the treatment condition. Interrater reliability was excellent for all creativity tasks.

Psilocybin influenced creativity in a time- and construct-dependent manner, acutely decreasing CT, fluency, and originality, while significantly increasing novelty at follow-up. Individuals under the effect of psilocybin reported significantly higher ratings of insightfulness. CT increased within both groups at each successive time-point. Both groups did not differ in terms of demographics.

DMT (Ayahuasca)

Frecska et al. (2012)

This observational study aimed to assess creativity and entoptic phenomena in a naturalistic setting after a two-week long series of ayahuasca ceremonies in Brazil. Forty healthy volunteers with a mean age of 30.9 participating in these ceremonies were

recruited. In addition, twenty-one subjects with a mean age of 27.1 were recruited from two other locations to provide control data.

On the day of the ceremonies, participants ingested a self-chosen dose of ayahuasca of at least 50 ml. Participants drank a total of 583 ± 315.8 ml over all sessions. The alkaloid concentrations of the beverage were analyzed and reported in a previous study to contain 0.73 mg/ml of N,N-Dimethyltryptamine (DMT) (Frecska, White, and Luna 2004). The main researcher did not participate in the organization of ayahuasca sessions. A separate group of the research staff was involved in the administration of the brew and test materials. Other members of the research team, blind to the identifying and grouping data, evaluated the tests. A third party performed the statistical analysis.

Subjects completed creativity tests between ninety and 180 minutes before the start of the sessions and again twenty-four to forty-eight hours after the last ayahuasca administration, when the acute effects of the concoction had ceased. These creativity tests measured fluency, flexibility, and originality. In addition, the number of highly original solutions was also calculated and considered as the most reliable index of creativity.

Repeated ingestion of ayahuasca resulted in a significantly increased number of highly original solutions. Both groups did not differ in baseline measures of creativity.

Kuypers et al. (2016)

This quasi-experimental open-label study aimed to assess creative thinking after administration of ayahuasca. Twenty-six healthy participants were recruited from two spiritual ayahuasca workshops. One different test group was formed from each of these workshops. Group 1 included fifteen participants with a mean age of 37.4. Group 2

included 11 participants with a mean age of 52.0. All individuals had prior experience with ayahuasca.

An initial ayahuasca dose was administered and, approximately one hour after, an optional dose was offered. The brew used in group 1 contained 0.65 mg/ml DMT and participants ingested a total of 75.5 ± 11.1 mg DMT. The brew used in group 2 contained 0.96 mg/ml DMT and a total of 42.8 ± 14.9 mg DMT was ingested.

Parallel versions of two creativity tests (one measuring both DT and CT, the other measuring only DT) were administered twice in a counterbalanced form: the first instance was three hours before dosing and the second was 1.5–2 hours after the initial dose, after which the optional dose was offered.

Age and education were significantly higher for group 2 compared to group 1. DT was shown to only change in one of the tests. Group 1 showed higher fluency and originality scores compared to group 2, while the latter showed higher ratio of originality/fluency than the former. In addition, fluency decreased in group 1 after ayahuasca ingestion, while increasing in group 2. Originality scores also improved under influence of ayahuasca compared to baseline. CT was shown to decrease after ingestion of ayahuasca when compared to baseline.

Uthaug et al. (2018)

This observational study aimed to assess sub-acute and long-term effects of ayahuasca on affect and creativity, as well if these effects depend on the degree of ego-dissolution experienced. Fifty-seven participants were recruited from ayahuasca ceremonies held in both the Netherlands and Colombia, divided into the Netherlands

group (n=30; 43.3% with no previous ayahuasca experience) and the Colombia group (n=27; 40.7% with no previous ayahuasca experience).

Three assessments were taken at baseline, twenty-four hours after, and four weeks after the ceremony. All participants completed the pre- and post-ceremony session, and thirty-one participants completed the four-week follow-up. At baseline, participants completed a thirty-minute test battery, where CT and DT were assessed, and again on-site after twenty-four hours. The follow-up assessment was administered through an online survey.

