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ORIGINAL INVESTIGATION

LSD enhances the emotional response to music

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Abstract
Rationale There is renewed interest in the therapeutic potential of psychedelic drugs such as lysergic acid diethylamide (LSD). LSD was used extensively in the 1950s and 1960s as an adjunct in psychotherapy, reportedly enhancing emotionality. Music is an effective tool to evoke and study emotion and is considered an important element in psychedelic-assisted psychotherapy; however, the hypothesis that psychedelics enhance the emotional response to music has yet to be investigated in a modern placebo-controlled study.
Objectives The present study sought to test the hypothesis that music-evoked emotions are enhanced under LSD.
Methods Ten healthy volunteers listened to five different tracks of instrumental music during each of two study days, a placebo day followed by an LSD day, separated by 5–7 days. Subjective ratings were completed after each music track and included a visual analogue scale (VAS) and the nine-item Geneva Emotional Music Scale (GEMS-9).
Results Results demonstrated that the emotional response to music is enhanced by LSD, especially the emotions "wonder", "transcendence", "power" and "tenderness".
Conclusions These findings reinforce the long-held assumption that psychedelics enhance music-evoked emotion, and provide tentative and indirect support for the notion that this effect can be harnessed in the context of psychedelic-assisted psychotherapy. Further research is required to test this link directly.

Keywords LSD · Serotonin 2A receptor · Psychotherapy · Psychedelic · Music · Emotion

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Introduction

Lysergic acid diethylamide (LSD) is a "classic" psychedelic[1] drug that elicits profound changes in consciousness with a remarkable potency (Schmid et al. 2015; Passie et al. 2008; Nichols 2004). Although much emphasis has been placed on their hallucinogenic properties, psychedelic drugs have a range of other interesting psychological effects. For example, they have marked effects on emotion, which is

[1] The word psychedelic is derived from combining the Greek words *psyché* meaning "mind" or "soul" and *dêlos*, meaning "to manifest" or "make visible". In addition to LSD, other drugs considered classic psychedelics include psilocybin (the major psychoactive constituent of magic mushrooms), mescaline (a psychoactive constituent of peyote and San Pedro cacti) and DMT (a major psychoactive ingredient in the Amazonian brew ayahuasca). All these drugs share the property of being agonists at the serotonin 2A receptor. The use of the term "psychedelics" in this paper refers specifically to classic psychedelics such as those listed above.

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one of the reasons why they were used in psychotherapy in the 1950s and 1960s. The dominant therapeutic model at the time maintained that by dismantling "ego defences", psychedelics facilitate emotional release (i.e. "catharsis") and insight (Busch and Johnson 1950; Leuner 1983; Cohen 1970). Broadly speaking, this approach is still adopted today in clinical studies with psychedelics (Bogenschutz et al. 2015; Johnson et al. 2014; Gasser et al. 2014a, b; Grob et al. 2011).

Music is a classic means of evoking emotion, and like LSD, it has also been used as an adjunct to psychotherapy (Koelsch 2014; Moore 2013). Music has accompanied ceremonial use of psychedelics for many centuries (Nettl 1956), was a staple component in psychedelic-assisted psychotherapy in the 1950s and 1960s (Bonny and Pahnke 1972; Grof 1980) and remains so today (Bogenschutz et al. 2015; Johnson et al. 2014; Gasser et al. 2014a, b; Grob et al. 2011). It has been proposed that listening to music during a psychedelic experience is useful for (1) encouraging the relinquishment of control, (2) facilitating emotional arousal and release, (3) promoting the occurrence of "peak" or spiritual-type experiences, (4) directing and/or structuring the experience and (5) stimulating the imagination (Bonny and Pahnke 1972; Grof 1980). Profound spiritual- or mystical-type experiences were reported by a majority of participants in a study with another psychedelic drug, psilocybin, while they listened to emotionally evocative music (Griffiths et al. 2006, 2011). This raises an important question: what is the role of music in producing such profound psychological experiences?

