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Sub-Acute Effects of Psilocybin on Empathy, Creative Thinking, and Subjective Well-Being

Natasha L. Mason, M.Sc., Ph.D. [a], Elisabeth Mischler, Ph.D.[b], Malin V. Uthaug, M.Sc., Ph.D.[a], and Kim P. C. Kuypers, Ph.D. [a]

[a]Department of Neuropsychology and Psychopharmacology, Faculty of Psychology and Neuroscience, Maastricht University, Maastricht, The Netherlands; [b]Central Customs Authority, Centre of Education and Science, Cologne, Germany

ABSTRACT

Creative thinking and empathy are crucial for everyday interactions and subjective well-being. This is emphasized by studies showing a reduction in these skills in populations where social interaction and subjective well-being are significantly compromised (e.g., depression). Anecdotal reports and recent studies suggest that a single administration of psilocybin can enhance such processes and could therefore be a potential treatment. However, it has yet to be assessed whether effects outlast acute intoxication. The present study aimed to assess the sub-acute effects of psilocybin on creative thinking, empathy, and well-being. Participants attending a psilocybin retreat completed tests of creative (convergent and divergent) thinking and empathy, and the satisfaction with life scale on three occasions: before ingesting psilocybin (N = 55), the morning after (N = 50), and seven days after (N = 22). Results indicated that psilocybin enhanced divergent thinking and emotional empathy the morning after use. Enhancements in convergent thinking, valence-specific emotional empathy, and well-being persisted seven days after use. Sub-acute changes in empathy correlated with changes in well-being. The study demonstrates that a single administration of psilocybin in a social setting may be associated with sub-acute enhancement of creative thinking, empathy, and subjective well-being. Future research should test whether these effects contribute to the therapeutic effects in clinical populations.

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Convergent thinking; creativity; divergent thinking; empathy; life satisfaction; psilocybin

Introduction

Creativity and empathy are crucial for everyday interactions and cooperation, allowing us to adapt to an ever-changing environment, and motivating our prosocial behaviors (Decety et al. 2016). Interestingly, they have been found to be positively related (Carlozzi et al. 1995), and it has been suggested that creative, flexible thinking is a prerequisite for empathy (Eslinger 1998). Previous research demonstrates a reduction in these skills in populations where social interactions and subjective well-being are compromised (Beck 1967; Neumann et al. 2011).

Creativity is a multicomponent construct, consisting of convergent (CT) and divergent thinking (DT) (Guilford 1967). CT is considered a process of generating a single optimal solution to a particular problem, emphasizing speed, accuracy, and logic. Conversely, DT is a process used to generate many new ideas, in a context where more than one solution is correct. An example of the latter is a brainstorming session, where generating many innovative ideas or solutions on a particular issue is the ultimate goal (Colzato, Szapora, and Hommel 2012). Although both CT and DT are important in creative activities, DT may be a more useful estimate of the potential for creative thought in daily life (Runco and Acar 2012).

Emotional, or affective, empathy (EE) refers to the sharing of emotions, or the ability to *feel* what another person is feeling. In contrast, cognitive empathy (CE) refers to mental perspective taking, or *recognizing* and *understanding* what another person is feeling (Deutsch and Madle 1975). Previous research suggests a specificity of the two constructs (Davis 1980), in that emotional empathy may depend on state variables, whereas cognitive empathy requires a (trait) ability to identify another's emotions (Hurlemann et al. 2010; Pokorny et al. 2017).

Both creative, flexible thinking and empathy deficits have been found in stress-related psychopathologies like depression, anxiety disorders, and post-traumatic stress disorder (PTSD) (Chamberlain et al. 2006; Cusi

CONTACT Natasha L. Mason Natasha.mason@maastrichtuniversity.nl Department of Neuropsychology and Psychopharmacology, Faculty of Psychology and Neuroscience, Maastricht University, P.O. Box 616, Maastricht 6200 MD, The Netherlands.

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et al. 2011; Donges et al. 2005; Lee and Orsillo 2014; Morrison et al. 2016; Nietlisbach et al. 2010; Palm and Follette 2011; Parlar et al. 2014). Hallmarks of these disorders are repetitive and rigid patterns of negative and compulsive thoughts, together with social difficulties and impaired empathic abilities (Aldao, Nolen-Hoeksema, and Schweizer 2010; Beck 1967; Dos Santos et al. 2016; Morrison et al. 2016; Nietlisbach and Maercker 2009; Todd et al. 2015), the latter of which, most evident in depression, may contribute to more pronounced symptoms (Cusi et al. 2011; Donges et al. 2005).

Importantly, previous research has found that these processes demonstrate plasticity and can be enhanced by interventions such as therapy programs, hormone administration, and mindfulness induction, as well as (positive) changes in mood (Ashby, Isen, and Turken 1999; Baas, De Dreu, and Nijstad 2008; Davis 2009; Donges et al. 2005; Forgeard and Eichner 2014; Hurlemann et al. 2010; Lee and Orsillo 2014; Palgi, Klein, and Shamay-Tsoory 2016). However, these interventions typically target only one of the two mentioned processes. Thus, by finding treatments that promote both processes, individual deficits could be further decreased, potentially enhancing well-being and quality of life.