Ayahuasca samples from each site were obtained and analyzed for alkaloid concentrations. Samples from the Netherlands contained 371.6 mg and 915.4 mg of DMT. Samples from Colombia contained 189.4 mg and 500.5 mg of DMT. The amount of ayahuasca consumed was not reported.

CT increased near-significantly twenty-four hours and significantly four weeks after the ceremony, compared to baseline. Neither country nor session × country affected CT. No DT parameters were affected by any of the main factors or their interaction. Experience with ayahuasca did not influence sub-acute outcomes.

Kiraga et al. (2021)

This observational study aimed to assess the subacute and long-term cognitive and psychological processes affected by ayahuasca in a naturalistic setting. Forty-three participants were recruited from ayahuasca retreats in the Netherlands.

Three assessments were taken: at baseline, twenty-four hours after, and a follow-up seven days after the ayahuasca ceremony. The average amount of DMT consumed,

based on participants' self-reports, was calculated to be 57.44 mg. Parallel versions of creativity tasks were used.

Results showed that CT increased significantly at follow-up compared to baseline, while DT decreased at one- and seven-days post-ceremony.

5-MeO-DMT

Uthaug et al. (2019)

This observational study aimed to assess whether inhalation of vapor from dried toad secretion containing 5-MeO-DMT in naturalistic settings would result in sub-acute and/or long-term improvements in measures of affect and cognition. A total of forty-two participants were recruited from three different locations (Czech Republic [N=25], Spain [N=10], and the Netherlands [N=7]) where sessions were conducted. Fifteen participants reported no previous experience with 5-MeO-DMT, while 92.9% had experience with other psychedelics.

Three assessments were taken: on site at baseline, twenty-four hours post-session after the acute effects subsided, and a follow-up assessment four weeks after through an online survey. The administered dose was not reported. Five samples of the substance were analyzed, containing an average of 266.88 mg/g 5-MeO-DMT. Only twenty-four participants completed the test battery at the final time-point.

A significant main effect of session and country on CT was verified. CT significantly increased twenty-four hours after drug intake and four weeks later, compared to baseline. The mean CT scores were significantly higher in the Dutch and Czech sample compared to the Spanish sample. There was no interaction between session

and country. No DT parameters were affected by any of the main factors or their interaction.

Discussion

An integrative review was conducted to evaluate the effect of SPs on creativity. The evidence reviewed reported the use of four psychedelic compounds and respective effects on different phases of the drugs' activity. All studies used process methods to assess components of creative cognition (CT and DT), with only one instance of product assessment.

Regarding DT (or its subcomponents), three studies reported increases in this construct during the acute phase (Zegans, Pollard, and Brown 1967; Kuypers et al. 2016; Prochazkova et al. 2018), with two instances of impairment (Mason et al. 2021; Kiraga et al. 2021), while two studies reported sub-acute increases (Frecska et al. 2012; Mason et al. 2019) and one study reported a decrease (Kiraga et al. 2021). Meanwhile, CT acutely decreased in two studies (Kuypers et al. 2016; Mason et al. 2021) and increased in one study (Prochazkova et al. 2018), sub-acutely increased in two studies (Uthaug et al. 2019; Kiraga et al. 2021), and increased long-term in four studies (Uthaug et al. 2018; Mason et al. 2019; Uthaug et al. 2019; Kiraga et al. 2021).

Taken together, current evidence does not seem to be conclusive enough to support most claims regarding the effects of SPs on creativity. Previous suggestions that SPs enhance DT initially, during the psychedelic state, while CT is fostered in later stages (Girn et al 2020) are only partly supported. Specifically, evidence is conflicting in whether DT is actually enhanced or hindered during the acute phase. In fact, the only modern RCT performed on this subject found that DT was acutely hindered, while

feelings of insightfulness increased and novelty was later enhanced (Mason et al. 2021). The authors proposed that SPs may acutely give way to insights that increase the potential for spontaneous creativity, while at the same time hindering the capacity for deliberate creativity, which in turn is potentially enhanced sub-acutely. On the other hand, in agreement with Girn et al (2020), the evidence found may indicate that CT is indeed enhanced in the later phases. This would suggest that in order to enhance the creative process, exploration of generated ideas should take place after the acute effects of SPs have subsided.