The significance of music in psychedelic-assisted psychotherapy has previously been discussed (Eagle 1972; Gaston and Eagle 1970; Bonny and Pahnke 1972; Turek et al. 1974) but has never been investigated in a modern placebo-controlled study. The present study sought to address this knowledge gap by testing the hypothesis that the emotional response to music is enhanced under LSD. Participants listened to five different instrumental music tracks on each of two study days: a placebo day followed by an LSD day, separated by 5–7 days. The question "How emotionally affected were you by the music?" was asked immediately after each track and served as the study's primary outcome. To probe more specific aspects of participants' emotional experiences during music listening, the Geneva Emotional Music Scale (GEMS-9) was also used (Zentner et al. 2008). The GEMS-9 has been developed to measure a range of emotions that can be experienced during music listening, and this was completed after each music track. It was predicted that it would be specifically emotions related to "transcendence" that would be enhanced, i.e. feeling "fascinated and overwhelmed" and "feelings of transcendence and spirituality", as defined by the GEMS-9.

Methods

Approvals

This study was approved by the National Research Ethics Service (NRES) London—West London and was conducted in accordance with the revised declaration of Helsinki (2000), the International Committee on Harmonisation Good Clinical Practice guidelines and NHS Research Governance Framework. Imperial College London sponsored the research which was conducted under a Home Office licence for research with schedule 1 drugs.

Recruitment and screening of participants

Participants were recruited via word of mouth and gave written informed consent before participating. They were briefed on the general experimental procedures, but no information regarding hypotheses of the experiments was shared. Prior to study enrolment, all participants were screened in a clinical research centre at the Hammersmith hospital campus of Imperial College London (the Wellcome Trust Clinical Research Facility, WTCRF). Demographic information was recorded and medical history taken. A physical examination was performed, including electrocardiogram (ECG), routine blood tests and blood pressure measurement. A psychiatric assessment was conducted and participants gave full disclosure of their drug taking histories. Participants completed the Beck Depression Inventory (BDI) (Beck et al. 1961) and the 60-item Neuroticism-Extraversion-Openness Five-Factor Inventory (NEO-FFI) personality scale (McCrae and Costa 1987) and were properly briefed on the study and the potential drug effects.

Key exclusion criteria were as follows: <21 years of age, personal history of diagnosed psychiatric illness, immediate family history of a psychotic disorder, an absence of previous experience with a classic psychedelic (e.g. LSD, mescaline, psilocybin/magic mushrooms or DMT/ayahuasca), having experienced a persistent adverse reaction after psychedelic drug use, pregnancy, problematic alcohol use (i.e. >40 units consumed per week) or a medically significant condition rendering the volunteer unsuitable for the study.

Drug dosing

One thousand micrograms of LSD freebase (certified 99.4 % purity) was reconstituted with 10 ml saline and sterile filtered, yielding a 100 μg:1 ml sterile solution. Since a primary motivation of the study was to determine a safe and appropriate dose of LSD for a subsequent neuroimaging study, the dosage of LSD varied among participants, i.e. one received 40 μg, two 50 μg, six 70 μg and one 80 μg. For each administration, the appropriate amount of LSD solution (e.g. 0.7 ml=70 μg)

was transferred to a 10-ml syringe and made up to 10 ml with saline. The 10-ml solution was then infused intravenously over a 3-min period, followed by a 60-s infusion ("flush") with 10 ml saline.

Study setting

Both study days were performed at the WTCRF at the Hammersmith Hospital. All experiments took place in a clinical room, consisting of a hospital bed, physiological monitoring equipment and en suite facilities. Since psychedelics have the potential to induce psychological distress, the clinical conditions of the room were adapted to promote feelings of comfort and safety, i.e. the lighting was dimmed and the room was decorated with soft furnishings (Johnson et al. 2008). The setting was identical for all study days.