Anecdotal evidence and (quasi-)experimental studies suggest that a single administration of a psychedelic drug like ayahuasca, LSD, or psilocybin can enhance creative, flexible thinking and emotional empathy in the neuro-typical population (Dolder et al. 2016; Harman et al. 1966; Krippner 1964; Kuypers 2018; Kuypers et al. 2016; Pokorny et al. 2017; Preller et al. 2015; Sessa 2008; Uthaug et al. 2018). Furthermore, clinical studies have found that administration of psilocybin can induce long-lasting positive psychological changes, such as symptom remission and enhancement of well-being, in clinical populations (Carhart-Harris et al. 2016; Griffiths et al. 2016; Johnson, Garcia-Romeu, and Griffiths 2017). However, the persistence of effects on creativity and empathy, and the relationship with subjective well-being, has yet to be assessed.

The present study was designed to assess the sub-acute effects of psilocybin on creative thinking, empathy, and subjective well-being. We hypothesized that divergent and convergent thinking, emotional empathy, and satisfaction with life would be enhanced sub-acutely with no effect on cognitive empathy (Pokorny et al. 2017). Furthermore, based on clinical research demonstrating reductions in creativity and empathy in individuals with compromised well-being, we hypothesized that enhancements in such processes would correlate with increased satisfaction with life. Finally, as psilocybin has been shown to induce long-lasting positive increases in well-being, we hypothesized that participants with previous psilocybin experience would have a higher baseline satisfaction with life score, compared to those who are psilocybin-naïve.

Methods

Participants

Participants were volunteers attending psilocybin retreats in the Netherlands, organized by the Psychedelic Society UK. In total, 55 participants (26 female) consented after goals and methods of the study were explained. Most participants were from Europe (80%), while the rest were from North America (7.3%), Africa (3.6%), Central America (1.8%), and Asia (1.8%), or undisclosed (5.4%). The highest completed levels of education were graduate school (41.8%), undergraduate school (41.8%), secondary school (7.3%), or undisclosed (9.1%). Mean (SD) participant age was 34.8 (8.9).

About half (52.7%) of the participants had used psilocybin before, and 49.1% had previously used a psychedelic other than psilocybin (LSD, ayahuasca, or DMT). Motivations for attending the retreat included "to understand myself" (83.6%), "curiosity" (80%), "to resolve problems" (49.1%), and "other" (18.2%). For 69.1% of the participants, this was the first time taking a psychedelic in a retreat setting.

The study was conducted in accordance with the Declaration of Helsinki and subsequent amendments concerning research in humans and was approved by the Ethics Review Committee of Psychology and Neuroscience. Participation was voluntary and no incentive to participate was provided. All volunteers gave their written informed consent to participate.

Study procedure

Psilocybin retreats

Prior to participation in the retreat, personal intakes were done by the facilitators, which included screening for (and excluding) individuals with psychiatric disorders or taking psychiatric medications, and medical factors like high blood pressure.

The setting in which psilocybin was taken was the same throughout all of the retreats. Participants stayed in a large house set in nature, hosted by at least two or more experienced psilocybin facilitators. They arrived the evening before psilocybin administration, and were able to get acquainted with each other, the facilitators, and the schedule of the retreat. The next day, participants received the psilocybin-containing truffles around noon, in a tea form. After ingestion,

participants were instructed to stay on the premises, and were able to do what they wanted, as long as they did not disturb other participants. Facilitators provided music, tools to draw and/or write, and food. In the evening, all participants and facilitators came back together as a group. The next morning, all participants had breakfast together and had a closing group meeting.

Psilocybin

Participants ingested the truffles in a tea form, guided by the facilitators. To do this, the truffles were crushed, and boiling hot ginger tea was added. After infusing for a few minutes, the participants drank the tea, and were subsequently free to add more water and repeat the process 2–3 times. Afterwards participants could eat the remaining truffle contents in the cup.

Previous experimental studies have demonstrated that subjective alterations after psilocybin intake begin 20–40 minutes following administration, peak around 60–90 minutes, and subside by six hours post-intake (Hasler et al. 2004). However anecdotal reports suggest that when ingested in tea form, subjective alterations are felt more quickly, and for a shorter amount of time (Erowid 2015).

Study procedure

Creativity, empathy, and well-being assessments were taken on three separate occasions: at baseline (the evening before ingesting psilocybin), the morning after ingesting psilocybin, and seven days after ingesting psilocybin. Participants completed pre- and post-psilocybin assessments at the retreat, with the investigators present. The third assessment was completed online. The total amount of psilocybin truffles taken by each participant was recorded, and a sample of the truffles was taken to determine concentrations of psilocybin and its metabolite, psilocin. The German Central Customs Authority determined the contents of psilocin and psilocybin after freeze-drying the truffles using a previously described HPLC method (Laussmann and Meier-Giebing 2010).