As previously mentioned, the psychedelic state is characterized by a state of hyperassociative and unconstrained cognition (Girn et al. 2020). Since associational fluency has been shown to be related to higher DT abilities (Benedek and Neubauer 2013; Beaty et al. 2014), in theory the psychedelic state could facilitate novel idea generation in early stages of the creative process. Moreover, SPs possess meaning-enhancing properties of otherwise irrelevant stimuli which could stimulate "out-of-the-box" ideation (Hartogsohn 2018; Preller et al. 2017). This review, however, shows that there is yet not enough evidence to either confirm or refute this possibility. Meanwhile, there is somewhat stronger evidence supporting the claim that CT is enhanced in the long-term, which would imply that SPs induce residual changes to the brain. Indeed, Pasquini, Palhano-Fontes, and Araujo (2020) found that, 24 hours after use, ayahuasca decreased connectivity within the default mode network. Suppression of this network could benefit CT considering its importance for goal-directed cognition (Anticevic et al. 2012).

Altogether, this review has shown that, considering the small number of studies available, knowledge of this topic is still lacking. This means that the findings in this review are undissociated from chance, Furthermore, most of the evidence discussed comes from naturalistic studies, which, alongside their intrinsic confounding factors,

present a significant risk of self-selection bias that limits the ability to extrapolate these findings to the general population. There is also no guarantee that practice effects did not take place in both observational and quasi-experimental studies. As such, while the findings hint at a possible long-term enhancement of CT, this possibility is reliant on further studies with a stronger methodological foundation.

Interestingly, Prochazkova et al. (2018) reported acute enhancements of both DT and CT when administering microdoses of psilocybin. Although these findings come from a single study, it could indicate that the effects of SPs on creativity are dose dependent, whereas doses small enough to not induce a psychedelic state may also benefit CT acutely. In other words, acute impairment of CT, as verified in other studies using hallucinogenic doses, may be tied to the psychedelic state itself, meaning that creativity may differently benefit from sub-hallucinogenic doses. Further studies with microdoses are needed to clarify this possibility.

Only one early study by Zegans et al. (1967) attempted to investigate the impact of individual differences on how SPs interact with creativity. This study suggests that a combination of affective, cognitive, and abstract skills may be determinant in eventual creative benefits. This may be further relevant due to semblance between SPs and psychosis, which intersect in terms of brain areas disrupted (Leptourgos et al. 2020; Lladó-Pelfort et al. 2017). Psychotic traits have been proposed to enhance creativity in the presence of protective factors such as increased intelligence or working memory capacity (Carson 2018). Further studies are needed addressing how individual traits such as level of cognitive abilities interact with the effects of SPs on creativity.

It should be stressed that assessing creativity is a difficult endeavour due to the conceptual issues associated with most psychometric instruments (Said-Metwaly, van den Noortgate, and Kyndt 2017). Moreover, most studies reviewed focused on process

components of creativity, while studies assessing personal traits, environmental factors, and productions are lacking.

It is therefore still unknown whether the claims that SPs possess the ability to enhance creativity in the individual are substantiated. For instance, enhancement of creativity could derive from increases in mood and openness that follow SP use (Turton, Nutt, and Carhart-Harris 2015; Forstmann et al. 2020; Nour, Evans, and Carhart-Harris 2017; Carhart-Harris et al. 2016), which in turn have been related to increased creativity (Baas, De Dreu, and Nijstad 2008; Li et al. 2014). It can also be argued that these drugs induce only subjective feelings of increased creativity that are biasedly attributed to their use, for instance due to expectation effects. Krippner (1977) proposed that SPs may only enhance creativity in individuals who were already talented before drug ingestion. Zegans et al. (1967) postulated that the effect of SPs on creativity may only become manifest in creative solutions to problems relevant to the individual's domain of interest. So far, studies have focused on creative processes using decontextualized tasks, even though a study by Harman et al. (1966) did attempt this approach, although using a non-psychometric method. Therefore, it may be relevant to design future studies specifically around subjects' domains.

