University of Tartu
Faculty of Social Sciences
Institute of Psychology

Marten Kase

Effects of LSD, DMT and psilocybin on cognitive and psychological functions: a systematic review of the literature

Master's thesis

Supervisors: Jaan Aru, PhD, Karl Kristjan Kaup, MSc

Tartu 2025

LSD, DMT ja psilotsübiini mõju kognitiivsetele ja psühholoogilistele funktsioonidele: süstemaatiline ülevaade kirjandusest

Kokkuvõte

Eesmärk: Läbi viia süstemaatiline ülevaade tänapäeva (1990–2025) platseebo-kontrolliga uuringutest, mis hindavad LSD, DMT ja psilotsübiini akuutset ja post-akuutset mõju kognitiivsetele ning psühholoogilistele funktsioonidele. **Meetod**: 28. veebruarist kuni 19. märtsini 2025 otsiti süstemaatiliselt platseebo-kontrolliga uuringuid andmebaasidest *PubMed* ja *APA PsycInfo*, mis uurisid, kuidas psühhedeelikumid mõjutavad empaatiat, reaktsiooniaega, emotsionaalset töötlemist, mälu, kognitiivset paindlikkust ja teisi kognitiivseid funktsioone. Täiendavaid otsinguid tehti andmebaasis *Google Scholar*. **Tulemused**: Süstemaatiline ülevaade hõlmas 30 uuringut. Psühhedeelikumid kaldusid suurendama emotsionaalset empaatiat, kuid ei mõjutanud kognitiivset empaatiat. Psühhedeelikumid halvendasid, parandasid või ei mõjutanud mälu olenevalt ülesandest ja hindamise ajastusest. Paljudes reaktsiooniaja ülesannetes täheldati annusest sõltuvat soorituse halvenemist, kuigi mõned uuringud ei leidnud mõjusid. Mõned uuringud leidsid psühhedeelikumide akuutse mõju korral negatiivsete stiimulite äratundmise halvenemist. Kognitiivse paindlikkuse tulemused olid vähem selged. **Piirangud**: Paljud uuringud olid tehtud väikese valimiga ja psühhedeelikumide ainulaadse subjektiivse mõju tõttu on usaldusväärset platseebot raske leida. Tulevased uuringud peaksid kasutama suuremaid valimeid ja uurima ka psühhedeelikumide pikemaajalisi mõjusid kognitiivsetele ning psühholoogilistele funktsioonidele.

Märksõnad: psilotsübiin, LSD, DMT, reaktsiooniaeg, kognitiivne paindlikkus, empaatia, emotsionaalne töötlemine, mälu.

Effects of LSD, DMT and psilocybin on cognitive and psychological functions: a systematic review of the literature

Abstract

Objective*:* To carry out a systematic review of modern-era (1990-2025) placebo-controlled studies assessing the acute and post-acute effects of LSD, DMT and psilocybin on cognitive and psychological functions. **Method**: From February 28 to March 19, 2025, PubMed and APA PsychINFO were systematically searched for placebo-controlled studies examining how psychedelics influence empathy, reaction time, emotional processing, memory, cognitive flexibility and related cognitive functions. Additional searches were done in Google Scholar. **Results*:*** The systematic review included 30 studies. Psychedelics tended to enhance emotional empathy, but had no effect on cognitive empathy. Psychedelics impaired, enhanced or had no effect on memory depending on the task and timing of the assessment. Dose-dependent impairments were seen in many of the reaction time tasks, although some studies found no effects. Some studies found impaired recognition of negative stimuli under the acute effects of psychedelics. The findings regarding cognitive flexibility were mixed. **Limitations*:*** Many studies had small samples and it is hard to find a reliable placebo due to psychedelics' unique subjective effects. Future studies should use bigger samples and also study more longitudinal effects of psychedelics on cognitive and psychological functions.

Keywords: psilocybin, LSD, DMT, reaction time, cognitive flexibility, empathy, emotional processing, memory.

Introduction

Psychedelics have recaptured the attention of scientists as recent research suggests that they may be suitable for therapeutic use in the treatment of anxiety, post-traumatic stress disorder (PTSD), alcoholism and tobacco addiction (Belouin and Henningfield, 2018; Nutt, 2019; Nutt et al., 2020). Classic psychedelics include psilocybin (i.e. magic mushrooms), LSD (lysergic acid diethylamide), DMT (dimethyltryptamine) and mescaline (found in several cacti species) (Andersen et al., 2020; Nutt et al., 2020). These substances produce altered states of consciousness (also known as psychedelic experience) that are characterized by geometric patterning (Bressloff et al., 2002), ego dissolution (Nour et al., 2016), changes in executive functions (Barrett et al., 2018), increased brain entropy (Carhart-Harris et al., 2014) and mystical experiences (Griffiths et al., 2006), although the exact mechanisms that underlie these phenomena still remain elusive (Girn, 2023) as several models have been proposed for explaining these effects (Kwan et al., 2022). The effects of classic psychedelics are primarily driven by activation of the 5-HT2A receptor, as their impact is significantly diminished when 5-HT2A antagonists, such as ketanserin, are administered (Preller et al., 2017).

Classic psychedelics have been used in healing settings since ancient times (Guerra-Doce, 2014), although they got more public attention after 1938, when Albert Hofmann synthesized LSD, which sparked interest due to its potential to treat mental health disorders (Hofmann et al., 2013). The first studies looked at the effects of LSD-assisted psychotherapy (Abramson et al., 1967; Busch and Johnson, 1950; Chandler and Hartman, 1960). After that, other classic psychedelics, e.g. psilocybin, also gathered research and public attention (Hofmann et al., 2013). Along with their therapeutic potential the effects of psychedelics on cognitive and psychological functioning also started to be investigated. Multiple studies demonstrated that psychedelics prolonged reaction times to auditory stimuli (Abramson et al., 1955; Dykstra & Appel, 1972), altered time perception (with effects varying across studies) (Deshon et al., 1952; Malitz et al., 1960), disrupted body schema (Liebert et al., 1957), and induced visual distortions (Fischer et al., 1970) (see Aday et al., 2021 for a review).

Most of the studies had many limitations, such as small sample sizes and unrefined methodological standards including no control groups and a lack of detailed reporting of

methodology (Aday et al., 2021). The research stopped in the 1970s as many classical psychedelics were associated with social unrest and anti-war protests related to the anti-Vietnam war movement (Wesson, 2011). There were also growing concerns about the potential dangers of psychedelic use, including psychosis and unpredictable behavior. As a result, research on these substances was largely limited until the early 2000s (Griffiths et al., 2006). In the 21st century, early research in Europe investigated the immediate psychological and physiological impacts of these substances (Griffiths et al., 2006; Vollenweider et al., 1998). Studies from this century have better methodological standards compared to the previous century studies, although they still have small sample sizes (Barrett et al., 2018; Carter et al., 2005) and placebo effect is a common problem in psychedelic research (Olson et al., 2020).

Most of the recent psychedelic research has focused on neuroimaging studies (Barrett et al., 2020) and therapeutic potential of psychedelics due to the current mental health crisis (Nutt et al., 2020). However, cognitive and psychological functions such as memory, empathy, emotional processing, cognitive flexibility, and reaction time remain less thoroughly studied in relation to the effects of psychedelics (Bălăeţ et al., 2022). These processes are typically measured during the acute effects or post-drug administration, using a variety of cognitive and psychological tests (Basedow et al., 2024). Although measuring these processes is crucial for understanding psychedelics' impact, there are also significant limitations in how these assessments reflect the psychedelic experience. The aim of this review is to explore these processes and their measurement in the context of psychedelic research. The review is organized into two main sections: (1) the effects of psychedelics on cognitive and psychological functions and (2) the limitations of current tests used to assess these functions.

Method

Data for this systematic review were collected following the systematic reviews and meta-analyses guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses [PRISMA]). The review was not registered.

Search

PubMed and APA PsycInfo were used to find articles that were published from January 1990 to March 2025. A search of Google Scholar was conducted to identify any additional relevant articles. The last date of the search was 18.03.2025. The following search terms were used: psychedelic* OR hallucinogen* OR psiloc* OR “shrooms” OR LSD OR ayahuasca OR DMT AND “reaction time” OR “response time” OR “cognitive flexibility” OR “task switching” OR “memory” OR “working memory” OR “short-term memory” OR “visuospatial memory” OR “autobiographical memory” OR “episodic memory” OR “semantic memory”, OR “emotional processing” OR “emotional face recognition” OR “empathy” OR “emotional empathy” OR “cognitive empathy” OR cognition. The literature search targeted the title and the abstract.

Eligibility criteria

Placebo-controlled trials in clinical and normative populations were included. The studies investigated acute and/or long-term effects of classic psychedelics on cognitive and psychological functions using behavioral or physiological measures. Exclusion criteria included studies that: 1) were not written in English, 2) were not available through institutional access, 3) were not peer-reviewed, 4) did not include placebo, 5) animal studies, 6) used self-reported methods (not experimental tests).

Data extraction

After removing duplicates, all remaining articles underwent title and abstract screening. Studies that did not fulfill the inclusion criteria were excluded. Full-text assessments were conducted to determine eligibility. For each included study, the following data were extracted: (1) publication year and author names; (2) participant demographics; (3) cognitive and/or

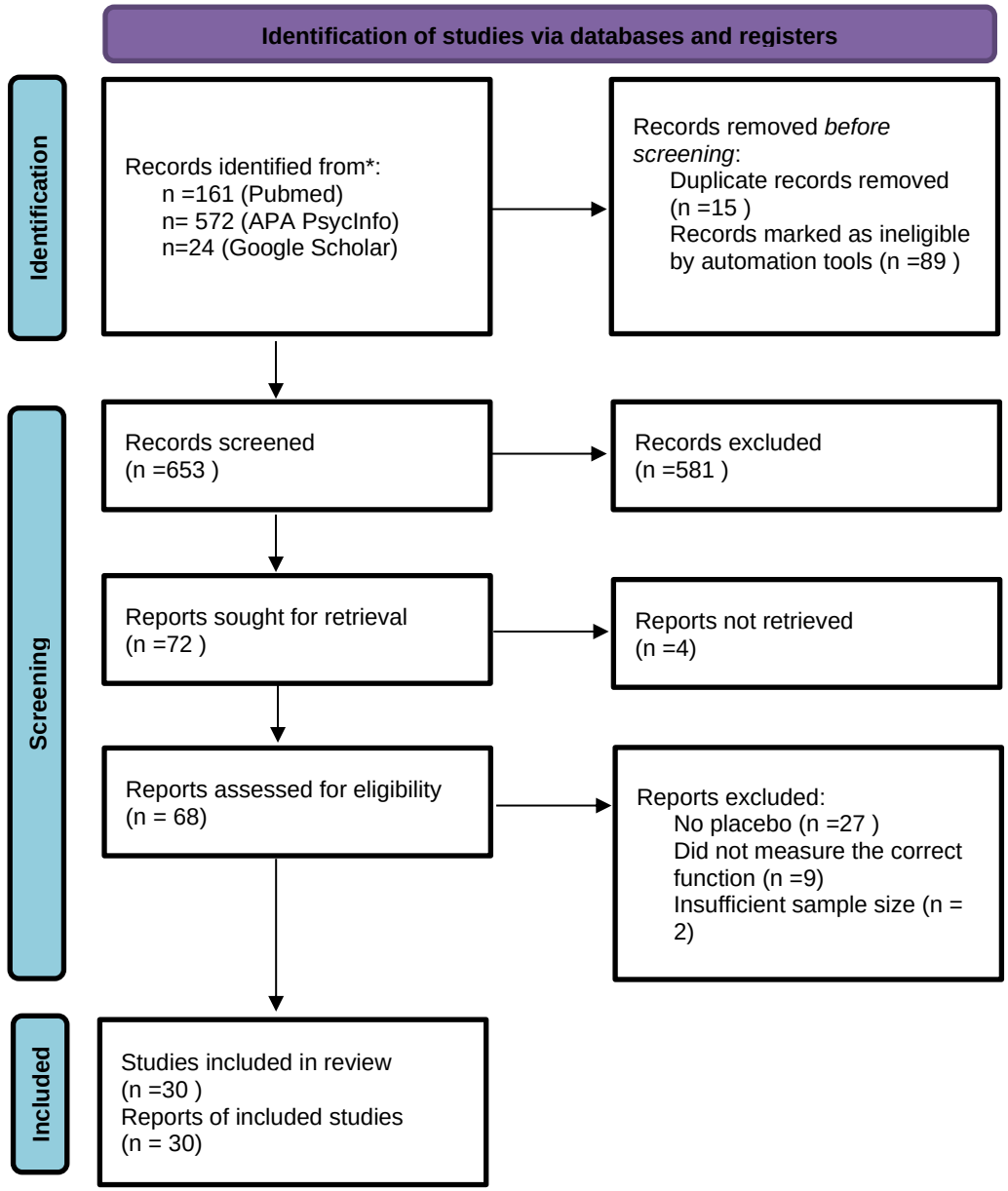
psychological assessment methods; (4) the specific psychedelic compound and administered dose; and (5) key findings along with measurement time points.

Identified studies

A flow diagram (Page et al., 2021) illustrating the different phases of the systematic review is presented in Figure 1.

Figure 1

PRISMA flow diagram for study selection.



Study selection

653 references were screened based on titles and abstracts, and 581 records were excluded in screening, leaving 72 potential research papers. Full-text reports of the 68 identified research papers were assessed according to eligibility criteria. The systematic search identified 30 eligible studies in total- 12 for reaction time, 4 for cognitive flexibility, 14 for memory, 8 for emotional processing and 6 for empathy. 29 studies were done in healthy volunteers and 1 study in people with depression.

Results

Psychedelics' effects on reaction time

Reaction time (RT) is measured by the elapsed time between stimulus onset and an individual's response on cognitive tasks. Higher levels of attention result in a shorter RT and vice versa. Many tests that measure RT also estimate attention and inhibitory control. Thus, these results are also reported in this paragraph.

The test for measuring RT in the analyzed experimental studies were the Psychomotor Vigilance Test (PVT; Dinges and Powell, 1985), the Digit Symbol Substitution Test (DSST; McLeod et al., 1982), the motor praxis (mpraxis) task (Gur et al., 2010), the Frankfurt Attention Inventory (FAIR; Moosbrugger and Oehlschlägel, 1996), a multiple-object tracking task (Pylyshyn and Storm, 1988), the Cambridge Neuropsychological Test Automated Battery (CANTAB) reaction time (RTI) and rapid visual information processing (RVP) test (Cambridge Cognition, 2016), the Attentional Blink task (Shapiro et al., 1997), the Stroop Test (Stroop, 1935), the Trail Making Test (TMT; Reitan and Wolfson, 1995) and the Go/No Go task (Nosek and Banaji, 2005) (see Table 1). Studies examining the effects of psychedelics on RT employed a range of dosages across various substances. Research with LSD used microdoses of 5, 10, and 20 μg (Hutten et al., 2020), 5 μg, 10 μg, 20 μg (Family et al., 2020), 6.5, 13, or 26 μg of LSD (Bershad et al., 2019) and 13 or 26 μg (de Wit et al., 2022). Medium doses of LSD were also used (50 μg (Wießner et al., 2022) and 100 μg (Schmidt et al., 2018). Psilocybin studies tested low to high doses of the drug- 115, 215, and 315 μg/kg (from low to high dose; Vollenweider et al., 2007), 10, 20, and 30 mg/70 kg (from

low to high dose; Barrett et al., 2018), 215 µg/kg of psilocybin (medium dose) (Carter et al., 2005) and 0.5 g of dried mushrooms, that is representative of the upper range used for microdosing (Cavanna et al., 2020). A high dose of psilocybin (260 µg/kg) was also used by Quednow and colleagues (2012). 15 mg of psilocybin (medium dose) was used by Mallaroni and colleagues (2023).