Experimental procedures

Participants were carefully prepared for the drug experience at screening, and the study was conducted in accordance with guidelines for the safe management of psychedelic drug sessions (Johnson et al. 2008). After screening, eligible participants attended the two study days, with at least 5 days in between, and were told they would receive LSD on one of these two occasions but were not told which. Placebo (10 ml saline) was always administered on the first day, thus avoiding potential carry-over effects (e.g. residual psychological effects) of LSD. Participants were blind to the condition (i.e. drug or placebo) but the researchers were not. Volunteers arrived at the research centre between 10.00 a.m. and 11.00 a.m. on testing days, were briefed about the study procedure, gave a urine test for drugs of abuse and pregnancy (where relevant) and carried out a breathalyser test for recent alcohol use. A cannula was inserted into a vein in the antecubital fossa by a medical doctor and secured. Subsequently, volunteers were encouraged to close their eyes and relax in a reclined position before a 10-ml solution of saline alone (placebo) or containing LSD was intravenously infused over a period of 3 min. Blood pressure was measured prior to dosing (baseline), 45 min after dosing and at the end of the study day (prior to discharge). Heart rate was recorded at regular intervals, together with self-ratings of the subjective intensity of the drug effects on a scale of 0 ("no effects") to 10 ("extremely intense effects"). These measurements were taken every 1–5 min during the first 45 min post-infusion and then continued in intervals of approximately 30–45 min until the end of the experiment. During the initial 45-min post-infusion, participants were encouraged to relax with their eyes closed and maintain a supine position while listening to music by the ambient music artists "Stars of The Lid". This music was only played during the initial 45 min and not during the subsequent psychological testing. Participants reported first noticing subjective drug effects between 5 to 15 min post-dosing, and these approached peak intensity between 45 to 90 min post-dosing. The duration of a subsequent plateau of drug effects varied among individuals but was generally maintained for approximately 3 h post-dosing. Psychological tests were performed within this time frame. Five music tracks were played to each participant during each session at the following time points post-dosing (minutes: mean, SD): 44±17 (track 1), 101±25 (track 2), 139±33 (tracks 3 and 4) and 250±53 (track 5). Once the subjective effects of LSD had sufficiently subsided, participants completed a 29-item questionnaire enquiring about the drug's subjective effects (see Carhart-Harris et al. 2012). Following this, the study psychiatrist assessed the participant's suitability for discharge. Participants remained in the research centre for an average of 6 h post-infusion. The results of other psychological tests performed during the study are published elsewhere (Carhart-Harris et al. 2014).

Stimulus selection and task design

Two playlists were compiled (A and B), each containing five different music tracks. One version was heard on the first study day and the other on the second, with the order of the playlists counterbalanced across participants. The emotional potency of the two lists was balanced based on pre-study ratings from a separate sample of nine participants. Pre-ratings were provided for 16 instrumental music tracks of the classical, neo-classical, ambient and new-age genres using the GEMS-9. In addition, the tracks were also rated for general liking and familiarity. It was from the subsequent ratings that ten tracks were selected for the study. Specifically, tracks were chosen that produced the highest liking and lowest familiarity, and a two-tailed paired *t* test confirmed no significant differences between the playlists on liking, familiarity and GEMS-9 scores. The final five tracks selected for each playlist consisted of neo-classical and ambient music composed by the following four contemporary musicians: Greg Haines, Ólafur Arnalds, Arve Henriksen and Brian McBride (see Table 1). Each music track and all rating scales were presented via PsychoPy presentation software (Peirce 2008). Before listening to a music track, participants were instructed to close their eyes and relax. Music was played via high-quality stereo headphones (Beyerdynamic DT990 Pro), and participants were allowed to adjust the volume via remote volume control. When the music ended, a pre-recorded voice instructed them to open their eyes. They were then presented with the question "How emotionally affected were you by the music?" Participants gave ratings via a continuous visual analogue scale from 0 ("not at all") to 100 ("very much"). Following this, a digitalised and shortened version of the full GEMS, the GEMS-9, was presented (Zentner et al. 2008). A particularly

Table 1 The two playlists utilised for the study

Stimulus	Artist name	Playlist A		Playlist B	
		Track title	Duration	Track title	Duration
1	Greg Haines	183 Times	09:08	Azure	14:14
2	Brian McBride	Toil theme part 2 & part 3	05:11	Supposed Essay on the Piano	04:10
3	Ólafur Arnalds	The Wait	03:35	Autumn Day	03:26
4	Brian McBride	Mélodrames Télégraphiés Part 2	04:12	Mélodrames Télégraphiés Part 1	05:25
5	Arve Henriksen	In the Light	05:29	Leaf and Rock	02:17

important instruction given prior to completing the questionnaire was that participants should rate how he or she personally felt *in response to* the music and not what he or she thought the music was trying to communicate to them or how he or she felt in general. The GEMS-9 consists of nine items or categories of emotion, with sub-items presented in brackets: wonder (filled with wonder, dazzled, moved), transcendence (fascinated, overwhelmed, feelings of transcendence and spirituality), power (strong, triumphant, energetic), tenderness (tender, affectionate, in love), nostalgia (nostalgic, dreamy, melancholic), peacefulness (serene, calm, soothed), joyful activation (joyful, amused, bouncy), sadness (sad, sorrowful) and tension (tense, agitated, nervous). Each item was scored from 0 to 4: 0 = "not at all", 1 = "somewhat", 2 = "moderately", 3 = "quite a lot" and 4 = "very much".