Picture concept task

In order to assess creativity, the picture concept task (PCT) was used (Kuypers et al. 2016). The PCT consists of 17 stimuli, each containing between 4 and 12 color pictures shown in a matrix of 2 × 2, 2 × 3, 3 × 3, or 3 × 4. Participants were instructed to find an association between one of the pictures in each row. Specifically, they were asked first to provide the correct solution, as there is only one correct answer. The number of correct answers served as the dependent measure of convergent thinking. In order to assess divergent thinking, participants were asked to provide as many alternative answers as possible. This is the regular instruction included in measures of divergent thinking, and it is used to calculate several parameters—i.e., fluency, originality, and the ratio of both—which reflect quantity and quality of divergent thinking. Fluency is defined as the number of alternative associations. The second parameter (i.e., originality) is calculated by evaluating the originality of the alternative association relative to those provided by all other participants in a session. Alternative answers that were uniquely reported by a single participant received an originality score of 2. Answers that were shared with a single participant were valued as 1, and answers that were shared by three or more participants were rated zero. Mean originality (creativity) scores and ratio originality scores weighed for fluency (originality/fluency) were used as measures of divergent thinking. Three parallel versions of the PCT were used at baseline and the two follow-up measures after the retreat to avoid learning effects; participants had 30 seconds per stimulus. Previous studies have found the PCT to be sensitive to the effects of psychedelics (Kuypers et al. 2016; Prochazkova et al. 2018; Uthaug et al. 2018).

Multifaceted empathy test

The multifaceted empathy test (MET) consists of 40 pictures of people in various emotional states, with 50% being positive and 50% negative (Dziobek et al. 2008). To assess cognitive empathy (CE), participants were asked to select the emotion word, out of four words, which matched the depicted emotion. To assess emotional empathy (EE), participants were asked to rate on a scale from 1 to 9 "how aroused does this picture make you feel" (implicit EE) and "how concerned do you feel for this person" (explicit EE). The number of correctly classified pictures (CE) and the implicit EE and explicit EE ratings per valence and averaged across valences were used as dependent variables. Previous validity and reliability analysis of the MET have shown to be in the good to highly satisfactory range (Dziobek et al. 2008), and previous studies have found it to be sensitive to the effects of psychedelics (Hysek et al. 2014; Kuypers et al. 2014, 2017; Pokorny et al. 2017; Preller et al. 2015; Schmid et al. 2014).

Satisfaction with Life Scale

The Satisfaction with Life Scale (SWLS) is a five-item questionnaire designed to measure global cognitive judgments of satisfaction with one's life (Diener et al. 1985), and has been used to measure the life satisfaction component of subjective well-being (Diener et al. 1985; Pavot et al. 1991). Individuals answer each item on a Likert scale ranging from 1 (strongly disagree) to 7 (strongly agree). The total score is then obtained by summing the ratings form each item. Sample items include "In most ways my life is close to my ideal" and "If I could live my life over, I would change almost nothing." The minimum possible score is 5, and the maximum possible score 35, with a score of 5–19 defined as dissatisfied to below average life satisfaction, 20–24 defined as average life satisfaction, and 29–35 defined as high to very high life satisfaction (Pavot and Diener 2013). The scale has previously been shown to be a valid and reliable measure of life satisfaction (Pavot and Diener 2009).

Psilocybin experience

The morning after ingesting psilocybin, participants were asked to retrospectively rate the intensity of various aspects of the acute psilocybin experience using 10 visual analog scales (VASs). The VASs were 10 cm horizontal lines, with a bottom anchor of "not more than usually" and a top anchor of "much more than usually." These items have previously been shown to be sensitive to the acute effects of psilocybin (Carhart-Harris et al. 2012).

Statistical analyses

Statistical analysis was conducted in IBM SPSS Statistics 24 using a linear repeated measures model analysis that included Session (three levels: baseline, morning after psilocybin, and seven days after psilocybin) as a within-subject factor. Due to small sample size at the seven-day follow-up, a separate linear repeated measures model analysis was done for each outcome variable. Similarly, as for the MET, if a main effect of Session was found on emotional or cognitive empathy, two further analyses were done, separating valence-specific (positive or negative emotion) responses.

The covariance structure was chosen according to best fit and could vary across outcome variables. Different covariance structures used included compound symmetry heterogenous (CSH) and first lag autoregressive (AR1) structures. If a main effect of Session was found, separate contrasts were performed between baseline and the follow-up sessions with Bonferroni adjustment for multiple comparisons.

In order to test whether people with previous psilocybin experience differed from psilocybin-naïve participants on outcome measures, a further mixed-model analysis was conducted, with Session (three levels: baseline, morning after psilocybin, and seven days after psilocybin) as a within-subject factor and previous experience with psilocybin (two levels: yes, no) as a between-subjects factor, though only for outcome parameters which showed a significant main effect of Session in the first analysis. The analysis was performed to determine whether sub-acute effects of psilocybin differed between experienced versus naïve psilocybin users.

In order to investigate the association between cognitive (creativity and empathy) and subjective (well-being) outcome parameters, Pearson's correlations were carried out using baseline change scores (Morning after—baseline; seven days after—baseline).