20 µg of LSD was found to reduce the number of correctly encoded digits measured up until 4 hours after consumption, but did not change accuracy in the DSST, which is a task that requires fast responding, working memory, and executive function for successful performance (Hutten et al., 2020). 5 µg and 20 µg (but not 10 µg) of LSD reduced attentional lapses (enhanced performance), as measured by the PVT which measures sustained attention. The tests were conducted up to 4 hours after drug administration. Notably, the cognitive effects of low-dose LSD were not uniformly experienced by all participants. 13 and 26 µg of LSD also did not significantly influence the results in the DSST measured 150 minutes after drug administration (de Wit et al., 2022). Non-significant results in the DSST were also found with 6.5, 13, or 26 µg of LSD when measured during expected peak drug effect (Bershad et al., 2019). However, a (15 mg) moderate dose of psilocybin delayed RT, reduced total correct answers and attempts in the DSST and delayed RT in the PVT, but did not significantly influence attentional lapses when measured during peak subjective effects (Mallaroni et al. 2023). 20–30 mg/70 kg of psilocybin (medium and high dose) significantly reduced attempted trials, accuracy and recall (only for 30 mg) in the DSST in participants with a history of classic psychedelic use (Barrett et al., 2018). In sum, only medium and high doses of psilocybin influenced the results in the DSST. 5 and 20 µg of LSD (microdoses) enhanced performance in the PVT, but 15 mg of psilocybin did not have a significant effect on it.

In addition to the DSST, Barrett et al. (2018) examined the effects of psilocybin (administered in doses of 10, 20, and 30 mg/70 kg) on psychomotor performance using the mpraxis task from the Penn Computerized Neurocognitive Battery (CNB). This task assesses psychomotor speed, with outcome measures including average response time and the number of squares correctly clicked (accuracy) during a timed response block. A main effect of drug condition was observed for response time, indicating that participants responded more slowly under the 20 mg and 30 mg psilocybin conditions compared to placebo. However, no significant differences were found in accuracy across conditions during the mpraxis task.

Additional studies have investigated the effects of LSD and psilocybin on RT, attention, and inhibitory control. Administration of low doses of LSD (5 μg, 10 μg, and 20 μg) did not result in significant changes in performance on the CANTAB RTI and RVP tests, when assessed 2–3 hours post-administration and at follow-up (Family et al., 2020). A higher dose of LSD (100 μg) was found to impair motor response inhibition on the Go/No-Go task, with measurements taken 200 minutes after administration (Schmidt et al., 2018). This impairment was correlated with subjective reports of cognitive dysfunction, which, according to the authors, may have exacerbated the failure to inhibit responses during No-Go trials. In one of the previous studies (Hutten et al., 2020), 63% of participants reported a perceived decline in performance, although performance enhancement was observed in 74% of participants on the PVT in the same study. These findings suggest that at higher doses, subjective beliefs about cognitive impairment may play a more pronounced role in influencing actual performance outcomes compared to lower doses.

The effects of microdosing psilocybin have also been studied. In particular, 0.5 grams of dried mushrooms (640.2 μg/g of psilocybin and 950.7 μg/g of psilocin) increased RT in the Stroop Test, which measures inhibitory control, selective attention and visual-verbal processing speed, and decreased visibility of the second target in the Attentional Blink task (Cavanna et al., 2022). However, these results were not significant after correction for multiple comparisons. Inhibitory control was also measured by the Go/ No Go task, where no significant changes were observed. There was a significant increase in the time required for part A of the TMT, that measures attention (sustained and shifting) and coordination, where the subject must connect numbers 1-25 in numerical order. There were no significant changes in the part B of the TMT, where it is required to alternate between numbers and letters (e.g., 1-A-2-B-...) while connecting circles. This part of the test measures task-switching ability, cognitive flexibility and working memory. Thus it seems that task-switching, cognitive flexibility and working memory seem to be less impacted by psilocybin microdosing than attention and coordination. All of the measures were taken 2-3 hours after drug administration.

The Stroop Test was also used in a study by Wießner et al. (2022), where 50 μg of LSD did not significantly change the results when measured 24 hours after drug administration. The LSD also did not change the results in the TMT. This discrepancy in the TMT results between the two studies (Cavanna et al., 2022; Wießner et al., 2022) could have been caused by the

different timing of the assessment. The effects of high dose psilocybin (260 μg/kg) in the Stroop Test were measured 85 minutes after the drug administration in another study (Quednow et al., 2012). Psilocybin selectively increased errors in high-conflict (incongruent) trials in the Stroop Test and slowed RT-s across all conditions and worsened Stroop interference, indicating reduced ability to inhibit distractions. These alterations were attenuated by ketanserin pretreatment. Thus, higher doses of psychedelics may be needed to cause significant changes in the Stroop Test.

Sustained attention has also been assessed using the FAIR, where psilocybin was shown to impair performance in a dose-dependent manner at doses of 115, 215, and 315 μg/kg (Vollenweider et al., 2007). Specifically, psilocybin significantly reduced the FAIR attentional performance capacity score P and the attentional continuity score C across all doses, while the FAIR score Q—reflecting the proportion of attentively made decisions relative to the total number of decisions—was significantly reduced only at the highest dose. Further support for psilocybin’s impairing effects on attention comes from a multiple-object tracking task, where a dose of 215 μg/kg significantly impaired participants' ability to track four targets, both when administered alone and following pretreatment with the 5-HT2A antagonist ketanserin (Carter et al., 2005). This impairment was observed 120 minutes post-administration. The lack of attenuation by ketanserin suggests that psilocybin's impact on attentional tracking may not be primarily mediated by 5-HT2A receptor mechanisms. Although participants reported that they could still comprehend the task instructions, they generally found the attention task substantially more challenging under the influence of psilocybin. Taken together, these findings indicate that psilocybin impairs attention across multiple assessment paradigms.

Table 1

Summary of Studies Investigating the Effects of Psychedelics on Reaction Time, Attention and Inhibitory Control

Study and sample	Tests and substance used	Results
Hutten et al., 2020- 24 healthy recreational psychedelic drug users (12 males; 12 females), aged 22.8 years on average (SD= 3.0)	DSST, PVT- 5,10,20 μg of LSD. Measurements were measured up until 4 hours after consumption.	20 μg of LSD reduced the number of correctly encoded digits ($p < 0.01$), but did not change accuracy in the DSST. 5 μg ($p< 0.01$) and 20 μg of LSD ($p< 0.01$) reduced attentional lapses in the PVT.
Family et al., 2020- healthy volunteers aged 55 to 75 years (21 males, 27 males; mean age 62.92 ± 5.78 years)	CANTAB tests RTI and RVP- 5 μg, 10 μg, 20 μg of LSD. Measurements were taken at baseline, 2-3 hours after drug administration and at the follow-up visit.	Post hoc tests on the RTI and RVP tasks did not reveal any significant differences between treatment groups at baseline (RTI: $F \leq 1.44$, $p \geq 0.11$; RVP: $F \leq 1.54$, $p \geq 0.07$), at dose 3, at dose 6, or during follow-up (all $p > 0.05$).
Cavanna et al., 2022- 34 participants (11 females; 31.26 ± 4.41 years; 74 ± 17 kg [mean ± STD]) were recruited by word-of-mouth, social media, and visits to workshops on psilocybin mushrooms and microdosing	Stroop Test, Attentional Blink task, TMT, Go / No Go Task- 0.5 grams of dried mushrooms (640.2 μg/g of psilocybin and 950.7 μg/g of psilocin). Measurements were taken 2-3 hours after drug administration.	Increased RT in the Stroop Test and decreased visibility of the second target in the Attentional Blink task. Both were significant only without correction for multiple comparisons. No significant changes were observed in the Go/ No Go task. There was a significant increase in the time required for part A of the TMT.

Table 1
(continued).

Vollenweider et al., 2007- 20 healthy subjects recruited through advertisement from local universities	FAIR- 115, 215 and 315 μg/kg of psilocybin. The test was conducted at 0, 105, 180, and 360 minutes after treatment.	Psilocybin significantly reduced the FAIR attentional performance capacity score P in a dose-dependent manner (interaction drug × session: $F(9, 135) = 10.3$, $p < .00001$), the FAIR score Q (interaction drug × session: $F(9, 135) = 2.69$, $p < .006$), and the attentional continuity performance score C (interaction drug × session: $F(9, 135) = 5.22$, $p < .00001$). Post hoc testing revealed that the reduction in the Q score was significant only after high-dose psilocybin and during the peak effect of the drug ($d = 0.95$).
Quednow et al., 2012- 16 healthy subjects (13 males, 3 females; mean age: 29.7 years, age range: 24–39) were recruited through advertisement from the local universities	Stroop Task- 260 μg/kg of psilocybin. Measurements were taken 85 minutes after treatment.	In *post-hoc* tests, psilocybin increased error rates in the conflict condition ($p<0.0001$). RT showed significant effects of drug ($F(3, 45)=9.51$, $p<0.0001$), condition ($F(3, 45)=61.6$, $p<0.00001$), and their interaction ($F(9, 135)=3.62$, $p<0.0005$). Psilocybin increased RT in all conditions (all $p<0.00003$).
Mallaroni et al., 2023- 22 healthy participants (11 women) aged 19–35 years (mean ± SD: 25 ± 4 years) were recruited by word of mouth and advertisement shared via Maastricht University social media platforms	DSST, PVT- 15 mg of psilocybin. Measurements were taken during peak subjective effects.	Psilocybin significantly delayed RT-s in the PVT ($F(2,41) = 4.94$, $p = 0.012$) and DSST ($F(2,39) = 15.85$, $p < 0.001$), reduced correct answers ($F(2,39) = 26.91$, $p < 0.001$) and attempts ($F(2,40) = 30.59$, $p < 0.001$) in the DSST compared to placebo. It did not significantly increase attentional lapses (PVT: $p = 0.124$).

Table 1
(continued).

de Wit et al., 2022- 56 participants (37 males) were healthy adults aged 18–35 who reported having used a psychedelic drug or MDMA at least once in their life-time	DSST- 13 or 26 μg LSD tartrate, which is equivalent to a dose of 10 or 20 μg of LSD base. Measurements were taken 150 minutes after drug administration and 3-4 days later.	There was a non-significant trend for a session × drug interaction in the direction of improved DSST performance after the drug ($F_{2,53} = 3.02$, $p = 0.057$, $\eta_p^2 = 0.102$).
Barrett et al., 2018- 20 healthy participants (mean age = 28.5 years, range = 22–43) with a history of both classic hallucinogen use and dissociative hallucinogen use	DSST, the motor praxis (mpraxis) task from the CNB- 10, 20, and 30 mg/70 kg psilocybin. Measurements were taken at baseline and 2 hours after administration.	There was a main effect of drug condition on response time, $F(4) = 6.52$, $p < .001$, but not on accuracy in the mpraxis task. Post hoc tests revealed that responses were slower during the 20 and 30 mg/70 kg psilocybin conditions compared to placebo. Analysis of attempted trials revealed significant main effects of drug condition, $F(4) = 23.52$, $p < .0001$, and time point, $F(3) = 123.28$, $p < .0001$, along with a significant drug condition × time point interaction, $F(12) = 10.28$, $p < .0001$, in the DSST. For accuracy measures, significant main effects were observed for both drug condition, $F(4) = 10.56$, $p < .0001$, and time point, $F(3) = 6.05$, $p < .0005$, with a significant interaction effect, $F(12) = 4.10$, $p < .0001$. Substitution recall accuracy showed significant main effects for drug condition, $F(4) = 11.59$, $p < .0001$, and time point, $F(3) = 40.92$, $p < .0001$, as well as a significant interaction, $F(12) = 2.07$, $p < .05$. All tests were two-tailed.
Carter et al., 2005- 8 healthy volunteers (5 men, 3 women) aged between 21 and 31 (mean = 27.0, SD = 2.7)	multiple-object tracking task- 215 μg/kg of psilocybin. Measurements were taken 120 minutes after drug administration during the peak effects.	Attentional tracking was significantly affected by drug administration ($F(3,21) = 3.64$, $p < .05$), with Tukey's post hoc analysis showing a significant reduction in performance from placebo and ketanserin, 120 min after drug intake, for both the psilocybin ($p < .01$) and psilocybin plus ketanserin ($p < .05$) conditions.

Table 1
(continued).

Bershad et al., 2019- 20 healthy subjects (12 women) aged 18 to 40 years	DSST- 6.5, 13, or 26 μg of LSD. Measurements were taken during expected peak drug effect.	LSD did not significantly affect the number of trials attempted ($F(3,54)= 0.55$, $p=0.65$) or correct trials ($F(3,54)= 0.41$, $p=0.75$).
Wießner et al., 2022- 24 healthy volunteers (8 women; mean (±SD) age = 35 (±11) years, range = 25–61)	TMT, Stroop Task- 50 μg of LSD. Measurements were taken 24h after dosing.	In TMT, there was no treatment effect and order effect but a period effect for basic duration (p = 0.032) with lower values in session 2. In Stroop, there was no treatment effect and order effect but a period effect for duration in colours (p = 0.007), words (p = 0.013) and colour words (p = 0.049) with lower values in session 2.
Schmidt et al., 2018- 18 healthy subjects (nine men, nine women; mean age: 31 ± 9 years, range: 25–58)	Go/No-Go task- 100 μg of LSD. Measurements were taken 200 min after drug administration.	Relative to placebo (M = 0.79, SD = 0.025), acute LSD administration (M = 0.77, SD = 0.044) significantly reduced the probability of inhibition, $t(17) = 2.19$, p = .043. LSD (M = 129.33, SD = 24.83) reduced the number of responses to Go trials compared with placebo (M = 151.00, SD = 12.84), $t(17) = 4.23$, p = .001. LSD (M = 432.64, SD = 12.89) prolonged *RT* to Go trials relative to placebo (M = 413.90, SD = 27.10), $t(17) = -3.42$, p = .003.

Psychedelics' effects on cognitive flexibility

Cognitive flexibility (CF) has been defined as the ability to appropriately adjust one's behavior according to a changing environment (Dajani and Uddin, 2015) and has been found to act as a buffer between stress and negative psychological outcomes (Gloster, Meyer, & Lieb, 2017). CF was assessed in analyzed studies by using tasks such as the Intra/Extra-Dimensional Shift Task (IED) (Owen et al., 1991), the Wisconsin Card Sorting Test (WCST; Heaton, 2005), the Cognitive Control Task (CCT; de Wit et al., 2012) and the probabilistic reversal learning task (Rostami Kandroodi et al., 2021) (see Table 2). The IED is based on the WCST paradigm, which requires participants to sort cards according to a rule that changes unpredictably. Studies investigating the effects of psychedelics on cognitive flexibility used

microdoses (5, 10, 20 µg; Hutten et al., 2020), low doses (50 µg; Wießner et al., 2022), and medium doses (75 µg and 100 µg; Kanen et al., 2023; Pokorny et al., 2020).

In a randomized, double-blind, placebo-controlled crossover study of 24 healthy participants, LSD (50 µg) reduced CF as measured by the WCST at baseline (two hours before drug administration) and 24 hours post-administration (Wießner et al., 2022). More specifically, LSD reduced categories achieved, conceptual level responses percentage and increased errors, particularly perseverative errors, indicating a tendency to stick to incorrect rules despite feedback. Similarly, a separate randomized, placebo-controlled within-subject study with 25 healthy participants demonstrated an acute reduction in CF following LSD (100 µg) administration, measured 220 minutes post-administration using the IED as there were more errors in the LSD condition compared to placebo or LSD+ketanserin (Pokorny et al., 2020). LSD also increased latency in the EDS stage (where participants had to shift attention to a previously irrelevant dimension) of the IED task compared to placebo. Thus, according to these two studies, medium doses of LSD impair CF acutely and post-acutely.