Data analysis

All statistical tests were performed in Statistical Package for the Social Sciences (SPSS) for Windows, Version 21.0. Scores for the question "How emotionally affected were you by the music?" for each stimulus were averaged for each subject per condition. A paired two-tailed *t* test was performed to test for significant difference between conditions.

Since the five possible ratings for the GEMS-9 were ascribed a relevant number (e.g. 0 = "not at all", 1 = "somewhat") and the resultant data was normally distributed, two-tailed paired *t* tests were used to analyse between-condition differences. Subsequent false discovery rate (FDR) control was used to correct for multiple comparisons (Benjamini and Hochberg 1995).

Finally, a Pearson correlational analysis was performed to evaluate a hypothesised relationship between the peak intensity of LSD's subjective effects and the intensity of emotional arousal in response to music under LSD (i.e. the average score for all music stimuli to the question "How emotionally affected were you by the music?") as well as the relationship between peak drug intensity and increases in the GEMS-9 item "transcendence".

Results

Participant demographics

Ten healthy volunteers participated in the study (one female; mean age=34.2±7.4, range=26–47 years). All had at least one previous experience with a classic psychedelic drug (mean estimated LSD uses=65±90, range=0–250) but not within 21 days of the study (mean last use of LSD=1829±2348, range=30–5000 days). Self-estimates of other drug use were as follows (mean, SD, range): weekly alcohol units=9.2±9.1, 0–26; daily cigarettes=3.5±6.6, 0–20; lifetime cannabis uses=822±377, 20–1000; lifetime MDMA uses=79±117, 3–400; lifetime psilocybin/magic mushroom uses=19.5±14, 6–40; lifetime ketamine uses=51±84, 0–200; and lifetime cocaine uses=23.1±31, 0–100. Beck Depression Inventory scores at baseline were 1.9±1.6, 0–4; NEO-FFI scores were as follows: neuroticism=13.2±6.5, 5–26; extraversion=32±8, 20–44; openness=31±3.8, 26–35; agreeableness=35.7±4.1, 32–45; and conscientiousness=34.2±6.5, 25–42.

Physiological effects of LSD

Measurements of blood pressure and heart rate under placebo and LSD are displayed in Table 2. Systolic blood pressure was slightly elevated under LSD relative to baseline and placebo, but these changes were not statistically significant after correcting for multiple comparisons.

Subjective effects of LSD

Subjective drug effects were first noticed between 5 to 15 min post-LSD and approached peak intensity between 45 and 90 min post-dosing. Drug effects maintained a subsequent plateau for approximately 3 h and showed a gradual decline in the following hours. These results suggest that compared with oral administration of LSD (Schmid et al. 2015; Passie et al. 2008; Nichols 2004), intravenous administration produces a quicker onset and (slightly) shorter lasting experience. Interestingly however, the speed of onset and duration of effects produced by oral and i.v. LSD are more similar than

Table 2 Physiological measurements for placebo and LSD displayed in rounded mean values+standard error of the mean

	Systolic blood pressure		Diastolic blood pressure		Heart rate	
	Placebo	LSD	Placebo	LSDcpr	Placebo	LSD
Baseline	125±5	123±4	72±4	78±4	78±5	77±5
45th minute	120±3	132±6	69±3	76±4	75±4	77±4
180th minute	n.a.	n.a.	n.a.	n.a.	65±3	79±5
End	118±3	134±5	68±3	74±4	68±3	74±4

when oral and i.v. psilocybin are compared (Carhart-Harris et al. 2012; Hasler et al. 2004).

LSD produced a range of subjective effects (see Fig. 3 in Supplementary material). The five VAS items that were scored highest under LSD were (in descending order) the following: "my thoughts wandered freely", "my imagination was extremely vivid", "I felt amazing", "things looked strange" and "I felt an inner warmth".

Effects of LSD on the emotional response to music

Mean scores for all music stimuli to the question "How emotionally affected were you by the music?" were significantly higher for the LSD condition (0.71±0.14) than for placebo (0.51±0.18, t=3.559, df=9, p=0.006; Fig. 1).

The effects of LSD on different music-evoked emotions

All nine factors on the GEMS-9 were scored higher in the LSD condition than placebo. Significant increases were observed for the items "wonder" (p=0.027), "transcendence" (p=0.027), "power" (p=0.027) and "tenderness" (p=0.027) (reported p values are FDR adjusted; Fig. 2).