Psilocybin experience ratings were analyzed separately using one-sample t tests comparing the scores on each VAS after psilocybin versus a zero distribution, since previous studies have shown that placebo scores are low, not rising above a 0 in a scale from 0 to 100 (Valle et al. 2016).

Results

In total, 55 participants completed parts of the test battery at baseline, 50 completed parts of the test battery the morning after taking psilocybin, and 22 completed parts of the test battery seven days after taking psilocybin. Incomplete or missing test batteries were due to time constraints and/or participant drop-out.

Psilocybin

The truffle sample (15 grams; Psilocybe Hollandia) contained 1.9 mg of psilocybin and 10.5 mg of psilocin. Participants ingested an average (SD) 34.2 (8.9) grams of truffles throughout the day. Once ingested, psilocybin is quickly metabolized to psilocin at a calculation factor of 0.719, resulting in a final (average) psilocin consumption of 27.1 mg.

Picture concept test

Convergent thinking

Analysis revealed a significant main effect of Session ($F_{2,37.48} = 5.94$, $p = .01$) on the number of correct associations (see Figure 1(d)). Compared to baseline, participants were able to identify a higher number of correct associations seven days after ingesting

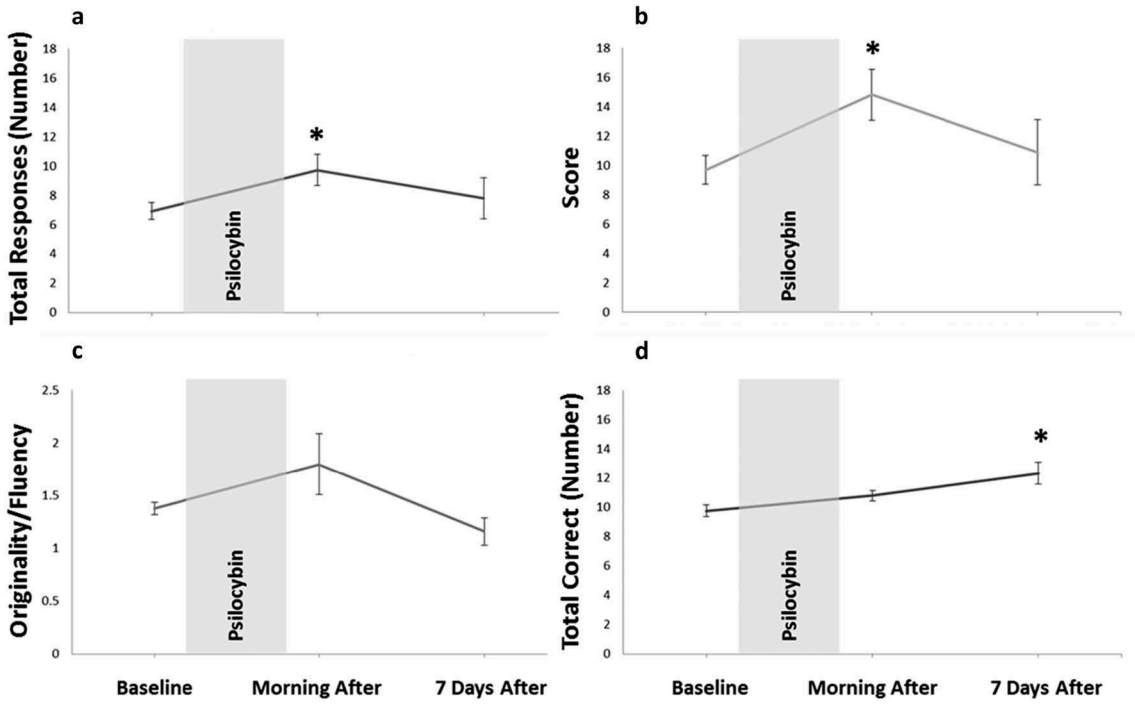

Figure 1. Mean (±SE) outcome variables of divergent and convergent thinking, measured before, the morning after, and seven days after psilocybin ingestion. Panels A to C depict outcome variables of divergent thinking; (a) fluency; (b) originality; (c) ratio; panel (d) depicts the outcome variable of convergent thinking (*p < .05).

psilocybin (p = .01; d = .46). There were no significant effects of psilocybin on convergent thinking the morning after taking psilocybin.

Divergent thinking

Analysis revealed a significant main effect of Session on Fluency ($F_{2,38.22}$ = 5.27, p = .01) and Originality ($F_{2,45.09}$ = 7.23, p = .002) (see Figure 1(a, b)). Compared to baseline, participants were able to come up with more associations (p = .01; d = .47), and had a higher originality score (p = .001; d = .55), the morning after taking psilocybin. There was no significant effect of session on Ratio ($F_{2,42.44}$ = 2.25, p = .12). Furthermore, there were no significant effects of psilocybin on Fluency, Originality, or Ratio seven days after taking psilocybin.

Multifaceted empathy test

Cognitive empathy

There was no significant effect of Session on cognitive empathy ($F_{2,23.26}$ = 3.18, p = .06); participants were able to recognize about 22 emotions on average in the three sessions (see Figure 2(c, d)).