Contrary to previous findings, a 75 µg dose of LSD enhanced aspects of cognitive flexibility in the probabilistic reversal learning task conducted five hours after administration (Kanen et al., 2023). Participants showed increased learning rates from rewards (biggest effects) and punishments, as well as exploration over rigid stimulus-response patterns measured by decreased stimulus stickiness. Microdoses of LSD have been found not to influence CF as measured with the CCT 2.5 hours after LSD consumption, that was used to assess participants' level of cognitive control, that is, the ease of shift between habitual and goal-directed behavior (Hutten et al., 2020).

Table 2

Summary of Studies Investigating the Effects of Psychedelics on Cognitive Flexibility

Study and sample	Tests and substance used	Results
Pokorny et al., 2020- 25 healthy participants (19 men, 6 women, mean age ± SD: 25.24 ± 2.79)	IED- 100 μg of LSD. Measurements were taken 220 minutes after the drug consumption.	Tukey post-hoc tests revealed that LSD significantly increased the number of errors in stage 8 (EDS) (M = 7.84, SD = 10.51, 95% CI [8.20, 14.62]) compared to placebo (M = 5.16, SD = 8.97, 95% CI [7.00, 12.48], $p < .0001$) and Ketanserin + LSD (M = 5.64, SD = 8.90, 95% CI [6.95, 12.38], $p < .01$). LSD also significantly increased latency in stage 8 (EDS) (M = 27.73, SD = 20.00, 95% CI [15.62, 27.83]) compared to placebo (M = 17.10, SD = 13.19, 95% CI [10.30, 18.35], $p < .0001$) and Ketanserin + LSD (M = 17.40, SD = 13.38, 95% CI [10.45, 18.62], $p < .0001$).
Wießner et al., 2022- 24 healthy volunteers (8 women; mean (±SD) age = 35 (±11) years, range = 25–61)	WCST- 50 μg of LSD. Measurements were taken 24 hours after dosing.	LSD led to fewer categories completed, $F(1, 20) = 8.11$, $p = .010$, $\eta_p^2 = 0.29$, and a lower percentage of conceptual level responses, $F(1, 20) = 6.78$, $p = .017$, $\eta_p^2 = 0.25$. LSD also resulted in an increase in total errors, both in absolute numbers, $F(1, 20) = 7.86$, $p = .011$, $\eta_p^2 = 0.28$, and as a percentage, $F(1, 20) = 8.35$, $p = .009$, $\eta_p^2 = 0.30$. There was an increase in the absolute number of conceptual level responses, $F(1, 20) = 6.32$, $p = .021$, $\eta_p^2 = 0.24$, and in perseverative responses, both in absolute terms, $F(1, 20) = 7.53$, $p = .013$, $\eta_p^2 = 0.27$, and percentage, $F(1, 20) = 6.19$, $p = .022$, $\eta_p^2 = 0.24$. Perseverative errors increased across several types: type 1 errors rose significantly in both absolute, $F(1, 20) = 7.38$, $p = .013$, $\eta_p^2 = 0.27$, and percentage terms, $F(1, 20) = 7.16$, $p = .015$, $\eta_p^2 = 0.26$, as did type 3 errors, in absolute terms, $F(1, 20) = 9.55$, $p = .006$, $\eta_p^2 = 0.32$, and percentage, $F(1, 20) = 10.30$, $p = .004$, $\eta_p^2 = 0.34$. Type 2 errors showed a marginal increase, in absolute terms, $F(1, 20) = 4.12$, $p = .056$, $\eta_p^2 = 0.17$. Non-perseverative errors also rose significantly, in absolute terms, $F(1, 20) = 6.43$, $p = .020$, $\eta_p^2 = 0.24$, and percentage, $F(1, 20) = 5.36$, $p = .031$, $\eta_p^2 = 0.21$.

Table 2
(continued).

Kanen et al., 2023- 19 healthy volunteers (mean age 30.6; 15 males	Probabilistic reversal learning task- 75 μg of LSD. Measurements were taken five hours after injection.	LSD enhanced the relationship between the number of correct responses during the acquisition phase and the number of perseverative errors made during the subsequent reversal stage (acquisition correct responses (LSD minus placebo) *v.* reversal perseverative errors (LSD minus placebo): linear regression coefficient β = 0.56, p = 0.002). Making fewer errors during the acquisition phase predicted more perseverative errors when on LSD (β = 0.44, p = 0.003) but not when under placebo (β = 0.04, p = 0.8). Perseverative errors, a subset of all reversal errors, alone did not differ between conditions (t_{18} = 0.03, p = 0.98, d = 0.01).
Hutten et al., 2020- 24 healthy recreational psychedelic drug users (12 males; 12 females), aged 22.8 years on average (*SD*= 3.0)	CCT- 5,10,20 μg of LSD. Measurements were taken 2.5 hours after drug administration.	No significant baseline differences were observed in accuracy (number correct: F(3, 69) = 1.74, p = 0.17, η_p^2 = 0.07) and RT (F(3, 69) = 0.29, p = 0.83, η_p^2 = 0.01). The devaluation ratio showed no significant group differences, though a marginal trend emerged (F(2.14, 49.13) = 3.03, p = 0.06, η_p^2 = 0.12).

Psychedelics' effects on memory

Memory is defined as the faculty of encoding, storing, and retrieving information. Memory can be categorized into short-term memory, working memory and long-term memory (Cowan, 2008). Most of the studies here looked at the effects of psychedelics on working memory, which refers to a system that provides temporary storage and manipulation of the information necessary for cognitive tasks.

The test for measuring memory in the analyzed experimental studies were the visual-manual delayed response task (DRT; Park and Holzman, 1992), the Spatial Span test (SSP) from the CANTAB (Cambridge Cognition, 2016), the letter N-back task (Jaeggi et al., 2008), Rey-Osterrieth Complex Figure (ROCF; Rey, 1999), the 2D Object-Location Memory Task

(OLMT; Rasch et al., 2007), the spatial working memory (SWM) and the paired associates learning (PAL) from the CANTAB (Cambridge Cognition, 2016), the Rey Auditory-Verbal Learning Test (RAVLT; Bezdicek et al., 2013), the Groton maze learning task (GMLT; Snyder, 2005), the Paired associative Learning Test (PALT; Dudysova et al., 2016), the Tower of London test (TOL; Phillips et al., 2001), the Spatial Memory Test (SMT; Mallaroni et al., 2023) and the Emotional Episodic Memory Task (Doss et al., 2024) (see Table 3). Some of these tests also involve other executive functions, for example, the letter N-back task also requires the use of selective attention and cognitive inhibition. Psilocybin dosages included low doses such as 115 μg/kg (Wittmann et al., 2007), 10 mg/70 kg (Barrett et al., 2018), and 15 mg (Doss et al., 2024), medium doses like 0.25 mg/kg (Vollenweider et al., 1998), 20 mg/70 kg (Barrett et al., 2018), 15 mg (Mallaroni et al., 2023) and 215 μg/kg (Carter et al., 2005), and high doses including 0.26 mg/kg (Nikolic et al., 2023), 30 mg/70 kg (Barrett et al., 2018) and 250 μg/kg (Wittmann et al., 2007). LSD was administered in dosages such as 5 μg, 10 μg, 20 μg of LSD (microdoses; Family et al., 2020), 13 or 26 μg (microdoses; de Wit et al., 2022), 50 μg (low dose; Wießner et al., 2022), 75 μg (medium dose; Speth et al., 2016) and 100 μg (medium dose; Pokorny et al., 2020).

Many studies looked at the effects of psychedelics on visuospatial or spatial working memory. Visuospatial working memory capacity measured with the SSP from the CANTAB was not influenced by psilocybin (0.215 mg/kg) (Carter et al., 2005). More specifically, no significant effect on the number of boxes remembered correctly in sequence ‘‘span length’’ was found for the drug. The SSP was administered 120 minutes after drug consumption during the peak effects. Higher dose of psilocybin (250μg/kg) impaired SSP performance in another study when measured at 0, 100 and 360 min after drug/placebo intake (Wittmann et al., 2007). Medium dose of psilocybin (115 μg/kg) did not impair SSP performance in the same study. Thus, only higher doses of psychedelics seem to impact visuospatial working memory as measured by the SSP.

In addition to the SSP, the SWM from the CANTAB has been used for measuring spatial working memory. Family and colleagues (2020) found that microdoses of LSD did not significantly influence the results in the SWM. PAL, which measures visual memory and learning, did not also change significantly. The measurements were taken between 2 and 3 h after LSD administration and at the follow-up visit. Different results in the SWM have been found with higher doses of LSD - a dose of 100 μg of LSD, compared to placebo,

significantly increased the number of between errors (participants forgot that they already collected a token from a certain box in a prior trial) and reduced strategic use in the SWM when assessed 220 minutes after administration (Pokorny et al., 2020). Importantly, these effects were only present when the cognitive load was high. Pre-treatment with ketanserin normalized LSD-induced spatial working memory and executive function deficits. Thus this effect seems to be 5-HT2A receptor dependent and medium to high LSD doses are needed to influence spatial working memory measured with the SWM.

Mallaroni et al. (2023) found that 15 mg of psilocybin significantly diminished scores in immediate and delayed (+30 minutes) SMT recall (measures visuospatial memory and reasoning). Psilocybin did not significantly change the results in the TOL, which measures planning, inhibition, impulsivity, and working memory, but delayed RT-s in comparison to placebo (implemented during peak subjective effects). 50 μg LSD (assessed 24 hours post-administration) was found to enhance visuospatial memory as measured by the ROCF and the OLMT (Wießner et al., 2022). Auditory-verbal memory consolidation was evaluated using the RAVLT, where no significant effects were observed. Collectively, these findings suggest that while psychedelics may acutely impair spatial working memory, they may enhance certain aspects of memory—particularly visuospatial and episodic memory—at sub-acute time points. However, differences in the cognitive tasks employed across studies may have influenced these outcomes.

Vollenweider et al. (1998) reported that psilocybin acutely (0.25 mg/kg) slowed RT in the DRT (used for measuring working memory) in 25 healthy volunteers. Performance as measured by the rate of correct responses did not differ significantly between the various conditions. The authors bring out that the impairment in RT did not correlate significantly with changes in the Altered State of Consciousness rating scale scores. The slowed RT was prevented by ketanserin. In a study by Barrett et al. (2018), psilocybin (administered at 10 mg/70 kg, 20 mg/70 kg, and 30 mg/70 kg) was found to impair working memory, as measured by the N-back task, and episodic memory, assessed via a word-encoding, recall, and recognition task. Psilocybin induced dose-dependent working memory deficits, most notably in the 2-back condition, increasing response times and reducing discriminability while leaving 0-back performance (an attentional measure) unaffected. Psilocybin also disrupted free recall (the retrieval of previously learned words) and regarding recognition memory (distinguishing

old from new words) reduced sensitivity (A') and impaired both recollection (conscious retrieval) and familiarity (automatic recognition).

However, in another study, 13 and 26 μg of LSD did not significantly change the results in the N-back task measured 150 min after drug administration, coinciding with the expected peak effect of the drug (de Wit et al., 2022). Interestingly, when subjects were asked to rate (on a 7-point scale) how well they thought they performed on the task, subjects in the high-microdose LSD group self-reported performing significantly above average relative to other participants. Bershad et al. (2019) found that different microdoses of LSD (6.5 μg, 13 μg or 26 μg) did not significantly affect working memory in 20 healthy participants measured with the dual *n*-back task, which requires the ability to manage two n-back tasks simultaneously.

Murphy and colleagues (2023) found in a home-administered randomized controlled trial that LSD did not significantly affect post-acutely measured results in National Institutes of Health (NIH) Cognition Battery that measures episodic memory, language (vocabulary and reading), processing speed, working memory, attention, inhibitory control and attention and the set-shifting component of executive function.

Speth and colleagues (2016) found significantly fewer mental spaces for the past under 75 μg of LSD. Interviews were conducted 2.5 h post-administration and later analyzed. Thus less attention is attributed to autobiographical memory. Nikolic and colleagues (2023) found that 0.26 mg/kg of psilocybin did not impair or improve memory consolidation measured with several tests (GMLT, RAVLT, PALT).

Psilocybin (15 mg) impaired the encoding of episodic memory, particularly for neutral and positive stimuli in a study by Doss et al. (2024). This was evidenced by reduced hit rates and high-confidence hit rates in the Emotional Episodic Memory Task conducted the day after drug administration. Contrary to the hypothesis that psychedelics would enhance familiarity, the study found that both psilocybin and 2C-B impaired estimates of familiarity. However, this impairment was likely due to a misattribution of heightened familiarity, as both drugs increased familiarity-based false alarms, especially for negative and positive stimuli. Memory performance was generally best for negative stimuli under placebo conditions, but psilocybin disrupted this pattern. Psilocybin selectively increased false alarms for emotional (negative and positive) stimuli, suggesting a distortion in how emotional memories are processed.

Table 3

Summary of Studies Investigating the Effects of Psychedelics on Memory

Study and sample	Tests and substance used	Results
Vollenweider et al., 1998- 25 healthy volunteers were recruited from university staff. Experiment 1- 15 subjects (eight male, seven female; mean age (± s.d.) 29.7 ± 5.3). Experiment 2- 10 subjects (five male, five female; age 28.4 ± 4.0)	DRT- 0.25 mg/kg of psilocybin. Measurements were taken 80 minutes post-administration.	Psilocybin significantly slowed RT-s ($p < 0.05$ to $p < 0.01$ vs. placebo), but did not significantly alter the rate of correct responses ($p > 0.05$).
Carter et al., 2005- 8 healthy volunteers (5 men, 3 women) aged between 21 and 31 (mean = 27.0, SD = 2.7)	SSP from the CANTAB- 215 μg/kg of psilocybin. Measurements were taken 120 minutes after drug consumption.	No significant effect on the number of boxes remembered correctly in sequence span length was found for drug ($F(3,21) = 0.57$, $p = 0.64$) or time ($F(1,7) = 1.56$, $p = .12$).
Wittmann et al., 2007- 12 young healthy volunteers (six men and six women; mean age 26.8 years, SD 3.6)	SSP from the CANTAB- medium (115 μg/kg), and high (250 μg/kg) dose of psilocybin. Measurements were taken at 0, 100 and 360 minutes after drug intake.	No overall effect for treatment, $F(2, 22) = 1.33$, $p =$ non-significant. There was a significant effect for measurement time, $F(2, 22) = 4.05$, $p = .032$, and a significant interaction effect, $F(2, 22) = 4.66$, $p = .003$. A priori contrasts revealed a significant difference only for the contrast between placebo and high dose psilocybin between t_1 and t_0 ($p < .011$).

Table 3
(continued).

Bershad et al., 2019- 20 healthy subjects (12 women) aged 18 to 40	dual *n*-back- 6.5, 13, or 26 μg of LSD. Measurements were taken 30- to 90-minute intervals after drug administration.	LSD did not significantly affect the number of trials attempted ($F(3,54)= 0.39$, $p=0.76$) or RT for correct trials ($F(3,54)= 0.10$, $p=0.96$) at any dose.
Wießner et al., 2022- 24 healthy volunteers (8 women; mean (±SD) age = 35 (±11) years, range = 25–61)	ROCF, OLMT, RAVLT- 50 μg of LSD. Measurements were taken 24 hours after dosing.	Compared to placebo, LSD increased ROCF immediate recall points ($p = 0.044$) and percentage ($p = 0.018$). LSD increased OLMT consolidation percentage ($p = 0.022$). No treatment effects were observed for ROCF copy and delayed recall points and percentage, OLMT consolidation points and RAVLT variables.
Pokorny et al., 2020- 25 healthy participants (19 men, 6 women, mean age ± SD: 25.24 ± 2.79, mean verbal IQ ± SD: 108.4 ± 9.2)	SWM- 100 μg of LSD. Measurements were taken 220 minutes after the administration.	Tukey post-hoc tests revealed that participants made significantly more between errors in the LSD condition ($M = 4.84$, $SD = 7.41$, 95% CI [5.79, 10.31]) than in the placebo condition when six boxes were presented ($M = 0.72$, $SD = 1.72$, 95% CI [1.34, 2.39], $p < .01$). LSD significantly increased between errors ($M = 12.68$, $SD = 12.03$, 95% CI [9.40, 16.74]) when eight boxes were presented, compared to both placebo ($M = 5.52$, $SD = 7.83$, 95% CI [6.12, 10.90], $p < .001$) and Ketanserin + LSD ($M = 7.48$, $SD = 8.36$, 95% CI [6.53, 11.63], $p < .001$). Tukey post-hoc tests also revealed that the strategy score was higher under LSD ($M = 17.84$, $SD = 3.88$, 95% CI [3.03, 5.40]) compared to placebo ($M = 16.52$, $SD = 3.72$, 95% CI [2.91, 5.18]) and Ketanserin + LSD ($M = 16.36$, $SD = 4.02$, 95% CI [3.14, 5.60]) when eight boxes were presented (both $p < .01$).