Conclusion

This integrative review presented data suggesting a possible relationship between SPs and creativity, specifically by enhancing CT in later phases, resulting in increased capacity for development of previously generated ideas after the acute effects subside. However, these findings are hampered by several limitations, namely the limited number of studies performed to date, small sample sizes, lack of RCTs, and significant

methodological limitations that compromise the strength of the evidence. It was shown that there is a trend to study the effects of SPs on creativity through process psychometric methods, measuring DT and CT and their subcomponents. On the other hand, research using person, press, or product approaches is lacking, as well as by investigating the role of individual characteristics.

Altogether, this review exposed the fragility in how the topic of SPs and creativity has been approached so far, calling for an increased number of studies and wider range of methods employed to provide a more comprehensive understanding of this subject. Nevertheless, it showed that this topic has great potential for further research, while providing a foundation that future studies can use to build upon. New RCTs will be particularly essential to provide a strong level of evidence.

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Authors	Year	Title	Journal
McGlothlin, W. H., S. Cohen, and M. S. McGlothlin.	1964	Short-term effects of LSD on anxiety, attitudes and performance.	The Journal of Nervous and Mental Disease
McGlothlin, W. H., S. Cohen, and M. S. McGlothlin.	1967	Long Lasting Effects of LSD on Normals.	Archives of General Psychiatry
Zegans, L. S., J. C. Pollard, and D. Brown.	1967	The Effects of LSD-25 on Creativity and Tolerance to Regression.	Archives of General Psychiatry
Frecska, E., C. E. Móré, A. Vargha, and L. E. Luna.	2012	Enhancement of Creative Expression and Entoptic Phenomena as After-Effects of Repeated Ayahuasca Ceremonies.	Journal of Psychoactive Drugs
Kuypers, K. P. C., J. Riba, M. de la Fuente Revenga, S. Barker, E. L. Theunissen, and J. G. Ramaekers.	2016	Ayahuasca enhances creative divergent thinking while decreasing conventional convergent thinking.	Psychopharmacology
Uthaug, M. V., K. van Oorsouw, K. P. C. Kuypers, M. van Boxtel, N. J. Broers, N. L. Mason, S. W. Toennes, J. Riba, and J. G. Ramaekers.	2018	Sub-acute and long-term effects of ayahuasca on affect and cognitive thinking style and their association with ego dissolution.	Psychopharmacology
Prochazkova, L., D. P. Lippelt, L. S. Colzato, M. Kuchar, Z. Sjoerds, and B. Hommel.	2018	Exploring the effect of microdosing psychedelics on creativity in an open-label natural setting.	Psychopharmacology
Mason, N. L., E. Mischler, M. V. Uthaug, and K. P. C. Kuypers.	2019	Sub-Acute Effects of Psilocybin on Empathy, Creative Thinking, and Subjective Well-Being.	Journal of Psychoactive Drugs

Uthaug, M. V., R. Lancelotta, K. van Oorsouw, K. P. C. Kuypers, N. Mason, J. Rak, A. Šuláková, et al.	2019	A single inhalation of vapor from dried toad secretion containing 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT) in a naturalistic setting is related to sustained enhancement of satisfaction with life, mindfulness-related capacities, and a decrement of psychopathological symptoms.	Psychopharmacology
Mason, N. L., K. P. C. Kuypers, J. T. Reckweg, F. Müller, D. H. Y. Tse, B. Da Rios, S. W. Toennes, P. Stiers, A. Feilding, and J. G. Ramaekers.	2021	Spontaneous and Deliberate Creative Cognition during and after Psilocybin Exposure.	Translational Psychiatry
Kiraga, M. K., N. L. Mason, M. V. Uthaug, K. I. M. van Oorsouw, S. W. Toennes, J. G. Ramaekers, and K. P. C. Kuypers.	2021	Persisting Effects of Ayahuasca on Empathy, Creative Thinking, Decentering, Personality, and Well-Being.	Frontiers in Pharmacology

Table 1: List of studies included in the integrative review.