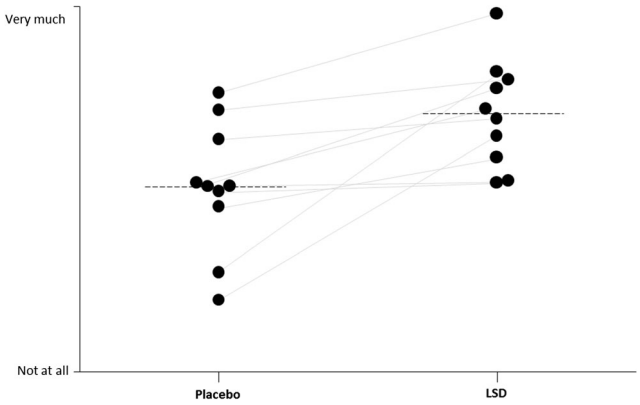

Fig. 1 Effect of LSD on music-evoked emotion. Each *data point* represents one participant's average response to the question "How emotionally affected were you by the music?" The *dashed horizontal line* represents the group average for each condition. The *lines connecting the data points* demonstrate the individual increases in emotional arousal to music from placebo to LSD. Participants gave significantly higher ratings under LSD than placebo (t=3.559, df=9, p=0.006), and every volunteer showed some degree of enhancement of emotional arousal to music under the drug

Correlation analyses

A significant positive relationship was found between ratings of the intensity of LSD's effects and emotional arousal to music (r=0.79, n=10, p=0.006), as well as between the former and increases in the GEMS-9 factor "transcendence" (r=0.79, n=10, p=0.006).

Discussion

The present study assessed the effects of LSD on music-evoked emotion. The primary hypothesis that LSD enhances music-evoked emotion was supported, as was the more specific hypothesis that emotions related to "transcendence" would be enhanced by the drug. Specifically, the emotions "wonder" (i.e. filled with wonder, dazzled, moved), "transcendence" (i.e. fascinated, overwhelmed, feelings of transcendence and spirituality), "tenderness" (i.e. tender, affectionate, in love) and "power" (i.e. strong, triumphant, energetic) showed the strongest enhancement.

The general popularity of music may be due to its ability to convey and modulate emotion (Juslin and Vastfjall 2008), and experimentally, music has been employed as a means to reliably evoke and thereby study emotion (Barrett et al. 2010), including its neurobiology (Koelsch 2014). In therapeutic settings, music has been used with the purpose of evoking, deepening and directing emotion (Moore 2013). The finding that LSD enhances the emotional response to music reinforces a long-held assumption that music takes on an intensified quality and significance under the influence of psychedelic drugs and that this effect may be harnessed for therapeutic purposes (Bonny and Pahnke 1972).

Typically, during psychedelic-assisted psychotherapy, music of the classical genre is played through headphones to individuals who lie supine on a bed or couch and close their eyes or wear eyeshades. These conditions are intended to promote an "inner exploration" where music constitutes the only external stimulus (Johnson et al. 2008). In such a setting, peak experiences or spiritual-type experiences are not uncommon

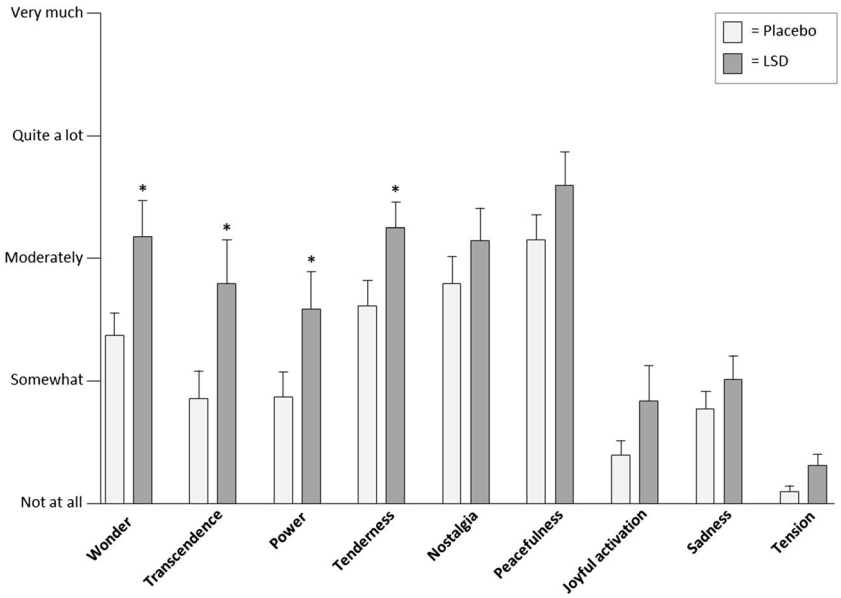

Fig. 2 Mean plus standard error values for the GEMS-9 scores for the complete playlist per condition. Scores were significantly higher for the LSD condition than placebo for the items "wonder" (p=0.027), "transcendence" (p=0.027), "power" (p=0.027) and "tenderness" (p=0.027). Reported p values are FDR adjusted. *p<0.05 after FDR correction for multiple comparisons