Table 3
(continued).

Speth et al., 2016- 20 healthy volunteers (four females, mean age=30.9±7.8, range=22–47), 19 of which were in the final analyses	Quantitative linguistic analysis- intravenous administration of LSD (75 μg). Interviews were conducted approximately 2.5 hours post-administration.	There were fewer references to the past after LSD (M = 0.079, SD = 0.20) than after placebo (M = 0.71, SD = 1.04).
Murphy et al., 2023- 80 healthy male volunteers (mean age = 36.9 ± 8.2 years)	NIH Cognition Battery- 14 doses of 10 μg LSD. Measurements were taken at baseline and 2 days after the last dose.	LSD did not significantly (all p>0.05) affect results in NIH Cognition Battery.
Family et al., 2020- healthy volunteers aged 55 to 75 years (21 males, 27 males; mean age 62.92 ± 5.78 years)	CANTAB tests PAL and SWM- 5 μg, 10 μg, 20 μg of LSD. Measurements were taken at baseline (i.e., prior to dosing), at dose 3 (between 2 and 3 h after dose administration), at dose 6 and during follow-up.	The one-way ANOVA analysis followed by Bonferroni post hoc test on the PAL and SWM, did not reveal any significant differences (all p>0.5) between treatment groups.

Table 3
(continued).

Mallaroni et al., 2023- 22 healthy participants (11 women) aged 19–35 years (mean ± SD: 25 ± 4 years) were recruited by word of mouth and advertisement shared via Maastricht University social media platforms.	SMT, TOL- 15 mg of psilocybin. Measurements were taken during peak subjective effects.	Psilocybin significantly diminished performance in both the immediate ($F(2,39) = 11.27$, $p < 0.001$) and delayed ($F(2,37) = 7.24$, $p = 0.002$) phases of the SMT. In the TOL, psilocybin did not alter accuracy ($F(2,41) = 0.7$, $p = 0.501$) but markedly delayed RT-s ($F(2,41) = 22.09$, $p < 0.001$) compared to placebo.
Doss et al., 2024- 20 participants (10 males, age: mean = 25.00 years, SD = 4.91)	Emotional Episodic Memory Task- 15 mg of psilocybin. Measurements were taken 185 minutes and 24 hours later.	Psilocybin impaired memory- trending main effects of drug on hit rates ($F_{2,38} = 2.61$, $p = .086$, $\eta_p^2 = 0.12$) and high-confidence hit rates ($F_{2,38} = 3.04$, $p = .060$, $\eta_p^2 = 0.18$). Psilocybin increased familiarity-based false alarms ($F_{2,36} = 3.33$, $p = .047$, $\eta_p^2 = 0.16$), especially for negative and positive stimuli and reduced familiarity for positive images ($p = .036$).
de Wit et al., 2022- 56 participants (37 males) were healthy adults aged 18–35 who reported having used a psychedelic drug or MDMA at least once in their life-time	N-back task- 13 or 26 μg LSD tartrate, which is equivalent to a dose of 10 or 20 μg of LSD base. Measurements were taken 150 minutes after drug administration	On the *n*-back task, neither dose of LSD significantly affected performance on two- or three-back trials during Sessions 1 and 4. The LSD (13 or 26 μg) groups did not differ from placebo on the N-back tasks on session 5.

Table 3
(continued).

Barrett et al., 2018- 20 healthy participants (11 females; mean age = 28.5 years, range = 22–43) with a history of both classic hallucinogen use and dissociative hallucinogen use	N-back task, a word-encoding , recall, and recognition task- 10, 20, and 30 mg/70 kg psilocybin. Measurements were taken during the acute effects.	Main effects of *n*-back condition ($F(2) = 38.53$, $p < .0001$) and drug condition ($F(4) = 3.47$, $p < .05$), as well as an interaction between drug and *n*-back condition ($F(8) = 3.51$, $p < .001$), were observed on discriminability. A main effect of *n*-back condition ($F(2) = 62.30$, $p < .0001$) and drug condition ($F(4) = 6.75$, $p < .001$), as well as an interaction between drug and *n*-back condition ($F(8) = 3.36$, $p < .005$), was observed on response bias. Main effects of drug condition ($F(4) = 8.50$, $p < .0005$) and *n*-back condition ($F(2) = 86.38$, $p < .0001$), as well as an interaction of drug and *n*-back conditions ($F(8) = 6.02$, $p < .0001$), were also observed on response time. Main effects of drug condition were observed on word recall accuracy ($F(4) = 11.22$, $p < .0001$). Main effects in the word recognition task of drug condition were observed on the area under the curve (AUC) of the ROC curves ($F(4) = 6.42$, $p < .0005$) and sensitivity (A'; $F(4) = 5.94$, $p < .0005$).
Nikolic et al., 2023- 20 healthy volunteers (10 M/10F, mean age = 36, SD = 8.1, range 28 - 53).	GMLT, RAVLT, PALT- 0.26 mg/kg of psilocybin. The dose was increased by 1 mg per 5 kg of body weight. Measurements were taken 8 to 24 hours after drug administration.	The main effect of the time of testing approached significance (participants made more errors after delay; $F(1, 15) = 4.172$, $p = 0.059$; one-way ANOVA did not find differences between groups).

Psychedelics' effects on emotional processing

Emotional processing refers to perceiving, expressing and managing emotions. Several tests were used in the current studies, such as the Facial Emotion Recognition Task (FERT; Bedi et al., 2010), the Reading the Mind in the Eyes Test (Baron-Cohen et al., 2001), the Emotional Go/Nogo Task (Kometer et al., 2012), the Emotional Images Task (Lang, 1999; Wardle, 2012), the Emotional Faces Task (Griffiths et al., 2015), the Cyberball Task (Williams and Jarvis, 2006), an emotional face discrimination task (Grimm et al., 2018), two facial affect

discrimination tasks (Schmidt et al., 2013), and paradigm of facial stimuli (Mueller et al., 2017) (see Table 4). For psilocybin, low doses included 0.16 mg/kg (Grimm et al., 2018), 115 μg/kg (Schmidt et al., 2013) and medium doses included 215 μg/kg (Kometer et al., 2012). In LSD studies, low doses included 13 μg (de Wit et al., 2022), 26 μg (de Wit et al., 2022) and medium doses included 100 μg (Dolder et al., 2016; Mueller et al., 2017) and high doses included 200 μg (Dolder et al., 2016).

Dolder et al. (2016) demonstrated that 100 μg and 200 μg doses of LSD impaired the recognition of fearful faces in the FERT, measured 5 and 7 hours post-administration (during the acute effects of the drug). In contrast, Mueller et al. (2017) found that 100 μg of LSD had no significant effect on RT, accuracy, or omission rates (absence of button presses) in an fMRI paradigm conducted 2.5 hours after consumption—timed to coincide with the subjective and pharmacological peak effects. During fMRI scanning, participants viewed a standardized set of facial stimuli consisting of 10 unique identities, each displaying neutral, 50% fearful, and 100% fearful expressions (totaling 30 stimuli). Brain activity, accuracy, and RT-s were recorded. The discrepancy between these studies may stem from differences in the tasks employed (FERT vs. fMRI-based emotion processing) or the timing of assessments relative to LSD's pharmacokinetic profile.

Kometer et al. (2012) found that a dose of 215 μg/kg psilocybin attenuated the recognition of negative facial expressions in the Reading the Mind in the Eyes Test (administered 130 minutes post-ingestion). In the Emotional Go/NoGo Task, where cues were defined by emotional valence (unlike the standard shape-based version), psilocybin disproportionately increased RT-s for negative and neutral words compared to positive words. It also significantly elevated error rates for neutral—but not positive or negative—words. Notably, error rates were higher for negative versus positive stimuli under psilocybin, an effect absent under placebo. These valence-specific effects on error rates were consistent across Go/NoGo conditions and unaffected by ketanserin pretreatment. Grimm et al. (2018) observed that a low psilocybin dose (0.16 mg/kg) slowed RTs across all affective categories (negative, neutral, positive) in an emotional face discrimination task during acute effects, though accuracy remained intact and no drug-by-face-type interaction emerged. Schmidt et al. (2013) reported that 115 μg/kg psilocybin impaired the discrimination of fearful (but not happy) faces relative to neutral ones. This suggests psilocybin’s behavioral effects are selectively modulated by stimulus valence. Collectively, low-to-medium psilocybin doses acutely impair

the processing of negative stimuli, an effect that appears partially independent of 5-HT2A receptor activation.

A study by de Wit et al. (2022) examined the effects of LSD microdoses (13 or 26 μg) on emotional and social processing using the Cyberball Task, the Emotional Images Task and the Emotional Faces Task. In the Emotional Images Task, neither LSD dose significantly affected ratings of positive or negative images during compared to placebo. However, in the Emotional Faces Task, 26 μg of LSD reduced false alarm rates for fearful faces on the first and last days of administration, without altering hit rates for any emotion. During the Cyberball Task, the same dose (26 μg) attenuated negative mood ratings in the social rejection, though it had no effect during social acceptance. These effects did not persist at follow-up (3–4 days post-session).

However, Bershad et al. (2019) observed no significant impact of LSD microdoses on the Cyberball Task. While their Emotional Images Task results were also unaffected, the highest dose (26 μg) slightly reduced positivity ratings for positive images. Similarly, psilocybin microdoses showed no measurable effects on emotional processing in the Emotional Go/NoGo Task (Marschall et al., 2021). Collectively, these studies suggest that LSD microdoses may transiently modulate specific aspects of emotional and social processing (e.g., fear perception, rejection sensitivity), but these effects are subtle, dose-dependent, and do not endure beyond acute administration.

Table 4

Summary of Studies Investigating the Effects of Psychedelics on Emotional Processing

Study and sample	Tests and substance used	Results
Dolder et al., 2016- 40 healthy participants were recruited from the University of Basel campus. Twenty-four subjects (12 men, 12 women; 33±11 years old (mean±SD); range, 25–60 years) participated in Study 1, and 16 subjects (8 men, 8 women; 29±6 years old; range, 25–51 years) participated in Study 2.	FERT- 100, 200μg of LSD. Measurements were taken 5 and 7 h after the 100 and 200 μg doses of LSD.	Both doses of LSD impaired impair the recognition of fearful faces (main effect of drug: $F_{1,36}$=20.71, p<0.001).
Kometer et al., 2012- 17 healthy, subjects (11 male subjects, 6 female subjects, mean age 26.0 ± 4.36 years) were recruited through advertisement from the University of Zürich	Reading the Mind in the Eyes Test, Emotional Go/Nogo Task- 215 μg/kg of psilocybin. Measurements were taken 130 minutes after drug administration.	Psilocybin modulated error rates depending on the valence of the facial expression [F(2,32) = 5.460, p < .01, η_p^2 = .254]. Psilocybin increased error rates for negative faces only after placebo (p < .05). Psilocybin increased RT much more for negative ($p < 1^{-6}$) and neutral ($p < 1^{-7}$) than for positive words (p < .01). Psilocybin significantly increased error rates only for neutral (p < .01) but not for positive (p = 1) or negative (p = 1) words.
Grimm et al., 2018- 25 healthy, subjects (16 male subjects, mean age 24.2 ± 3.42 years, all students or university-educated persons; 18 in analysis)	modified version of an emotional face discrimination task in the MRI scanner- 0.16 mg/kg of psilocybin. Measurements were taken during the acute effects.	An increase in RT for all three categories of affective stimuli was found (F(1,17)=24.03, p<0.001).

Table 4
(continued).

de Wit et al., 2022- 56 participants (37 males) were healthy adults aged 18–35 who reported having used a psychedelic drug or MDMA at least once in their life-time	Cyberball, Emotional Images Task, Emotional Faces Task- 13 or 26 μg LSD tartrate, which is equivalent to a dose of 10 or 20 μg of LSD base. Measurements were taken 150 min after drug administration and 3-4 days later.	In the Emotional Images Task LSD did not significantly alter positive ratings of positive images or negative ratings of negative images. In Emotional Faces Task 26 μg of LSD decreased false alarm rates on fear faces only, during the first and last days of drug administration (main effect of drug $F_{2,52} = 3.26$, $p = 0.046$, $\eta_p^2 = 0.111$; 26 μg vs. placebo, $p < 0.050$). On the Cyberball, 26 μg of LSD decreased negative mood ratings during the social rejection phase (main effect of drug, $F_{2,53} = 3.65$, $p = 0.033$, $\eta_p^2 = 0.121$; 26 μg vs. placebo, $p < 0.05$). 3-4 days later these results were not significant.
Marschall et al., 2021- 52 participants were included for S1 (session 1) and S3, consisting of 29 females and a mean age of 29.75 (ranging from 29–60) years and 44 were included for S2 and S4, consisting of 21 females and a mean age of 30.6 (ranging from 20–60) years	Emotional go/no-go task- the doses contained 0.7 g of dried psilocybin-containing Galindoi truffles, which corresponds to around 1/10th of a medium-high dose. Measurements were taken 1.5 hours after drug administration.	The analysis showed a significant main effect of emotion, $F(5, 195) = 40.14$, $p < 0.001$, $\eta^2 = 0.20$, but no significant main effect of condition, $F(1, 39) = 0.88$, $p = 0.35$, $\eta^2 = 0.009$.

Table 4
(continued).

Schmidt et al., 2013- healthy university students were separated into two groups: S-ketamine group (N=21, 12 males, mean age=26±5.39) and psilocybin group (N=21, 13 males, mean age=23±2.22)	Facial affect discrimination tasks- 115 μg/kg of psilocybin. Measurements were taken 110 minutes following psilocybin administration.	A significant treatment × valence interaction for psilocybin (from $F(1,40) = 4.11$; $p < 0.05$; $\eta_p^2 = 0.09$) revealed reduced d' for fearful faces ($p < 0.001$) but not for happy faces ($p = 0.87$) relative to placebo.
Mueller et al., 2017- 20 healthy subjects (9 men, 11 women; mean age 32 ± 10.2 years; 19 of them with an academic background)	paradigm of facial stimuli- 100 μg of LSD. Measurements were taken 2.5 hours after LSD consumption.	There were no significant differences in average response times between the two conditions ($M = 964 \pm 128$ ms for LSD; $M = 910 \pm 289$ ms for placebo), $t(21) = 2.00$, $p = .06$. Response accuracy did not differ significantly between conditions ($M = 93.1\% \pm 10.8\%$ for LSD; $M = 97.3\% \pm 3.3\%$ for placebo), $t(21) = –1.80$, $p = .08$. The proportion of missed button presses showed no significant difference ($M = 4.5\% \pm 9.3\%$ for LSD; $M = 1.3\% \pm 1.8\%$ for placebo), $t(21) = 1.50$, $p = .16$.

Table 4
(continued).