Emotional empathy

Analysis revealed a significant main effect of Session ($F_{2,48.31}$ = 4.29, p = .02) on average Explicit EE (see Figure 2(b)). Compared to baseline, participants felt more concern for people depicting emotions the morning after ingesting psilocybin (p = .02; d = .45). When assessing valence-specific responses, analysis revealed a significant main effect of Session ($F_{2,38.04}$ = 5.87, p = .01) on concern ratings of negative emotions; compared to baseline, individuals' concern for negative emotions was increased the morning after taking psilocybin (p = .01; d= .49) without effects on day 7. There was no significant effect of Session ($F_{2,51.42}$ = 2.58, p= .09) on concern ratings of positive Explicit EE.

Analysis revealed a significant main effect of Session ($F_{2,23.71}$ = 10.64, p = .001) on average Implicit EE ratings (see Figure 2(a)). Compared to baseline, participants felt more aroused by the emotional content of the stimuli the morning after ingesting psilocybin (p< .001; d = .71). When assessing valence-specific responses, analysis revealed a significant main effect of Session on both positive ($F_{2,25.72}$ = 7.89, p = .002) and negative ($F_{2,19.18}$ = 4.93, p= .02) emotions. Separate contrasts indicated that, compared to baseline, individuals' arousal to both positive (p = .001; d= .61) and negative (p = .01; d= .48)

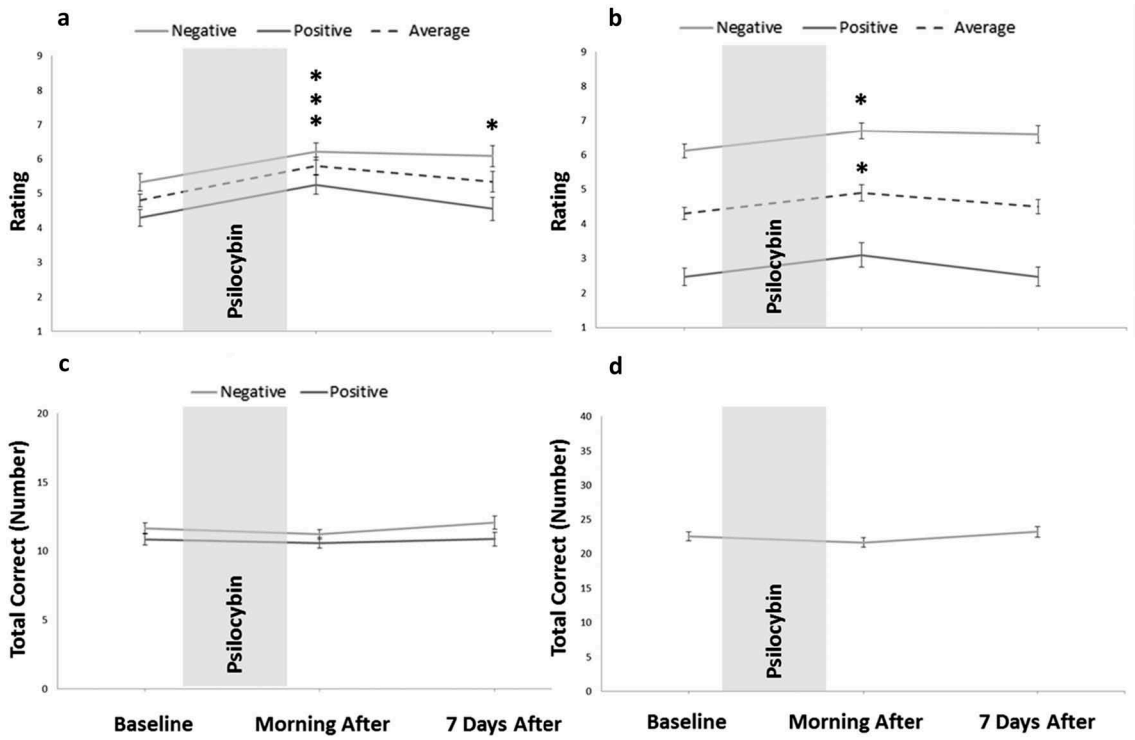

Figure 2. Mean (±SE) outcome variables of implicit emotional empathy (a), explicit emotional empathy (b), and cognitive empathy (c; total (d)), measured before, the morning after, and seven days after psilocybin ingestion (*$p < .05$).

emotions was higher the morning after ingesting psilocybin. Furthermore, implicit arousal to negative stimuli, but not positive stimuli, remained increased seven days after ingesting psilocybin ($p = .05$; $d = .41$).

Satisfaction with Life Scale

Analysis revealed a significant main effect of Session ($F_{2,48.31} = 17.83$, $p < .001$) on individuals' responses to the SWLS (see Figure 3(a)). Contrasts indicated that, compared to baseline, satisfaction with life significantly increased both the morning after ($p < .001$; $d = .77$) and seven days after ($p = .001$; $d = .50$) ingesting psilocybin.