(Pahnke 1963; Richards 2009; Griffiths et al. 2006, 2011) and these effects have been found to correlate with sustained improvements in well-being and life satisfaction (Griffiths et al. 2008) and increases in the personality trait openness (MacLean et al. 2011). It is unclear however, how important music is in determining this.

Emotions of transcendence and wonder are traditionally thought of as core constituents of peak and spiritual experiences (Maslow 1993; Richards 2009). Thus, the enhancement of these emotions suggests that the music×LSD combination may contribute to the occurrence of spiritual-type or peak experiences. If spiritual-type experiences are predictive of therapeutic/beneficial effects of psychedelics (Griffiths et al. 2008; MacLean et al. 2011; Garcia-Romeu et al. 2014), and if the likelihood of their occurrence can be increased by music, then this would substantiate the view that music is an important element in psychedelic-assisted therapy.

Limitations

This study has some important limitations. LSD has previously been found to enhance suggestibility (Carhart-Harris et al. 2014; Middlefell 1967; Solursh and Rae 1966), and this may have contributed to the present findings. Participants were not informed of our hypotheses regarding music listening, but it would not have been difficult for them to have intuited them. Thus, participants might have given higher ratings for the question "How emotionally affected were you by the music", simply to reinforce their own expectations or to confirm (their perception of) the researchers'. The difficulty of maintaining the study blind (due to the conspicuous subjective effects of LSD) may have compounded any such biases. Measures to reduce expectation or increase uncertainty about the experimental aims could be introduced in future studies, e.g. by including (1) variable doses of LSD and a larger sample size to examine dose dependency and (2) an active control or comparator drug (see Studerus et al. 2012). Randomising or at least balancing the order of the LSD and placebo sessions would also be worth incorporating into the design of future studies. However, it is unlikely that order could have significantly contributed to the present outcomes, given that order effects are typically sensitive to such things as learning/practice, fatigue and habituation, and playlists were balanced across participants and days.

Another significant limitation of the present study is that we did not assess emotions pre- and post-music but rather simply asked how much the participant had been affected by the music. Without pre- versus post-ratings implemented in a factorial design, the present results may be vulnerable to the interpretation that they were driven by a general drug effect rather than a specific effect of music in combination with drug. The correlation between drug effect intensity and increased feelings of "transcendence" to music could be construed as supportive of this interpretation. Alternatively however, stronger drug effects may have simply enhanced a true music× LSD interaction. The GEMS-9 instructions explicitly request that the participant rate according to how the music made them feel and not how they felt in general or what emotions they thought the music was intended to convey. Thus, while no formal tests for an interaction between drug and music on mood and emotion were performed, the questions were intentionally constructed to enquire about *the effect of music on emotion* (i.e. the interaction between drug and music was implicit in the structure of the question). Nevertheless, to properly investigate an interaction between drug and music on emotion, future studies incorporating a factorial design (with

pre- and post-music listening ratings) will need to be performed. The absence of such a design in the present study prevents us from rejecting the possibility that the results were driven by a general drug effect.

Finally, it is important to emphasise that this was a pilot study with a limited sample size. Moreover, only one female was recruited, all participants were psychedelic experienced and only specific music styles or genres were included. Inferences on the present results can therefore not be generalised beyond the music styles used in the present study, and neither can they be easily generalised to larger populations. Future studies could assess the importance of specific genres or styles of music and the effect of individual music taste in determining outcomes in response to psychedelics. Similarly, non-musical "sound/noise" could be included as an additional control variable.

Conclusions

The results of the present study provide tentative support for the hypothesis that psychedelics enhance the emotional response to music; however, extension studies are required to confirm and extend the inferences that have been discussed here. Future studies are warranted to test the importance of music as a component in psychedelic-assisted psychotherapy and to understand *how* psychedelics enhance the emotional response to music via their effect on brain activity.

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