Bershad et al., 2019- healthy subjects (N = 20; 12 women) aged 18 to 40 years	Emotional Images Task, Cyberball Task- 6.5, 13, or 26 μg of LSD. Measurements were taken 30- to 90-minute intervals after drug administration.	In the Emotional Images Task, participants rated positive pictures as more positive, $F(2, 38) = 194.28$, $p < .001$; pairwise comparisons (negative vs. neutral, negative vs. positive, and positive vs. neutral) were all significant at $p < .001$. Higher doses of LSD appeared to reduce positivity ratings for positive images, as reflected in a significant Dose × Emotion interaction, $F(6, 114) = 2.35$, $p < .05$; post hoc comparisons showed a significant difference between the 13 μg dose and placebo ($p < .05$), and a marginal difference between the 26 μg dose and placebo ($p = .06$). Participants accurately perceived that they received fewer throws during rejection and felt less included in the game, as indicated by main effects of condition on perceived throws, $F(1, 19) = 221.10$, $p < .001$, and sense of inclusion, $F(1, 19) = 599.20$, $p < .001$. LSD did not significantly influence mood responses to rejection.

Psychedelics' effects on empathy

Empathy can be categorized as cognitive or emotional. Cognitive empathy involves knowing how other people think and feel, while emotional empathy involves feeling another person's emotions. In most of the analyzed studies empathy was measured acutely or post-acutely with the Multifaceted Empathy Test (MET, Dziobek et al., 2008) that was developed to assess cognitive and emotional aspects of empathic functioning. Emotional empathy is categorized into two in this test: 1) implicit empathy, often referred to as "arousal," includes the automatic, unconscious aspect of emotional empathy in which the sharing of emotions arouses the observing individual, 2) explicit empathy, which is a deliberate and conscious process requiring mental effort and conscious processing, enabling us to respond appropriately and empathetically toward other people's emotions.

Studies investigating the effects of psychedelics on empathy employed LSD doses of 100 μg (medium dose), 200 μg (high dose) (Dolder et al., 2016), 25, 50, 100, and 200 μg (from low

to high dose) (Holze et al., 2021). Psilocybin studies utilized a dose of 0.215 mg/kg (medium dose) (Jungwirth et al., 2024; Pokorny et al., 2017) and a dose of 15 mg (medium dose) (Mallaroni et al., 2023). Investigations on ayahuasca reported DMT concentrations ranging from 14.1 to 20.1 mg (medium to high dose) (Uthaug et al., 2021) (see Table 5).

Dolder and colleagues (2016) looked at the effects of 100 μg and 200 μg of LSD on empathy. Most significantly, 200 μg of LSD enhanced implicit and explicit emotional empathy as measured with the MET 7 h and 30 minutes after the administration, that accounts for 50% of the peak subjective effects. The valence-specific analysis showed that higher dose of LSD significantly increased explicit and implicit emotional empathy scores for positive emotional stimuli. Both doses of LSD significantly reduced cognitive empathy, for the lower dose the MET was performed 5 h and 30 minutes after the administration. Similar results were found in another study where 200 μg of LSD increased implicit and explicit emotional empathy measured with the MET 6 h after administration (Holze et al., 2021). It is interesting to note that ketanserin did not have an effect on the result- thus the effects of LSD on empathy could be 5-HT2A receptor independent. Lower doses of LSD (25, 50, 100 μg) did not significantly impact empathy, but the authors bring out that the results could have been different when measured at 3 h, which is approximately 50% of the peak subjective effects for lower doses.

0.215 mg/kg of psilocybin was found to increase explicit and implicit emotional empathy independent of stimuli valence (Pokorny et al., 2017). The MET was performed 160 minutes after the administration when the peak perceptual/visual effect of psilocybin had already markedly subsided. Psilocybin did not significantly influence cognitive empathy. The same dose of psilocybin was administered to 51 people with depression in another study (Jungwirth et al., 2024). Psilocybin significantly enhanced explicit emotional empathy, particularly due to increased empathy toward positive stimuli, compared to the placebo group, with effects lasting at least two weeks. At baseline participants showed significantly stronger empathy towards negative compared to positive stimuli, which could be linked to depression. However, no significant correlations between increased empathy and improvement in depressive symptoms were found in the present study. On the contrary to the previous studies, 15 mg of psilocybin has been found to have no effect on empathy measured with the MET 270 minutes after drug administration (Mallaroni et al., 2023).

While the impact of ayahuasca on empathy has been less extensively studied, Uthaug et al. (2021) observed a notable treatment × time interaction in implicit emotional empathy, revealing that ayahuasca (contained 14.1–20.1 mg of DMT) boosted emotional empathy in response to negative stimuli. The MET was performed post-acutely.

Table 5

Summary of Studies Investigating the Effects of Psychedelics on Empathy

Study and sample	Tests and substance used	Results
Dolder et al., 2016- 40 healthy participants were recruited from the University of Basel campus. 24 (12 men, 12 women; 33±11 years old (mean±SD); range, 25–60 years) participated in Study 1, and 16 subjects (8 men, 8 women; 29±6 years old; range, 25–51 years) participated in Study 2	MET- 100, 200µg of LSD. MET was performed 5 hours and 30 minutes after the low LSD dose and 7 hours and 30 minutes after the high LSD dose.	The post hoc tests showed that the 200 µg dose, but not the 100 µg dose, of LSD produced a significant effect on explicit ($p < .01$) and implicit ($p = .01$) empathy compared with placebo. The valence-specific analysis showed that LSD significantly increased explicit and implicit emotional empathy for positive emotional stimuli ($F(1, 36) = 24.32$, $p < .001$ and $F(1, 36) = 10.47$, $p < .01$, respectively). LSD decreased cognitive empathy ($F(1, 36) = 16.87$, $p < .001$). The post hoc tests showed that this effect was significant for both doses of LSD compared with the placebo (both $p < .05$).
Holze et al., 2021- 16 healthy subjects (eight men and eight women; mean age ± SD: 29 ± 6.4 years; range: 25–52 years) were recruited by word of mouth or an advertisement.	MET- 25, 50, 100, 200 µg of LSD. Measurements were taken 6 hours after administration.	There were significant main effects of LSD on explicit and implicit emotional empathy ratings ($F_{4,44} = 4.64$, $p < 0.01$, and $F_{4,44} = 4.82$, $p < 0.01$, respectively). 200 µg of LSD significantly affected explicit ($p < 0.05$) and implicit ($p < 0.01$) empathy scores compared with placebo.
Pokorny et al., 2017- 33 healthy subjects were recruited through advertisements at universities (17 men, 15 women, mean age 26.72 ± 5.34 years, range 20–38 years)	MET- 0.215 mg/kg of psilocybin. Measurements were taken 160 minutes after drug administration.	Psilocybin increased implicit ($F(1,30)= 4.77$, $p<.05$) and explicit ($F(1,30) =7.74$, $p<.01$) emotional empathy.

Table 5 (continued).

Jungwirth et al., 2024- 51 depressed patients (19 men, 32 women; mean age ± SD = 36.7 ± 10.4)	MET- 0215 mg/kg of psilocybin. Measurements were taken 2 days, 8 days and 14 days after drug administration.	Psilocybin enhanced explicit emotional empathy ($F(2.43, 102) = 5.83$, $p = .006$, $\eta^2 = 0.01$).
Mallaroni et al., 2023- 22 healthy participants (11 women) aged 19–35 years (mean ± SD: 25 ± 4 years) were recruited by word of mouth and advertisement shared via Maastricht University social media platforms	MET- 15 mg of psilocybin. Measurements were taken 270 minutes after drug administration.	Implicit emotional empathy (positive: $p = .616$; negative: $p = .962$), explicit emotional empathy (positive: $p = .172$; negative: $p = .257$), and cognitive empathy (positive: $p = .23$; negative: $p = .459$) were all unaffected ($F(2, 41) < 1.84$, $p > .05$).
Uthaug et al., 2021- 30 visitors of ayahuasca ceremony (12 males, 18 female; a mean (SD) age of 40.18 (10.10))	MET- ayahuasca that contained 14.1-20.1 mg of DMT. Measurements were taken post-session.	Ayahuasca boosted emotional empathy in response to negative stimuli ($F_{1, 16} = 5.11$; $p = .038$, partial $\eta^2 = 0.20$).

Table 6

The Effects of Psychedelics on Task and Functions they assess

Task	Functions	The effects of psychedelics
the Digit Symbol Substitution Test (DSST)	working memory, visual processing, motor speed and attention	13 and 26 μg of LSD did not influence (de Wit et al., 2022), 20 μg of LSD impaired performance (Hutten et al., 2020), 6.5, 13 and 26 μg of LSD did not influence (Bershad et al., 2019), 15 mg of psilocybin impaired performance (Mallaroni et al. 2023), 20–30 mg/70 kg of psilocybin impaired performance (Barrett et al., 2018)
the Psychomotor Vigilance Test (PVT)	sustained attention	5 μg and 20 μg of LSD enhanced performance (Hutten et al., 2020), 15 mg of psilocybin delayed RT (Mallaroni et al. 2023)
mpraxis task from the Penn Computerized Neurocognitive Battery (CNB)	psychomotor speed	20 mg and 30 mg psilocybin slowed response times (Barrett et al., 2018)
a multiple-object tracking task (Carter et al., 2005)	attention	215 μg/kg of psilocybin impaired performance (Carter et al., 2005)
the Cambridge Neuropsychological Test Automated Battery (CANTAB) reaction time (RTI) and rapid visual information processing (RVP) test	RVP measures visual attention, RTI measures RT	5 μg, 10 μg, and 20 μg of LSD did not significantly change the results (Family et al., 2020)

Table 6 (continued).

the Frankfurt Attention Inventory (FAIR)	attention, inhibition	115, 215, and 315 μg/kg of psilocybin impaired performance (Vollenweider et al., 2007)
the Attentional Blink task	attention	0.5 grams of dried mushrooms did not significantly impair performance (Cavanna et al., 2022)
the Stroop Test	inhibition	0.5 grams of dried mushrooms did not significantly impair performance (Cavanna et al., 2022), 50 μg of LSD did not significantly change the results (Wießner et al., 2022), 260 μg/kg of psilocybin impaired performance (Quednow et al., 2012)
the Trail Making Test (TMT)	attention and coordination	0.5 grams of dried mushrooms increased time (Cavanna et al., 2022), 50 μg of LSD did not significantly change the results (Wießner et al., 2022)
the Go/ No Go task	inhibition	100 μg of LSD impaired performance (Schmidt et al., 2018), 0.5 grams of dried mushrooms did not significantly impair performance (Cavanna et al., 2022)
Intra/Extra-Dimensional Shift Task (IED)	CF, attention, discriminative learning, reversal learning	100 μg of LSD impaired performance (Pokorny et al., 2020)
the Wisconsin Card Sorting Test (WCST)	CF, working memory, inhibition	50 μg of LSD impaired performance (Wießner et al., 2022)

Table 6 (continued).

The Cognitive Control Task (CCT)	cognitive control	5, 10, and 20 μg of LSD did not significantly change the results (Hutten et al., 2020)
the probabilistic reversal learning task	reinforcement learning, CF	75 μg of LSD enhanced performance (Kanen et al., 2023)
the Spatial Span test (SSP; from CANTAB)	visuospatial working memory	was not influenced by psilocybin (0.215 mg/kg) (Carter et al., 2005), 250μg/kg of psilocybin impaired performance, whereas 115 μg/kg had no significant effect (Wittmann et al., 2007)
the visual-manual delayed response task (DRT)	working memory, RT	0.25 mg/kg of psilocybin slowed RT (Vollenweider et al., 1998)
the letter N-back task	working memory, inhibition, attention	10 mg/70 kg, 20 mg/70 kg, and 30 mg/70 kg of psilocybin impaired performance (Barrett et al., 2018), 13 and 26 μg of LSD did not significantly change the results (de Wit et al., 2022)
the dual *n*-back task	working memory, inhibition	6.5 μg, 13 μg and 26 μg of LSD did not significantly change the results (Bershad et al., 2019)

Table 6 (continued).

National Institutes of Health (NIH) Cognition Battery-NIH-TB Flanker Inhibitory Control and Attention Test (Executive/Attention), NIH-TB Dimensional Change Card Sort Test (Executive/Shifting), NIH-TB List Sorting Working Memory Test (Working Memory), NIH-TB Picture Sequence Memory Test (Episodic Memory), NIH-TB Oral Reading Recognition Test (Language), NIH-TB Picture Vocabulary Test (Language), NIH-TB Pattern Comparison Processing Speed Test (Processing Speed)	attention, inhibition, working memory, episodic memory, word pronunciation, letter recognition, receptive vocabulary, reaction time	14 doses of 10 μg LSD did not significantly change the results (Murphy et al., 2023)
a word-encoding, recall, and recognition task (Barrett et al., 2018)	short-term memory performance, episodic memory	10 mg/70 kg, 20 mg/70 kg, and 30 mg/70 kg of psilocybin impaired performance (Barrett et al., 2018)
Rey-Osterrieth Complex Figure (ROCF)	visual perception, visuoconstructional abilities and spontaneous memory retention	50 μg LSD enhanced performance (Wießner et al., 2022)
The 2D Object-Location Memory Task (OLMT)	visuospatial memory consolidation	50 μg LSD enhanced performance (Wießner et al., 2022)
the SWM and the PAL from the CANTAB	SWM measures spatial working memory, PAL measures visual memory and learning	5 μg, 10 μg, 20 μg of LSD did not significantly influence the results (Family et al., 2020), 100 μg of LSD impaired performance (Pokorny et al., 2020)

Table 6 (continued).

the Rey Auditory-Verbal Learning Test (RAVLT)	auditory-verbal memory consolidation	50 μg LSD did not significantly change the results (Wießner et al., 2022), 0.26 mg/kg of psilocybin did not significantly influence the results (Nikolic et al., 2023)
the Groton maze learning task (GMLT)	spatial memory	0.26 mg/kg of psilocybin did not significantly influence the results (Nikolic et al., 2023)
the Paired associative Learning Test (PALT)	assesses the influence of sleep on declarative memory processes	0.26 mg/kg of psilocybin did not significantly influence the results (Nikolic et al., 2023)
the Tower of London test (TOL)	planning, inhibition, impulsivity, working memory	15 mg of psilocybin delayed RT (Mallaroni et al., 2023)
the Spatial Memory Test (SMT)	visuospatial memory and reasoning	15 mg of psilocybin impaired performance (Mallaroni et al., 2023)
the Emotional Episodic Memory Task	emotional episodic memory	15 mg of psilocybin impaired performance (Doss et al., 2024)
the Facial Emotion Recognition Task (FERT)	recognition of four basic emotions	100 μg and 200 μg doses of LSD impaired the recognition of fearful faces (Dolder et al., 2016),
the Reading the Mind in the Eyes Test	inferring emotional states from the eye region	215 μg/kg psilocybin attenuated the recognition of negative facial expressions (Kometer et al., 2012)

Table 6 (continued).

the Emotional Go/Nogo Task	inhibition	psilocybin increased RT-s for negative and neutral words compared to positive words, elevated error rates for neutral words and error rates were higher for negative versus positive stimuli under psilocybin (Kometer et al., 2012), 0.7 g of dried psilocybin-containing Galindoi truffles (microdose) did not significantly influence the results (Marschall et al., 2021)
the Emotional Images Task	rating the positivity and negativity of images with emotional content	13 and 26 μg of LSD did not significantly influence the results (de Wit et al., 2022), 13 and 26 μg of LSD did not significantly influence the results (Bershad et al., 2019)
the Emotional Faces Task	sensitivity to the perception of emotions	26 μg of LSD reduced false alarm rates for fearful faces (de Wit et al., 2022)
the Cyberball Task	reaction to social exclusion	26 μg of LSD attenuated negative mood ratings (de Wit et al., 2022), 6.5, 13, and 26 μg of LSD did not significantly influence the results (Bershad et al., 2019)
an emotional face discrimination task (Grimm et al., 2018)	RT to different emotions	psilocybin dose (0.16 mg/kg) slowed RTs across all affective categories (Grimm et al., 2018)

Table 6 (continued).