Previous experience with psilocybin

Twenty-nine participants reported previously using psilocybin, whereas 21 reported being psilocybin

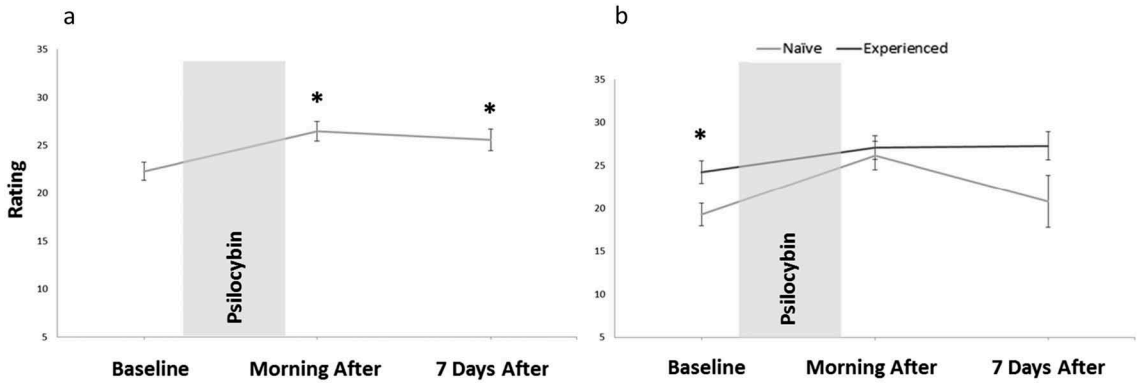

Figure 3. Panel A depicts the total group mean (±SE) ratings of satisfaction with life measured before, the morning after, and seven days after psilocybin ingestion. In panel B, a second analysis was performed to assess differences in satisfaction with life between those who had previous experience with psilocybin (experienced) and those who had not (naïve). Mean (±SE) ratings per group are shown (*$p < .05$).

naïve, and five chose not to disclose their previous drug use history. The latter were thus not included in this analysis. The analysis revealed a significant main effect of Session ($F_{2,52.44}$ = 16.768, p< .000) and Psilocybin experience ($F_{1,46.93}$ = 5.39, p= .025) on individuals' response to the SWLS (Figure 3(b)). Contrasts indicated that those who had previous experience with psilocybin reported a significantly higher quality of life at baseline compared to those who were psilocybin naïve (p= .012; d= .39). The sub-acute effects of psilocybin did not differ between participants who had used psilocybin vs. those who had not for any other outcome measures.

Correlations

Analysis showed medium to strong positive correlations between changes in implicit and explicit EE towards a positive stimulus and changes in satisfaction with life. Specifically, as changes in arousal to pictures of people in positive mood states increased, changes in satisfaction with life also increased, when comparing baseline to both the morning after psilocybin intake (Spearman correlation (r_s) = .43, p= .05) and seven days after intake (r_s = .61, p= .02). Furthermore, as changes in ratings of concern for people in various emotional states increased between baseline and the morning after intake, ratings of satisfaction with life increased between baseline and seven days after intake (r_s = .57, p= .03). Finally, as changes in ratings of concern for people in positive mood states increased, changes in quality of life increased between baseline and seven days after psilocybin intake (r_s = .58, p= .03). No significant correlations were found between outcome variables of the PCT and ratings of quality of life, or between variables of the PCT and the MET.

Psilocybin experience

Mean (SE) ratings on the different VAS items after psilocybin are shown in Figure 4. The one-sample t tests showed psilocybin-induced significant increases in all VAS items (t_{49} = 14.56–23.73; p≤ .000; d= 2.05–3.35).

Discussion

We believe that this study demonstrates the first attempt to assess the sub-acute influence of psilocybin on creative thinking, empathy, and their relationship with well-being. Using a naturalistic approach, significant sub-acute enhancements of outcome measures of divergent thinking (DT), convergent thinking (CT), emotional empathy (EE), and satisfaction with life (LS), after ingestion of psilocybin