Authors	Year	Type of study	Sample population/size			Drug and dose	Phase	Creativity tests	Outcomes
McGlothlin et al.	1964	Quasi-experimental	**G1** Experimental group (n=8–15; =5)		**G2** Control group (n=14; ♀=5)	LSD; 200 µg	Sub-acute	Associational fluency; Ideational fluency; Alternate uses; Alternate signs; Consequences; Remote Associations Test	DT: ≈ CT: ≈
McGlothlin et al.	1967	Quasi-experimental	**G1** Experimental group (n=24; ♀=0)	**G2** Control group 1 (n=24; ♀=0)	**G3** Control group 2 (n=24; ♀=0)	LSD; 200 µg and 25 µg	Long-term	Fluency, Alternate Uses, Hidden Figures, and Plot Titles tests; Thematic Apperception Test; Draw-a-	DT: ≈ CT: ≈

								Person Test; Remote Associations Test		
Zegans et al.	1967	Randomized controlled trial	**G1**		**G2**	LSD; 0.5 µg/kg body weight	Acute	Remote Associates Test; Modified Word Association Test; Mosaic Design Test	Originality: ↑ Product: ↓ CT: ≈	
			Experimental group (n=20; ♀=0)		Control group (n=11; ♀=0)					
Prochazkova et al.	2018	Quasi-experimental; open-label; naturalistic	Healthy volunteers (n=38; ♀=15)			Psilocybin (Truffles); 350.9 µg, 526.35 µg, or 701.8 µg	Acute	Alternate Uses Task; Picture Concept Task	DT: ↑ CT: ↑	
Mason et al.	2019	Observational; naturalistic	N=55 (50 on session 1, 22 on session 2); ♀=26			Psilocybin (Truffles); average 4.332 mg	Sub-acute	Picture Concept Task	**24h+** DT: ↑ CT: ≈	**7 days +** DT: ≈ CT: ↑
Mason et al.	2021	Randomized controlled trial	Healthy participants (n=60); ♀=25			Psilocybin; 0.17 mg/kg body weight	Acute; Long-term	Picture Concept Task; Alternate Uses Task	**Acute** Fluency: ↓ Originality: ↓ CT: ↓	**Long-term** Novelty: ↑
Frecska et al.	2012		**G1**		**G2**		Sub-acute		Originality: ↑	

		Observational; naturalistic	Healthy volunteers (n=40; ♀=23)	Control group (n=21; ♀=11)	DMT (Ayahuasca); 0.73 mg/ml		Torrance Tests of Creative Thinking		
Kuypers et al.	2016	Quasi-experimental, open-label	**G1** Healthy volunteers (n=15; ♀=10)	**G2** Healthy volunteers (n=11; ♀=7)	DMT (Ayahuasca); G1: 75.5 ± 11.1 mg; G2: 42.8 ± 14.9 mg	Acute	Pattern/Line Meanings task; Picture Concept Task	**G1** DT: ↑ CT: ↓	**G2** DT: ↑ CT: ↓
Uthaug et al.	2018	Observational; naturalistic	**G1** Healthy volunteers (n=23); volunteers w/ psychiatric disorders (n=7); 60% ♀	**G2** Healthy volunteers (n=15); volunteers w/ psychiatric disorders (n=6); unknown (n=6); 66.7% ♀	DMT (Ayahuasca); G1: 1.858~4.577 mg/ml; G2: 0.947~ 2,5025 mg/ml	Sub-acute; Long-term	Picture Concept Task	**Sub-acute** DT: ≈ CT: ≈	**Long-term** DT: ≈ CT: ↑
Kiraga et al.	2021	Observational; naturalistic	N=43 (20 on session 1; 19 on session 2); ♀=21		DMT (Ayahuasca); 19.20~75.00 mg	Sub-acute; Long-term	Picture Concept Task	**Sub-acute** DT: ↓ CT: ≈	**Long-term** DT: ↓ CT: ↑
Uthaug et al.	2019	Observational; naturalistic	Healthy volunteers (n=32); Volunteers w/ psychiatric disorders (n= 10); ♀=40%; 42 on session 1; 24 on sessions 2		5-MeO-DMT (Dried toad secretion); 203.6~307.3 mg/g	Sub-acute; Long-term	Picture Concept Task	**Sub-acute** DT: ≈ CT: ↑	**Long-term** DT: ≈ CT: ↑

Table 2: Results of the selected studies for the integrative review. Abbreviations: n – number; ♀ – female; G – group; DT – Divergent thinking; CT – Convergent thinking; ↑ – significant improvement; ↓ – significant impairment; ≈ – no significant changes.