two facial affect discrimination tasks (Schmidt et al., 2013)	emotion recognition	115 μg/kg psilocybin impaired the discrimination of fearful faces (Schmidt et al., 2013)
paradigm of facial stimuli (Mueller et al., 2017)	emotion recognition	100 μg of LSD had no significant effect (Mueller et al., 2017)
the Multifaceted Empathy Test (MET)	implicit and explicit emotional empathy, cognitive empathy	200 μg of LSD enhanced implicit and explicit emotional, 100 μg and 200 μg reduced cognitive empathy (Dolder et al. 2016), 200 μg of LSD increased implicit and explicit emotional empathy, but 25, 50, 100 μg of LSD had no effect on it (Holze et al., 2021), 0.215 mg/kg of psilocybin increased explicit and implicit emotional (Pokorny et al., 2017), 0.215 mg/kg of psilocybin enhanced explicit emotional empathy (Jungwirth et al., 2024), 15 mg of psilocybin had no effect (Mallaroni et al., 2023), ayahuasca increased implicit emotional empathy (Uthaug et al., 2021)

Discussion

The effects of psychedelics on cognitive and psychological functions

This systematic review included 30 placebo-controlled studies (see Table 6) mostly done in healthy volunteers. Psychedelics enhanced implicit and explicit emotional empathy, but most of the time had no effect on cognitive empathy (Dolder et al., 2016; Holze et al., 2021;

Jungwirth et al., 2024; Pokorny et al., 2017; Uthaug et al., 2021). Psychedelics impaired (Barrett et al., 2018; Doss et al., 2024; Mallaroni et al., 2023; Pokorny et al., 2020; Vollenweider et al., 1998; Wittmann et al., 2007), enhanced (Wießner et al., 2022) or had no effect (Bershad et al., 2019; Carter et al., 2005; de Wit et al., 2022; Family et al., 2020; Murphy et al., 2023; Nikolic et al., 2023) on memory depending on the task, dosage and timing of the assessment. Dose-dependent impairments were seen in many tasks assessing RT, attention and inhibition (Barrett et al., 2018; Carter et al., 2005; Cavanna et al., 2022; Hutten et al., 2020; Mallaroni et al. 2023; Schmidt et al., 2018; Vollenweider et al., 2007; Quednow et al., 2012), although some studies found no effects (Bershad et al., 2019; de Wit et al., 2022; Family et al., 2020; Wießner et al., 2022). Regarding emotional processing, several studies found impaired recognition of specifically negative stimuli (Dolder et al., 2016; Kometer et al., 2012; Schmidt et al., 2013). The results on CF were less clear as there were also less studies about this compared to other cognitive or psychological functions. Most of the studies assessed the acute effects of psychedelics. Post-acute measurements were usually taken hours or days later.

Many tests for measuring RT also assessed attention and inhibitory control as they are intertwined. Microdoses of LSD (5–26 μg) showed mixed results, with one study reporting enhanced sustained attention (Hutten et al., 2020) and others showing no significant changes (Bershad et al., 2019; de Wit et al., 2022). Medium (15–30 mg) and high (≥215 μg/kg) doses of psilocybin impaired performance in several attention tasks (Barrett et al., 2018; Quednow et al., 2012; Vollenweider et al., 2007). Higher doses of LSD (50–100 μg) and psilocybin also slowed RT and reduced inhibitory control (Schmidt et al., 2018; Quednow et al., 2012), whereas microdoses of psilocybin (0.5 g dried mushrooms) showed non-significant trends toward impaired RT (Cavanna et al., 2022). Overall, while low doses of psychedelics may have subtle or negligible effects on RT and attention, medium to high doses tended to impair performance.

Only 4 CF articles met criteria for placebo-controlled study standards. All of these studies were done with LSD (microdoses to medium doses) in healthy volunteers. Two of them found that LSD impairs CF acutely (Pokorny et al., 2020) and postacutely (Wießner et al., 2022), whereas one study found enhanced CF during LSD subjective effects (Kanen et al., 2023). The difference in the results could have been influenced by different tests used as the IED and the WCST are based on the same principle, but the probabilistic reversal learning task can be

looked at as a reinforcement learning test. Microdoses of LSD did not influence CF that is in line with several previous studies that have found no significant effects of microdosing on cognition (Bershad et al., 2019; Cavanna et al., 2022).

Psilocybin and LSD exerted dose- and time-dependent effects on memory, with acute impairments often observed in working and episodic memory tasks, particularly at medium to high doses (Barrett et al., 2018; Mallaroni et al., 2023; Pokorny et al., 2020; Vollenweider et al., 1998; Wittmann et al., 2007). However, some studies reported no acute effects on working memory (Bershad et al., 2019; Carter et al., 2005; de Wit et al., 2022; Family et al., 2020) or subacute improvements in memory consolidation and visuospatial memory (Wießner et al., 2022). Changes in autobiographical memory during acute effects were also observed (Speth et al., 2016). Psilocybin was found to impair episodic memory (Barrett et al., 2018; Doss et al., 2024). Regarding memory consolidation it was found that psilocybin does not affect daytime or sleep-related declarative memory consolidation in healthy volunteers (Nikolič et al., 2023).

Research on psychedelics' modulation of emotional processing revealed dose- and valence-dependent effects, primarily characterized by attenuated responses to negative stimuli without consistent alterations in positive emotion perception. Medium to high doses of LSD (100–200 μg) impaired fear recognition in the FERT during acute effects (Dolder et al., 2016), though discrepant fMRI findings suggest task-dependent variability (Mueller et al., 2017). Psilocybin demonstrated valence-specific blunting of negative emotion processing: medium doses (215 μg/kg) reduced recognition of negative facial expressions (Kometer et al., 2012), while low doses (0.16 mg/kg) slowed RT-s across emotional stimuli without affecting accuracy (Grimm et al., 2018). Microdoses of LSD (13–26 μg) showed limited acute effects, with isolated reductions in fear false alarms and transient mood improvements during social rejection (Cyberball Task; de Wit et al., 2022). Neither LSD nor psilocybin microdoses reliably altered emotional processing in standardized tasks (Bershad et al., 2019; Marschall et al., 2021).

As mentioned, Grimm et al. (2018) showed 0.16 mg/kg of psilocybin slowed RTs for negative, neutral and positive faces without having a significant effect on accuracy. The same authors bring out an interesting point regarding the findings of Kometer et al. (2012) and Quednow et al. (2012). Research on psilocybin's effects has shown differing results depending on the task paradigm. In an emotional go/no-go task, psilocybin significantly increased RTs more for negative and neutral words compared to positive ones (Kometer et al., 2012), but

slowed RT across all conditions in a Stroop test in another study (Quednow et al., 2012). These findings suggest that psilocybin's effects are highly dependent on the specific cognitive and emotional demands of the task as the Stroop test does not engage emotional processing compared to an emotional go/no-go task.

Current studies on empathy demonstrated that psychedelics exert distinct, dose-dependent effects on cognitive and emotional empathy. All of the studies on empathy were conducted with MET, which makes it easier to compare the results and makes them more reliable. High dose of LSD (200 μg) enhanced both implicit and explicit emotional empathy, particularly for positive stimuli, when measured during the subacute phase, while both medium (100 μg) and high doses simultaneously reduced cognitive empathy (Dolder et al., 2016). Similar results on emotional empathy were found by Holze and colleagues (2021). Psilocybin showed more variable outcomes: a dose of 0.215 mg/kg increased emotional empathy independent of stimuli valence in healthy volunteers (Pokorny et al., 2017) and depressed patients (Jungwirth et al., 2024), with the latter study showing again increased empathy toward positive stimuli. However, a higher 15 mg dose showed no significant effects on empathy (Mallaroni et al., 2023).

Ayahuasca appeared to specifically enhance emotional empathy for negative stimuli when measured post-acutely (Uthaug et al., 2021). A recent meta-analysis that looked at the effects of classical psychedelics on the MET and incorporated open-design studies, brought out that these drugs significantly enhance explicit and implicit emotional empathy without affecting measures of cognitive empathy (Olami and Peled-Avron, 2024), which is similar to the results found in this review. As mentioned in the review, the increase in emotional empathy could be caused by ego dissolution that blurs the boundaries between the self and others.

Most studies found that higher doses of psychedelics have greater effects on psychological and cognitive functions than low- or microdoses. The effects of ketanserin (5-HT2A receptor antagonist) in attenuating these psychedelic effects showed mixed results. Ketanserin was effective in attenuating psilocybin's effects in attention tasks (Stroop Task - Quednow et al., 2012; FAIR task - Vollenweider et al., 2007) and blocked LSD-induced impairments in CF (IED task) and working memory (SWM task) (Pokorny et al., 2020). Ketanserin also reduced reaction time deficits in the working memory DRT task (Vollenweider et al., 1998). However, ketanserin did not affect performance in a multiple-object tracking attention task (Carter et al.,

2005), in the Emotional Go/No-Go task (Kometer et al., 2012) and did not alter LSD's effects on empathy (Holze et al., 2021). These results demonstrate that ketanserin inhibits psychedelic-induced impairments in cognitive flexibility and memory, but its effects on attention are task-dependent. Importantly, ketanserin doesn't significantly affect emotional processing or empathy, suggesting these psychedelic effects may involve non-5-HT2A receptors (Preller et al., 2017).

Drawbacks of measuring psychedelics' effects

Tests for measuring cognitive and psychological functions have many drawbacks. They are difficult to perform under the acute effects of psychedelics as they have an effect on top-down and bottom-up processes in the brain. However, this does not mean that attention is necessarily disturbed, it's just that information is processed in a different way or different aspects of the environment catch attention. For instance, under the effects of psilocybin, subjects reported that they understood the task requirements, but it was still harder to perform (Carter et al., 2005). It was reported that all of the dots became more dynamic and one participant compared it to children chasing each other. This increase in salience of all of the dots may have made it more difficult both to selectively track the target dots and to ignore the other ones. These effects can also be attributed to expanded attention that encompasses more of the dots. After pretreatment with 5-HT2A receptor antagonist, subjects reported that they no longer experienced the ‘‘personalities’’ within the stimulus, but reported difficulties with maintaining attention.

Dolder and colleagues (2016) found that moderate to high doses impaired the recognition of fearful faces but did not significantly affect the recognition of neutral, angry, or happy faces. This finding could mean that the effects of LSD vary depending on the emotional content of the sensory stimulus and thus different aspects of the environment catch attention. While the impaired recognition of fearful faces might suggest a more positive subjective experience—potentially due to a diminished perception of fear— psychedelic experiences are often emotionally ambivalent (Gashi et al., 2021). Dolder and colleagues' (2016) findings with psilocybin were not replicated in subsequent studies using LSD (Mueller et al., 2017) or psilocybin at different doses (Grimm et al., 2018). Additionally, a less explored area is how various types of open-eye visuals induced by psychedelics—such as enhancements, transformations, and overlays—impact attention allocation (Swanson, 2024). For example,

transformations and overlays might have bigger effects on attentional tasks performance as they change visual stimuli more profoundly, that may result in broadened attention (Carter et al., 2005). Investigating these aspects could provide insights into the interplay between perception and attention during psychedelic states.

Although only placebo-controlled studies were used in this systematic review, placebo (or nocebo) could have had an effect as it is a common problem in psychedelic research (Olson et al., 2020). It has been found that expectancy for escitalopram (a common SSRI) was associated with improved therapeutic outcomes to escitalopram, expectancy for psilocybin was not predictive of response to psilocybin (Szigeti et al., 2024). This suggests that the effects of psilocybin, and also maybe other psychedelics, cannot be fully explained by placebo alone. Self-reported expectancy may be a worse predictor of drug effects for psychedelics as they have a strong effect on cognition and consciousness (Nutt et al., 2020). Incorporating a similar approach into studies analyzed in this review—by asking participants to report their expectations before administration—could help disentangle the influence of expectancy on results.

The last result (Szigeti et al., 2024) is somewhat opposite to the Olson et al. study (2020) where the participants did not receive any drug (but believed that they did) but some participants felt the psychedelic effects measured with the "Five Dimensional Altered States of Consciousness" scale. These effects were induced through contextual factors and confederate behavior, highlighting the important role of environment and suggestion in shaping subjective experiences. Although it is important to note that most of the participants did not experience significant psychedelic effects.

Cognitive tests were employed at different timepoints during the trip, which make the results inconclusive and most of the analyzed studies had small samples, which is important as psychedelic experiences are often personal (Bălăeţ, 2022). Many of the participants were university students or part of an academic staff. The content of the trip is also time-dependent and depends on the individual (Lawrence et al., 2022). Among classical psychedelics, the cognitive and psychological effects of psilocybin and LSD have been studied more extensively than those of DMT and mescaline. Thus, it is possible that effects may vary by the classical psychedelic used. When administered intravenously, DMT induces vivid, immersive visions that are largely unaffected by whether the user's eyes are open or closed. Griffiths et

al. (2019) found that DMT users more frequently reported "complete" mystical experiences compared to users of psilocybin and LSD. This intensity makes it particularly challenging to assess DMT's effects on cognitive and psychological functions during the acute phase. DMT's psychological effects remain minimally reduced with repeated use compared to other classical psychedelics (Strassman et al., 1994). Thus, if it did not have intense visual effects, it could be better than other classical psychedelics for studying its effects of cognition as its results would not differ in naive and experienced users as the latter may have gotten used to psychedelic effects.

However, when DMT is ingested in combination with an MAOI agent, it becomes active orally and significantly longer lasting: this combination is known as ayahuasca (Brito-da-Costa et al., 2020). In addition to DMT ayahuasca also contains harmala alkaloids that can also have an effect on the psyche. The effects of ayahuasca last longer (4-6 hours) and it has more somatic effects (such as vomiting) compared to synthesized DMT (effects last approximately 5–20 minutes). The subjective experience is also different as the effects of ayahuasca seem to be milder (Lawrence et al., 2022; Riba et al., 2001). Ayahuasca also has more somatic effects (such as vomiting) compared to DMT and its hallucinogenic effects can last up to 4 to 6 hours. Mescaline in general has received less attention than other classical psychedelics as it has more somatic effects, for example, it can cause nausea (Deniker, 1957), and its effects can last longer than 10 to 12 hours (Vamvakopoulou et al., 2023). These effects complicate the use of ayahuasca and especially mescaline in cognitive and psychological studies, although for different reasons, making these psychedelics commonly less explored compared to psilocybin and LSD.

Some of the studies used other drugs as comparison to classic psychedelics, for example, 2C-B, DXM and ketamine were used (Barrett et al., 2018; Doss et al., 2024; Mallaroni et al., 2023; Schmidt et al., 2013), that caused similar effects to classical psychedelics. Their effects are different from usual placebo and thus it will be harder for participants to guess which psychedelic they got. As they still have considerable effect on the state of consciousness they could induce analogous expectancy to classical psychedelics. In future studies, it might be possible to use non-hallucinogenic psychedelics to see if they elicit the same changes in cognitive and psychological functions.

Conclusions

The recent resurgence in psychedelic research supports the potential of classical psychedelics to treat certain mental health disorders in controlled clinical settings (Andersen et al., 2020). However, their effects on cognitive and psychological functions remain less thoroughly explored. This review synthesized findings from 30 placebo-controlled studies investigating the acute and post-acute effects of psilocybin, DMT, and LSD on empathy, memory, emotional processing, reaction time, and cognitive flexibility. Psychedelics consistently enhanced emotional empathy, while effects on cognitive empathy were mixed or absent. Memory outcomes varied by task, dose and timing, ranging from impairments to no effect or improvement. Dose-dependent impairments were common in attention, reaction time, and inhibition, though some studies reported no changes. Emotional processing was often disrupted, especially in response to negative stimuli. Evidence on cognitive flexibility was limited and inconclusive. Most studies assessed only acute effects and many had small sample sizes. Placebo effects—particularly challenging in psychedelic research—also remain a significant methodological concern. Future research should explore how changes in cognitive and psychological functions relate to therapeutic benefits and integrate findings from both controlled trials and open-label studies to build a more comprehensive understanding.