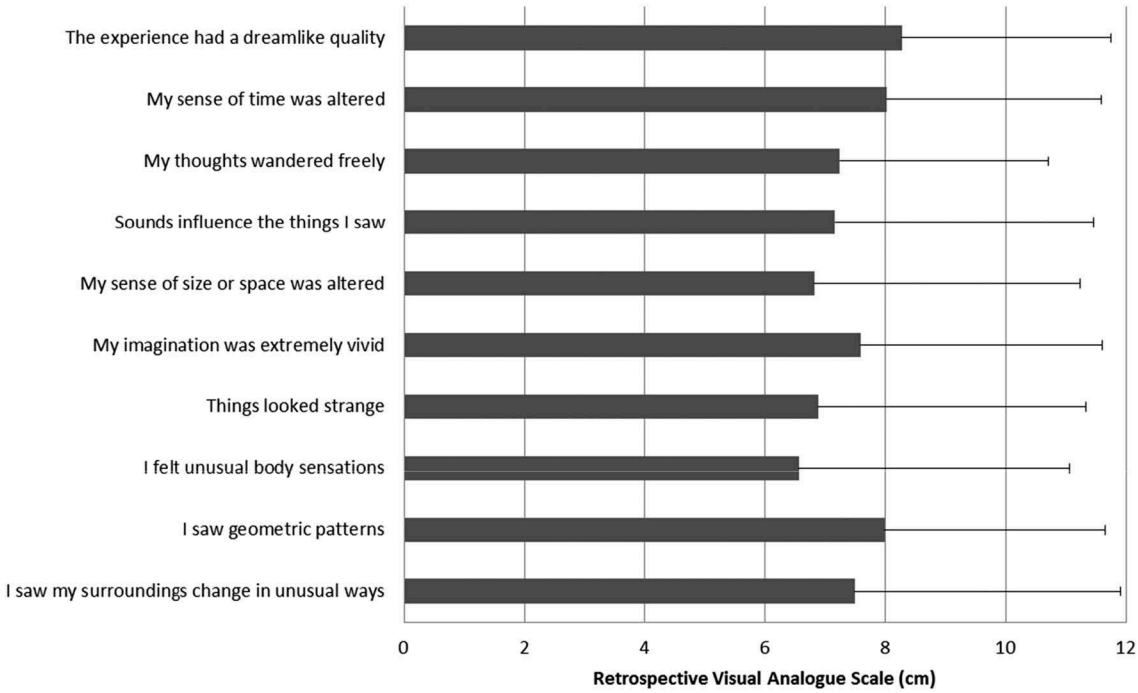

Figure 4. Mean (±SE) of visual analogue scale item scores on a 10 cm scale. Scores are retrospective of the psilocybin experience.

at a psychedelic retreat, were demonstrated relative to baseline. Correlational analyses suggest a positive relationship between sub-acute enhancements in EE and LS.

The findings demonstrate a time- and construct-related differentiation of effects of psilocybin on creativity; whereas DT was shown to increase the morning after ingesting psilocybin relative to baseline, CT was unaffected. Seven days after ingestion, DT performance returned to baseline, whereas CT was enhanced. Previous research has shown that ayahuasca, a South American plant tea consisting of the similar-acting 5-HT_{2A} agonist N,N-Dimethyltryptamine (DMT), acutely enhanced DT and impaired CT in individuals participating in an ayahuasca ceremony (Kuypers et al. 2016). Furthermore, a similar study demonstrated persisting sub-acute enhancements of CT one month after participation in an ayahuasca ceremony (Uthaug et al. 2018). Taken together, our findings suggest that whereas psychedelic-induced enhancements of DT outlast the acute phase, decrements in CT do not. This discrepancy in acute versus sub-acute effects after a psychedelic is interesting in light of therapeutic implications, as both DT and CT are important components in the therapeutic process. Specifically, it has been suggested that DT can enhance psychological flexibility by allowing individuals to generate new, more effective strategies that facilitate adaptive interpretations and coping abilities (Forgeard and Elstein 2014). Consequently, the ability of psilocybin to enhance DT sub-acutely could help patients to relive events, recall various associations, and consider their situation from another perspective (Bouso et al. 2008; Frecska, Bokor, and Winkelman 2016; Frecska et al. 2012). Longer-term effects on CT could then be studied in a subsequent integration session where patients discuss their acute experiences and decide on a strategy to help them cope with intensive emotions (Kuypers et al. 2016).

Findings demonstrate a time-, component-, and valence-differentiation of effects of psilocybin on empathy; whereas explicit and implicit EE were shown to increase the morning after psilocybin use, CE was unaffected. Furthermore, enhancement in implicit EE to pictures depicting negative emotions persisted until seven days after use. The sub-acute enhancements in EE are in line with previous studies assessing acute effects of psilocybin, as well as other serotonergic psychedelics like LSD and MDMA, on empathy. Specifically, psilocybin, LSD, and MDMA have been found to enhance EE on the MET (Hysek et al. 2014; Kuypers et al. 2014, 2017; Pokorny et al. 2017; Preller et al. 2015; Schmid et al. 2014) without impairing CE. Taken together, these findings suggest that psilocybin (sub)-acutely increases individuals' ability to *feel* what other people are feeling, without affecting individuals' ability to *understand* what other people are feeling. Furthermore, psilocybin-induced increments in arousal to the (negative) emotion of others outlast induced increments in the ability to feel for others.

Self-rated LS increased after psilocybin ingestion compared to baseline, both the morning after and seven days after use. Specifically, at baseline, participants reported a mean (±SE) score of 22.3 (.96), a morning-after score of 26.5 (1.03), and seven-day-after score of 25.6 (1.11). Scores between 20–24 reflect an "average" LS, defined by general satisfaction, but with a desire for improvement in major domains (e.g., work/school, family) (Pavot and Diener 2013). A score of 25–29 is considered a "high" score, suggestive of an enjoyable life and satisfaction in the major domains. Based on interpretation scores, results suggest that psilocybin ingestion increased individuals' LS from "average" to "high" until at least seven days after use. This finding is consistent with previous studies showing acute (Schmid et al. 2014), sub-acute (Barbosa, Giglio, and Dalgalarrondo 2005; Uthaug et al. 2018), and long-term (Barbosa et al. 2009; Bouso et al. 2012; Garcia-Romeu, Griffiths, and Johnson 2015; Griffiths et al. 2011; Grob et al. 2011; Lawn et al. 2017; Osorio et al. 2015; Thomas et al. 2013) positive psychological changes after psychedelic use. We also assessed whether there was a relationship between previous experience with psilocybin and baseline LS scores. In line with the aforementioned research, it was found that those who had previously used psilocybin reported higher LS at baseline compared to those who were psilocybin naïve; however, this was not related to differences between groups on performance measures. Altogether, these results add to the growing body of literature suggesting beneficial subjective psychological effects of psychedelic use outlasting acute intoxication.