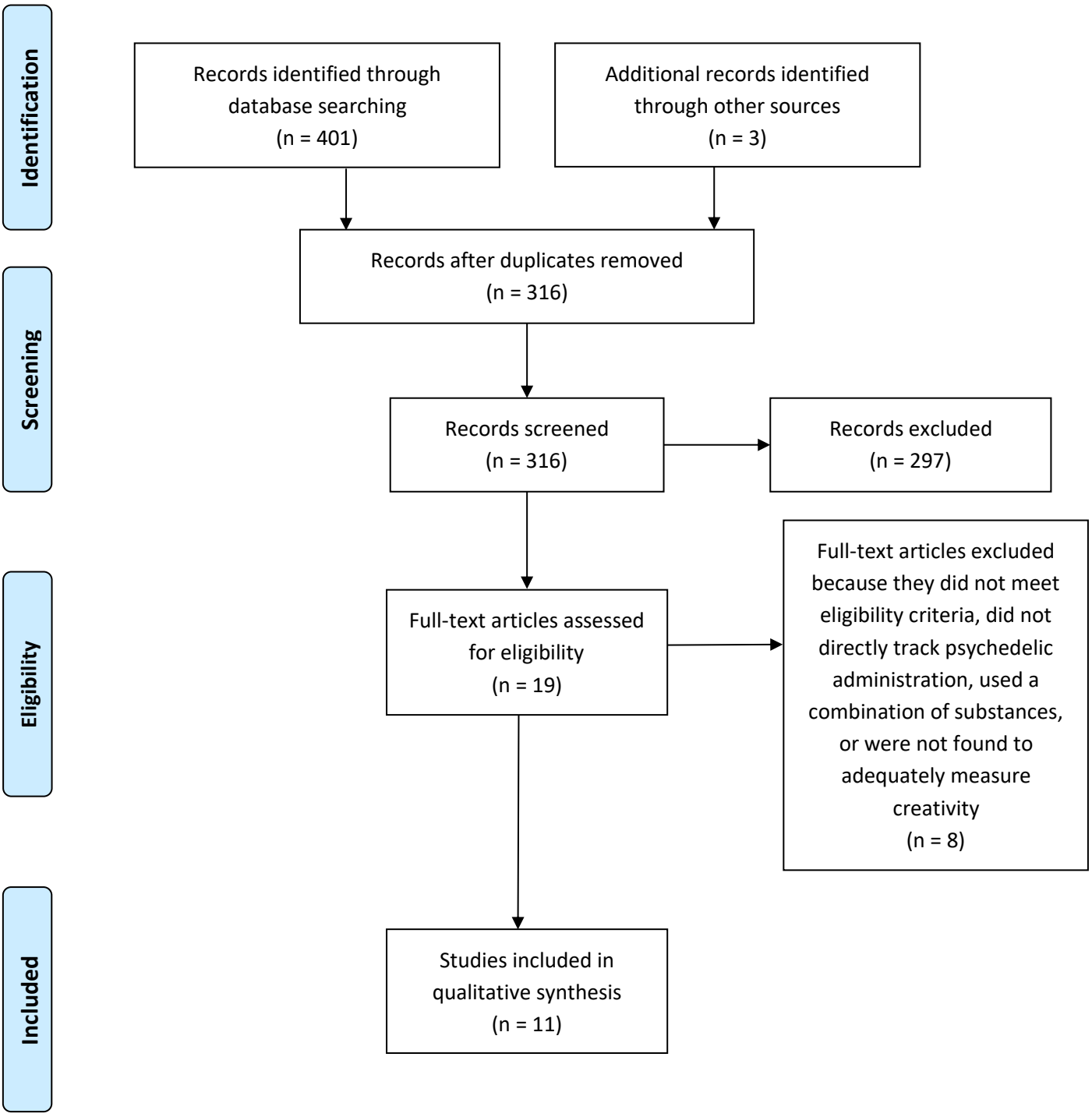

Figure 1: Flow diagram identifying the different stages of the integrative review.