References

Abramson, H. A. (1967). *The use of LSD in psychotherapy and alcoholism*. Bobbs-Merrill.

Abramson, H. A., Jarvik, M. E., & Hirsch, M. W. (1955). Lysergic acid diethylamide (LSD-25): X. Effect on reaction time to auditory and visual stimuli. *The Journal of Psychology: Interdisciplinary and Applied, 40*, 39–52. https://doi.org/10.1080/00223980.1955.9712962

Aday, J. S., Wood, J. R., Bloesch, E. K., & Davoli, C. C. (2021). Psychedelic drugs and perception: a narrative review of the first era of research. *Reviews in the Neurosciences*, *32*(5), 559–571. https://doi.org/10.1515/revneuro-2020-0094

Andersen, K. A. A., Carhart-Harris, R., Nutt, D. J., & Erritzoe, D. (2020). Therapeutic effects of classic serotonergic psychedelics: A systematic review of modern-era clinical studies. *Acta Psychiatrica Scandinavica, 143*(2), 101–118. https://doi.org/10.1111/acps.13249

Bălăeț, M. (2022). Psychedelic cognition—The unreached frontier of psychedelic science. *Frontiers in neuroscience*, *16*, 832375. https://doi.org/10.3389/fnins.2022.832375

Baron-Cohen, S., Wheelwright, S., Hill, J., Raste, Y., & Plumb, I. (2001). The "Reading the Mind in the Eyes" Test Revised Version: A Study with Normal Adults, and Adults with Asperger Syndrome or High-functioning Autism. *Journal of Child Psychology and Psychiatry*, *f*(2), 241–251. https://doi.org/10.1111/1469-7610.00715

Barrett, F. S., Carbonaro, T. M., Hurwitz, E., Johnson, M. W., & Griffiths, R. R. (2018). Double-blind comparison of the two hallucinogens psilocybin and dextromethorphan: effects on cognition. *Psychopharmacology*, *235*(10), 2915–2927. https://doi.org/10.1007/s00213-018-4981-x

Barrett, F. S., Krimmel, S. R., Griffiths, R. R., Seminowicz, D. A., & Mathur, B. N. (2020). Psilocybin acutely alters the functional connectivity of the claustrum with brain networks that support perception, memory, and attention. *NeuroImage*, *218*, 116980. https://doi.org/10.1016/j.neuroimage.2020.116980

Basedow, L. A., Majić, T., Hafiz, N. J., Algharably, E. A. E., Kreutz, R., & Riemer, T. G. (2024). Cognitive functioning associated with acute and subacute effects of classic psychedelics and MDMA - a systematic review and meta-analysis. Scientific Reports, *14*(1). https://doi.org/10.1038/s41598-024-65391-9

Bedi, G., Hyman, D., & de Wit, H. (2010). Is Ecstasy an "Empathogen"? Effects of ±3,4-Methylenedioxymethamphetamine on Prosocial Feelings and Identification of Emotional States in Others. *Biological Psychiatry*, *68*(12), 1134–1140. https://doi.org/10.1016/j.biopsych.2010.08.003

Belouin, S. J., & Henningfield, J. E. (2018). Psychedelics: Where we are now, why we got here, what we must do. *Neuropharmacology*, *142*, 7–19. https://doi.org/10.1016/j.neuropharm.2018.02.018

Bershad, A. K., Schepers, S. T., Bremmer, M. P., Lee, R., & de Wit, H. (2019). Acute Subjective and Behavioral Effects of Microdoses of Lysergic Acid Diethylamide in Healthy Human Volunteers. *Biological Psychiatry*, *86*(10), 792–800. https://doi.org/10.1016/j.biopsych.2019.05.019

Bezdicek, O., Stepankova, H., Moták, L., Axelrod, B. N., Woodard, J. L., Preiss, M., Nikolai, T., Růžička, E., & Poreh, A. (2013). Czech version of Rey Auditory Verbal Learning test: Normative data. *Aging, Neuropsychology, and Cognition*, *21*(6), 693–721. https://doi.org/10.1080/13825585.2013.865699

Bressloff, P. C., Cowan, J. D., Golubitsky, M., Thomas, P. J., & Wiener, M. C. (2002). What Geometric Visual Hallucinations Tell Us about the Visual Cortex. *Neural Computation*, *14*(3), 473–491. https://doi.org/10.1162/089976602317250861

Brito-da-Costa, A. M., Dias-da-Silva, D., Gomes, N. G. M., Dinis-Oliveira, R. J., & Madureira-Carvalho, Á. (2020). Toxicokinetics and Toxicodynamics of Ayahuasca Alkaloids N,N-Dimethyltryptamine (DMT), Harmine, Harmaline and Tetrahydroharmine: Clinical and Forensic Impact. *Pharmaceuticals*, *13*(11), 334. https://doi.org/10.3390/ph13110334

Busch, A. K., Johnson, W. C. (1950). L.S.D. 25 as an aid in psychotherapy; preliminary report of a new drug. *Diseases of the Nervous System*, 11, 241–243.

Cambridge Cognition. 2016. CANTAB® [cognitive assessment software]. All rights reserved. www.cantab.com

Carhart-Harris, R. L., Bolstridge, M., Rucker, J., Day, C. M. J., Erritzoe, D., Kaelen, M., Bloomfield, M., Rickard, J. A., Forbes, B., Feilding, A., Taylor, D., Pilling, S., Curran, V. H., & Nutt, D. J. (2016). Psilocybin with psychological support for treatment-resistant depression: an open-label feasibility study. *The Lancet Psychiatry*, *3*(7), 619–627. https://doi.org/10.1016/s2215-0366(16)30065-7

Carhart-Harris, R. L., Leech, R., Hellyer, P. J., Shanahan, M., Feilding, A., Tagliazucchi, E., ...Nutt, D. (2014). The entropic brain: a theory of conscious states informed by neuroimaging research with psychedelic drugs. *Frontiers in Human Neuroscience*, *8*. https://doi.org/10.3389/fnhum.2014.00020

Carter, Olivia L, David C Burr, John D Pettigrew, Guy M Wallis, Felix Hasler, and Franz X . (2005). "Using Psilocybin to Investigate the Relationship Between Attention, Working Memory, and the Serotonin 1a and 2a Receptors." *Journal of Cognitive Neuroscience*, *17*(10), 1497–1508. https://doi.org/10.1162/089892905774597191

Cavanna, F., Muller, S., de la Fuente, L. A., Zamberlan, F., Palmucci, M., Janeckova, L., ... & Tagliazucchi, E. (2022). Microdosing with psilocybin mushrooms: a double-blind placebo-controlled study. *Translational Psychiatry*, *12*(1), 307. https://doi.org/10.1038/s41398-022-02039-0

Chandler, A. L., & Hartman, M. A. (1960). Lysergic acid diethylamide (LSD-25) as a facilitating agent in psychotherapy. *A.M.A. Archives of General Psychiatry, 2,* 286–299. https://doi.org/10.1001/archpsyc.1960.03590090042008

Cowan, N. (2008). Chapter 20 What are the differences between long-term, short-term, and working memory? *Progress in Brain Research*, 323–338. https://doi.org/10.1016/s0079-6123(07)00020-9

Dajani, D. R., & Uddin, L. Q. (2015). Demystifying cognitive flexibility: Implications for clinical and developmental neuroscience. *Trends in neurosciences*, *38*(9), 571-578. https://doi.org/10.1016/j.tins.2015.07.003

Deniker, P. (1957). Biological changes in man following intravenous administration of mescaline. *The Journal of nervous and mental disease*, *125*(3), 427-431. https://doi.org/10.1097/00005053-195707000-00013

Deshon, H. J., Rinkel, M., & Solomon, H. C. (1952). Mental changes experimentally produced by L. S. D. (d-Lysergic acid diethylamide tartrate). *The Psychiatric Quarterly*, *26*(1–4), 33–53. https://doi.org/10.1007/bf01568448

Dinges, D. F., & Powell, J. W. (1985). Microcomputer analyses of performance on a portable, simple visual RT task during sustained operations. *Behavior Research Methods, Instruments, & Computers*, *17*(6), 652–655. https://doi.org/10.3758/bf03200977

de Wit, H., Molla, H. M., Bershad, A., Bremmer, M., & Lee, R. (2022). Repeated low doses of LSD in healthy adults: A placebo-controlled, dose–response study. *Addiction Biology*, *27*(2). https://doi.org/10.1111/adb.13143

de Wit, S., Watson, P., Harsay, H. A., Cohen, M. X., van de Vijver, I., & Ridderinkhof, K. R. (2012). Corticostriatal Connectivity Underlies Individual Differences in the Balance between Habitual and Goal-Directed Action Control. *The Journal of Neuroscience*, *32*(35), 12066–12075. https://doi.org/10.1523/jneurosci.1088-12.2012

Dolder, P. C., Schmid, Y., Müller, F., Borgwardt, S., & Liechti, M. E. (2016). LSD Acutely Impairs Fear Recognition and Enhances Emotional Empathy and Sociality. *Neuropsychopharmacology*, *41*(11), 2638–2646. https://doi.org/10.1038/npp.2016.82

Doss, M. K., Mallaroni, P., Mason, N. L., & Ramaekers, J. G. (2024). Psilocybin and 2C-B at Encoding Distort Episodic Familiarity. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *9*(10), 1048-1057. https://doi.org/10.1016/j.bpsc.2024.06.008

Dudysová, D., Fajnerová, I., Nekovářová, T., Ngo, H. V. V., & Kopřivová, J. (2016). Czech version of paired associative learning test–a pilot study. *Psychiatrie*, *20*(4), 174-177.

Dziobek, I., Rogers, K., Fleck, S., Bahnemann, M., Heekeren, H. R., Wolf, O. T., & Convit, A. (2007). Dissociation of Cognitive and Emotional Empathy in Adults with Asperger Syndrome Using the Multifaceted Empathy Test (MET). *Journal of Autism and Developmental Disorders*, *38*(3), 464–473. https://doi.org/10.1007/s10803-007-0486-x

Dykstra, L. A., & Appel, J. B. (1972). Lysergic Acid Diethylamide and Stimulus Generalization: Rate-Dependent Effects. *Science*, *177*(4050), 720–722. https://doi.org/10.1126/science.177.4050.720

Family, N., Maillet, E. L., Williams, L. T. J., Krediet, E., Carhart-Harris, R. L., Williams, T. M., Nichols, C. D., Goble, D. J., & Raz, S. (2019). Safety, tolerability, pharmacokinetics, and pharmacodynamics of low dose lysergic acid diethylamide (LSD) in healthy older volunteers. *Psychopharmacology*, *237*(3), 841–853. https://doi.org/10.1007/s00213-019-05417-7

Fischer, R., Hill, R., Thatcher, K., & Scheib, J. (1970). Psilocybin-induced contraction of nearby visual space. *Agents and Actions*, *1*(4), 190–197. https://doi.org/10.1007/bf01965761

Gashi, L., Sandberg, S., & Pedersen, W. (2021). Making "bad trips" good: How users of psychedelics narratively transform challenging trips into valuable experiences. *International Journal of Drug Policy*, *87*, 102997. https://doi.org/10.1016/j.drugpo.2020.102997

Girn, M., Rosas, F. E., Daws, R. E., Gallen, C. L., Gazzaley, A., & Carhart-Harris, R. L. (2023). A complex systems perspective on psychedelic brain action. *Trends in Cognitive Sciences*, *27*(5), 433–445. https://doi.org/10.1016/j.tics.2023.01.003

Gloster, A. T., Meyer, A. H., & Lieb, R. (2017). Psychological flexibility as a malleable public health target: Evidence from a representative sample. *Journal of Contextual Behavioral Science*, *6*(2), 166–171. https://doi.org/10.1016/j.jcbs.2017.02.003

Griffiths, R. R., Hurwitz, E. S., Davis, A. K., Johnson, M. W., & Jesse, R. (2019). Survey of subjective "God encounter experiences": Comparisons among naturally occurring experiences and those occasioned by the classic psychedelics psilocybin, LSD, ayahuasca, or DMT. *PLOS ONE*, *14*(4), e0214377. https://doi.org/10.1371/journal.pone.0214377

Griffiths, S., Jarrold, C., Penton-Voak, I. S., & Munafò, M. R. (2015). Feedback training induces a bias for detecting happiness or fear in facial expressions that generalises to a

novel task. *Psychiatry Research*, 230(3), 951–957. https://doi.org/10.1016/j.psychres.2015.11.007

Griffiths, R. R., Richards, W. A., McCann, U., Jesse, R. (2006). Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. *Psychopharmacology*, *187*, 268–283. https://doi.org/10.1007/s00213-006-0457-5

Grimm, O., Kraehenmann, R., Preller, K. H., Seifritz, E., & Vollenweider, F. X. (2018). Psilocybin modulates functional connectivity of the amygdala during emotional face discrimination. *European Neuropsychopharmacology*, *28*(6), 691-700. https://doi.org/10.1016/j.euroneuro.2018.03.016

Gur, R. C., Richard, J., Hughett, P., Calkins, M. E., Macy, L., Bilker, W. B., Brensinger, C., & Gur, R. E. (2010). A cognitive neuroscience-based computerized battery for efficient measurement of individual differences: Standardization and initial construct validation. *Journal of Neuroscience Methods*, *187*(2), 254–262. https://doi.org/10.1016/j.jneumeth.2009.11.017

Guerra-Doce, E. (2015). Psychoactive Substances in Prehistoric Times: Examining the Archaeological Evidence. *Time and Mind*, *8*(1), 91–112. https://doi.org/10.1080/1751696x.2014.993244

Heaton, K. R., Chelune, G. J., Talley, J. L., Kay, G. G., Curtiss, G., & Cunha, J. A. (2005). Manual do teste Wisconsin de Classificação de Cartas. *São Paulo: Casa do Psicólogo*, *346*.

Hofmann, A. (2013). *LSD: My problem child*. Oxford University Press, USA.

Holze, F., Avedisian, I., Varghese, N., Eckert, A., & Liechti, M. E. (2021). Role of the 5-HT2A receptor in acute effects of LSD on empathy and circulating oxytocin. *Frontiers in Pharmacology*, *12*, 711255. https://doi.org/10.3389/fphar.2021.711255

Hutten, N. R., Mason, N. L., Dolder, P. C., Theunissen, E. L., Holze, F., Liechti, M. E., ... & Kuypers, K. P. (2020). Mood and cognition after administration of low LSD doses in healthy volunteers: A placebo controlled dose-effect finding study. *European*

Neuropsychopharmacology, *41*, 81-91. https://doi.org/10.1016/j.euroneuro.2020.10.002

Jaeggi, S. M., Buschkuehl, M., Jonides, J., & Perrig, W. J. (2008). Improving fluid intelligence with training on working memory. *Proceedings of the National Academy of Sciences*, *105*(19), 6829–6833. https://doi.org/10.1073/pnas.0801268105

Jungwirth, J., von Rotz, R., Dziobek, I., Vollenweider, F. X., & Preller, K. H. (2024). Psilocybin increases emotional empathy in patients with major depression. *Molecular Psychiatry*. https://doi.org/10.1038/s41380-024-02875-0

Kanen, J. W., Luo, Q., Rostami Kandroodi, M., Cardinal, R. N., Robbins, T. W., Nutt, D. J., Carhart-Harris, R. L., & den Ouden, H. E. M. (2022). Effect of lysergic acid diethylamide (LSD) on reinforcement learning in humans. *Psychological Medicine*, *53*(14), 6434–6445. https://doi.org/10.1017/s0033291722002963

Kometer, M., Schmidt, A., Bachmann, R., Studerus, E., Seifritz, E., & Vollenweider, F. X. (2012). Psilocybin biases facial recognition, goal-directed behavior, and mood state toward positive relative to negative emotions through different serotonergic subreceptors. *Biological psychiatry*, *72*(11), 898-906. https://doi.org/10.1016/j.biopsych.2012.04.005

Kwan, A. C., Olson, D. E., Preller, K. H., & Roth, B. L. (2022). The neural basis of psychedelic action. *Nature Neuroscience*, *25*(11), 1407–1419. https://doi.org/10.1038/s41593-022-01177-4

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (1997). International affective picture system (IAPS): Technical manual and affective ratings. *NIMH Center for the Study of Emotion and Attention*, *1*(39-58), 3.