We hypothesized that changes in empathy and creativity would correlate with changes in satisfaction with life. Correlational analysis suggested a positive relationship between changes in LS and changes in implicit EE ("arousal"). Morning-after change score increases in arousal in response to positive emotions correlated with morning-after and seven-day-after change score increases in subjective ratings of LS. This relationship could be due to an increase in positive empathy, the phenomenon of sharing and understanding other's positive emotions (Morelli, Lieberman, and Zaki 2015). Specifically, it has been demonstrated that the ability to share, celebrate, and enjoy others' positive emotions correlates with increased prosocial behavior and well-being (Morelli, Lieberman, and Zaki 2015). Furthermore, it has been hypothesized that enhanced positive empathy may increase subjective well-being (Morelli, Lieberman, and Zaki 2015), although

directionality has not been established. Our results could provide limited evidence for directionality, as they demonstrate that an earlier (morning after) increase in positive arousal strongly correlates with a later (seven days after) increase in well-being. However, future research should more formally assess a causal relationship between (positive) empathy and well-being. Alternatively, because psilocybin acutely enhances response bias towards positive emotions (Kometer et al. 2012), individuals may feel more "aroused" when viewing positive emotions because they are paying more attention to them. The shift of emotional bias to positive emotions is a proposed mechanism of antidepressant effects (Kometer et al. 2012), increasing individuals' psychological well-being. Importantly, previous studies have implicated empathic deficits in symptom severity of depression (Cusi et al. 2011; Derntl et al. 2012). Therefore, enhancing implicit emotional empathy could decrease depressive symptom severity by shifting emotional biases towards positive emotions.

Correlational analysis also suggested a relationship between changes in LS and changes in explicit EE. Morning-after change score increases in concern for emotional pictures and seven-day-after change score increases in concern for negative pictures correlated with seven-day-after change score increases in subjective LS. This is consistent with previous findings of a relationship between empathic concern and well-being (Gleichgerrcht and Decety 2013; Thomas et al. 2007).

A relationship was not found between changes in DT or CT and LS. However, the therapeutic implications of enhanced creativity are still relevant. It may be that, while not directly increasing subjective well-being, enhancements in constructs of creativity open up a "window of opportunity" where therapeutic interventions could prove more effective.

The current study is not without its limitations. The small sample size restricts the generalizability of the data, and high drop-out rates result in loss of statistical power at the seven-day follow-up. Additional factors that restrict generalizability include the selection bias, as individuals chose to attend the retreat for various reasons. Due to the non-random sample, as well as the lack of placebo control, it could be argued that sub-acute enhancements are due to uncontrolled factors such as psychological expectations, or the environment in which the drug is taken. Previous research has shown that both factors, termed *set* and *setting*, play an important role in the outcome of a psychedelic experience (Lawn et al. 2017; Shewan, Dalgarno, and Reith 2000). However, previous studies demonstrating significant enhancement of psychedelics on creativity, empathy, and positive psychological outcomes have been found in a wide range of settings, including clinical (Garcia-Romeu, Griffiths, and Johnson 2015; Griffiths et al. 2016, 2011, 2006; Osorio et al. 2015), experimental (Hysek et al. 2014; Kuypers et al. 2014, 2017; Pokorny et al. 2017; Preller et al. 2015; Schmid et al. 2014), and naturalistic environments (Barbosa et al. 2009; Barbosa, Giglio, and Dalgalarrondo 2005; Bouso et al. 2012; Kuypers et al. 2016; Uthaug et al. 2018). Taken together, this is a strong indicator that the present study effects are directly related to drug intake. That being said, future placebo-controlled experimental studies could ideally control for the potential influence of non-pharmacological factors. Finally, future longitudinal clinical research into the therapeutic mechanisms of psilocybin could further assess the role of creativity and empathy in symptom alleviation in the pathological population.

In conclusion, the present study demonstrates that psilocybin, taken in a naturalistic setting, promotes constructs of creativity and empathy, and enhances subjective well-being. These findings highlight the possible underlying role of enhanced creativity and empathy in the therapeutic potential of psychedelics. Importantly, the effects outlast the acute state, potentially opening up a "window of opportunity" where therapeutic interventions could prove more effective. These findings add further support to growing evidence suggesting that psychedelics may hold therapeutic value for treating stress-related mood disorders.

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ORCID

Natasha L. Mason http://orcid.org/0000-0001-7115-0389
Kim P. C. Kuypers http://orcid.org/0000-0001-7634-3809

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