Lawrence, D. W., Carhart-Harris, R., Griffiths, R., & Timmermann, C. (2022). Phenomenology and content of the inhaled N, N-dimethyltryptamine (N, N-DMT) experience. *Scientific Reports*, *12*(1). https://doi.org/10.1038/s41598-022-11999-8

Liebert, R. S. (1957). Studies in the Effects of Lysergic Acid Diethylamide (LSD-25). *A.M.A. Archives of Neurology & Psychiatry*, *77*(2), 193. https://doi.org/10.1001/archneurpsyc.1957.02330320091012

Malitz, S., Esecover, H., Wilkens, B., & Hoch, P. H. (1960). Some observations on psilocybin, a new hallucinogen, in volunteer subjects. *Comprehensive Psychiatry*, *1*(1), 8–17. https://doi.org/10.1016/s0010-440x(60)80045-4

Mallaroni, P., Mason, N. L., Reckweg, J. T., Paci, R., Ritscher, S., Toennes, S. W., Theunissen, E. L., Kuypers, K. P. C., & Ramaekers, J. G. (2023). Assessment of the Acute Effects of 2C-B vs. Psilocybin on Subjective Experience, Mood, and Cognition. *Clinical Pharmacology & Therapeutics*, *114*(2), 423–433. https://doi.org/10.1002/cpt.2958

Marschall, J., Fejer, G., Lempe, P., Prochazkova, L., Kuchar, M., Hajkova, K., & van Elk, M. (2021). Psilocybin microdosing does not affect emotion-related symptoms and processing: A preregistered field and lab-based study. *Journal of Psychopharmacology*, *36*(1), 97-113. https://doi.org/10.1177/02698811211050556

McLeod, D. R., Griffiths, R. R., Bigelow, G. E., & Yingling, J. (1982). An automated version of the digit symbol substitution test (DSST). *Behavior Research Methods & Instrumentation*, *14*(5), 463–466. https://doi.org/10.3758/bf03203313

Moosbrugger, H., & Oehlschlägel, J. (1996). FAIR: Frankfurter Aufmerksamkeits-Inventar [FAIR: Frankfurt Attention Inventory]. *Bern, Switzerland: Huber*.

Mueller, F., Lenz, C., Dolder, P. C., Harder, S., Schmid, Y., Lang, U. E., Liechti, M. E., & Borgwardt, S. (2017). Acute effects of LSD on amygdala activity during processing of fearful stimuli in healthy subjects. *Translational Psychiatry*, *7*(4), e1084–e1084. https://doi.org/10.1038/tp.2017.54

Murphy, R. J., Sumner, R., Evans, W., Ponton, R., Ram, S., Godfrey, K., Forsyth, A., Cavadino, A., Krishnamurthy Naga, V., Smith, T., Hoeh, N. R., Menkes, D. B., & Muthukumaraswamy, S. (2023). Acute Mood-Elevating Properties of Microdosed Lysergic Acid Diethylamide in Healthy Volunteers: A Home-Administered Randomized Controlled Trial. *Biological Psychiatry*, *94*(6), 511–521. https://doi.org/10.1016/j.biopsych.2023.03.013

Nikolič, M., Viktorin, V., Zach, P., Tylš, F., Dudysová, D., Janků, K., ... & Páleníček, T. (2023). Psilocybin intoxication did not affect daytime or sleep-related declarative

memory consolidation in a small sample exploratory analysis. *European Neuropsychopharmacology*, *74*, 78-88. https://doi.org/10.1016/j.euroneuro.2023.04.019

Nosek, B. A., & Banaji, M. R. (2001). The Go/No-go Association Task. *Social Cognition, 19*(6), 625–666. https://doi.org/10.1521/soco.19.6.625.20886

Nour, M. M., Evans, L., Nutt, D., & Carhart-Harris, R. L. (2016). Ego-Dissolution and Psychedelics: Validation of the Ego-Dissolution Inventory (EDI). *Frontiers in Human Neuroscience*, *10*. https://doi.org/10.3389/fnhum.2016.00269

Nutt, D., Erritzoe, D., Carhart-Harris, R. (2020). Psychedelic Psychiatry's Brave New World. *Cell*, *181*(1), 24–28. https://doi.org/10.1016/j.cell.2020.03.020

Nutt, D. (2019). Psychedelic drugs—a new era in psychiatry? Dialogues in Clinical *Neuroscience*, *21*(2), 139–147. https://doi.org/10.31887/dcns.2019.21.2/dnutt

Olami, A., & Peled-Avron, L. (2024). Effects of classical psychedelics on implicit and explicit emotional empathy and cognitive empathy: a meta-analysis of MET task. *Scientific Reports*, *14*(1), 24480. https://doi.org/10.1038/s41598-024-74810-w

Olson, J. A., Suissa-Rocheleau, L., Lifshitz, M., Raz, A., & Veissière, S. P. L. (2020). Tripping on nothing: placebo psychedelics and contextual factors. *Psychopharmacology*, *237*(5), 1371–1382. https://doi.org/10.1007/s00213-020-05464-5

Owen, A. M., Roberts, A. C., Polkey, C. E., Sahakian, B. J., & Robbins, T. W. (1991). Extra-dimensional versus intra-dimensional set shifting performance following frontal lobe excisions, temporal lobe excisions or amygdalo-hippocampectomy in man. *Neuropsychologia*, *29*(10), 993–1006. https://doi.org/10.1016/0028-3932(91)90063-e

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., … Moher, D. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Systematic Reviews*, *10*(1). https://doi.org/10.1186/s13643-021-01626-4

Park, S., & Holzman, P. S. (1992). Schizophrenics show spatial working memory deficits. *Archives of general psychiatry*, *49*(12), 975-982.

Phillips, L. H., Wynn, V. E., McPherson, S., & Gilhooly, K. J. (2001). Mental planning and the Tower of London task. *The Quarterly Journal of Experimental Psychology Section A*, *54*(2), 579–597. https://doi.org/10.1080/713755977

Pylyshyn, Z. W., & Storm, R. W. (1988). Tracking multiple independent targets: Evidence for a parallel tracking mechanism. *Spatial vision*, *3*(3), 179-197.

Pokorny, T., Duerler, P., Seifritz, E., Vollenweider, F. X., & Preller, K. H. (2019). LSD acutely impairs working memory, executive functions, and cognitive flexibility, but not risk-based decision-making. *Psychological Medicine*, *50*(13), 2255–2264. https://doi.org/10.1017/s0033291719002393

Pokorny, T., Preller, K. H., Kometer, M., Dziobek, I., & Vollenweider, F. X. (2017). Effect of Psilocybin on Empathy and Moral Decision-Making. *International Journal of Neuropsychopharmacology*, *20*(9), 747–757. https://doi.org/10.1093/ijnp/pyx047

Preller K. H., Herdener, M., Pokorny, T., Planzer, A., Kraehenmann, R., Stämpfli, P., ... Vollenweider, F. X. (2017). The Fabric of Meaning and Subjective Effects in LSD Induced States Depend on Serotonin 2A Receptor Activation. *Current Biology*, *27*(3), 451–457. https://doi.org/10.1016/j.cub.2016.12.030

Quednow, B. B., Kometer, M., Geyer, M. A., & Vollenweider, F. X. (2012). Psilocybin-induced deficits in automatic and controlled inhibition are attenuated by ketanserin in healthy human volunteers. *Neuropsychopharmacology*, *37*(3), 630-640. https://doi.org/10.1038/npp.2011.228

Rasch, B., Büchel, C., Gais, S., & Born, J. (2007). Odor Cues During Slow-Wave Sleep Prompt Declarative Memory Consolidation. *Science*, *315*(5817), 1426–1429. https://doi.org/10.1126/science.1138581

Riba, J., Rodríguez-Fornells, A., Urbano, G., Morte, A., Antonijoan, R., Montero, M., Callaway, J. C., & Barbanoj, M. J. (2001). Subjective effects and tolerability of the South American psychoactive beverage Ayahuasca in healthy volunteers. *Psychopharmacology*, *154*(1), 85–95. https://doi.org/10.1007/s002130000606

Reitan, R. M., & Wolfson, D. (1995). Category test and trail making test as measures of frontal lobe functions. *The Clinical Neuropsychologist*, *9*(1), 50–56. https://doi.org/10.1080/13854049508402057

Rey, A. (1999). Teste de cópia e de reprodução de memória de figuras geométricas complexas: Manual. *Adaptação e Padronização Brasileira*, *1*.

Rostami Kandroodi, M., Cook, J. L., Swart, J. C., Froböse, M. I., Geurts, D. E. M., Vahabie, A.-H., Nili Ahmadabadi, M., Cools, R., & den Ouden, H. E. M. (2021). Effects of methylphenidate on reinforcement learning depend on working memory capacity. *Psychopharmacology*, *238*(12), 3569–3584. https://doi.org/10.1007/s00213-021-05974-w

Shapiro, K. L., Raymond, J. E., & Arnell, K. M. (1997). The attentional blink. *Trends in cognitive sciences*, *1*(8), 291-296.

Schmidt, A., Kometer, M., Bachmann, R., Seifritz, E., & Vollenweider, F. (2013). The NMDA antagonist ketamine and the 5-HT agonist psilocybin produce dissociable effects on structural encoding of emotional face expressions. *Psychopharmacology*, *225*(1), 227–239. https://doi.org/10.1007/s00213-012-2811-0

Schmidt, A., Müller, F., Lenz, C., Dolder, P. C., Schmid, Y., Zanchi, D., Lang, U. E., Liechti, M. E., & Borgwardt, S. (2017). Acute LSD effects on response inhibition neural networks. *Psychological Medicine*, *48*(9), 1464–1473. https://doi.org/10.1017/s0033291717002914

Snyder, P. J., Bednar, M. M., Cromer, J. R., & Maruff, P. (2005). Reversal of scopolamine-induced deficits with a single dose of donepezil, an acetylcholinesterase inhibitor. *Alzheimer's & Dementia*, *1*(2), 126–135. https://doi.org/10.1016/j.jalz.2005.09.004

Strassman, R. J. (1994). Dose-Response Study of N,N-Dimethyltryptamine in Humans. *Archives of General Psychiatry*, *51*(2), 98. https://doi.org/10.1001/archpsyc.1994.03950020022002

Stroop, J. R. (1935). Studies of interference in serial verbal reactions. *Journal of experimental psychology*, *18*(6), 643.

Szigeti, B., Weiss, B., Rosas, F. E., Erritzoe, D., Nutt, D., & Carhart-Harris, R. (2024). Assessing expectancy and suggestibility in a trial of escitalopram v. psilocybin for depression. *Psychological Medicine*, *54*(8), 1717–1724. https://doi.org/10.1017/s0033291723003653

Swanson, L. R. (2024). Psychedelic visuals in context. *Philosophical Perspectives on Psychedelic Psychiatry*, 116-138.

Uthaug, M. V., Mason, N. L., Toennes, S. W., Reckweg, J. T., de Sousa Fernandes Perna, E. B., Kuypers, K. P. C., van Oorsouw, K., Riba, J., & Ramaekers, J. G. (2021). A placebo-controlled study of the effects of ayahuasca, set and setting on mental health of participants in ayahuasca group retreats. *Psychopharmacology*, *238*(7), 1899–1910. https://doi.org/10.1007/s00213-021-05817-8

Vamvakopoulou, I. A., Narine, K. A., Campbell, I., Dyck, J. R., & Nutt, D. J. (2023). Mescaline: The forgotten psychedelic. *Neuropharmacology*, *222*, 109294. https://doi.org/10.1016/j.neuropharm.2022.109294

Vollenweider, F. X., Csomor, P. A., Knappe, B., Geyer, M. A., & Quednow, B. B. (2007). The effects of the preferential 5-HT2A agonist psilocybin on prepulse inhibition of startle in healthy human volunteers depend on interstimulus interval. *Neuropsychopharmacology*, *32*(9), 1876-1887. https://doi.org/10.1038/sj.npp.1301324

Vollenweider, F. X., Vollenweider-Scherpenhuyzen, M. F. I., Bäbler, A., Vogel, H., & Hell, D. (1998). Psilocybin induces schizophrenia-like psychosis in humans via a serotonin-2 agonist action. *NeuroReport*, *9*(17), 3897–3902. https://doi.org/10.1097/00001756-199812010-00024

Wardle, M. C., Garner, M. J., Munafò, M. R., & de Wit, H. (2012). Amphetamine as a social drug: effects of d-amphetamine on social processing and behavior. *Psychopharmacology*, *223*(2), 199–210. https://doi.org/10.1007/s00213-012-2708-y

Wesson, D. R. (2011). Psychedelic Drugs, Hippie Counterculture, Speed and Phenobarbital Treatment of Sedative-Hypnotic Dependence: A Journey to the Haight Ashbury in the

Sixties. *Journal of Psychoactive Drugs*, *43*(2), 153–164. https://doi.org/10.1080/02791072.2011.587708

Williams, K.D., Jarvis, B. (2006) Cyberball: A program for use in research on interpersonal ostracism and acceptance. *Behavior Research Methods*, *38*, 174–180. https://doi.org/10.3758/BF0319276

Wießner, I., Olivieri, R., Falchi, M., Palhano-Fontes, F., Oliveira Maia, L., Feilding, A., B. Araujo, D., Ribeiro, S., & Tófoli, L. F. (2022). LSD, afterglow and hangover: Increased episodic memory and verbal fluency, decreased cognitive flexibility. *European Neuropsychopharmacology*, *58*, 7–19. https://doi.org/10.1016/j.euroneuro.2022.01.114

Wittmann, M., Carter, O., Hasler, F., Cahn, B. R., Grimberg, U., Spring, P., ... & Vollenweider, F. X. (2007). Effects of psilocybin on time perception and temporal control of behaviour in humans. *Journal of Psychopharmacology*, *21*(1), 50-64. https://doi.org/10.1177/0269881106065859

Lihtlitsents lõputöö reprodutseerimiseks ja üldsusele kättesaadavaks tegemiseks

Mina, Marten Kase ,

1. annan Tartu Ülikoolile tasuta loa (lihtlitsentsi) minu loodud teose
   „LSD, DMT ja psilotsübiini mõju kognitiivsetele ja psühholoogilistele funktsioonidele: süstemaatiline ülevaade kirjandusest“ ,

   mille juhendaja(d) on Jaan Aru ja Karl Kristjan Kaup ,

reprodutseerimiseks eesmärgiga seda säilitada, sealhulgas lisada Tartu Ülikooli digitaalarhiivi kuni autoriõiguse kehtivuse lõppemiseni;

2. annan Tartu Ülikoolile loa teha punktis 1 nimetatud teos üldsusele kättesaadavaks Tartu Ülikooli veebikeskkonna, sealhulgas digitaalarhiivi kaudu Creative Commonsi litsentsiga CC BY NC ND 4.0, mis lubab autorile viidates teost reprodutseerida, levitada ja üldsusele suunata ning keelab luua tuletatud teost ja kasutada teost ärieesmärgil, kuni autoriõiguse kehtivuse lõppemiseni;

3. olen teadlik, et punktides 1 ja 2 nimetatud õigused jäävad alles ka autorile;

4. kinnitan, et lihtlitsentsi andmisega ei riku ma teiste isikute intellektuaalomandi ega isikuandmete kaitse õigusaktidest tulenevaid õigusi.

Marten Kase

12.05.2025