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ORIGINAL INVESTIGATION

Tripping on nothing: placebo psychedelics and contextual factors

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Abstract

Rationale Is it possible to have a psychedelic experience from a placebo alone? Most psychedelic studies find few effects in the placebo control group, yet these effects may have been obscured by the study design, setting, or analysis decisions.

Objective We examined individual variation in placebo effects in a naturalistic environment resembling a typical psychedelic party.

Methods Thirty-three students completed a single-arm study ostensibly examining how a psychedelic drug affects creativity. The 4-h study took place in a group setting with music, paintings, coloured lights, and visual projections. Participants consumed a placebo that we described as a drug resembling psilocybin, which is found in psychedelic mushrooms. To boost expectations, confederates subtly acted out the stated effects of the drug and participants were led to believe that there was no placebo control group. The participants later completed the 5-Dimensional Altered States of Consciousness Rating Scale, which measures changes in conscious experience.

Results There was considerable individual variation in the placebo effects; many participants reported no changes while others showed effects with magnitudes typically associated with moderate or high doses of psilocybin. In addition, the majority (61%) of participants verbally reported some effect of the drug. Several stated that they saw the paintings on the walls "move" or "reshape" themselves, others felt "heavy… as if gravity [had] a stronger hold", and one had a "come down" before another "wave" hit her.

Conclusion Understanding how context and expectations promote psychedelic-like effects, even without the drug, will help researchers to isolate drug effects and clinicians to maximise their therapeutic potential.

Keywords Placebo effects · Context · Setting · Psilocybin · Expectation · Contact high

Introduction

Is it possible to have a psychedelic experience from a placebo? Although placebos can have robust effects across various domains (Kaptchuk and Miller 2015), psychedelic studies generally report few effects in the placebo control group (e.g. Liechti et al. 2017; Studerus et al. 2010b). However, in naturalistic environments, people sometimes report having a *contact high*, in which they experience drug-like effects without consuming a drug but merely by being around others who have (Tart 1971). One person, for example, reported a "delightful" 4-h high without consuming anything and then "came down about the same time as did the others" who had taken a psychedelic (Shulgin and Shulgin 1995). Contact highs are well-known among recreational drug users (Tart 1971; Gordon 1974), yet almost nobody has studied them; we know of only two relevant studies, both focusing on marijuana (Carlin et al. 1972; Simmons 1973). In 1974, Gordon (p. 21) argued that the "very oddity [of the contact high] may well keep researchers from admitting to its existence, let alone trying to understand it or … its rather far-reaching implications for psychological and social health". Indeed, it appears that no related studies have been published in the four decades since.

These contact highs are not simply due to accidental consumption of a drug, such as passive inhalation of

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marijuana, as the term is sometimes broadly used (Keup 1971; Zeidenberg et al. 1977). Instead, similar to placebo effects (Enck et al. 2013), these highs may result from classical conditioning as well as the physical and social setting (Carlin et al. 1972). Psychedelic drugs are commonly consumed in familiar environments conducive to the experience. A typical psychedelic party has lights, music, and art that may draw attention to changes in perception; its social setting promotes the spreading of emotions (i.e. *emotional contagion*; Hatfield et al. 1993) and observational learning of drug effects (i.e. *social modelling*; Colloca and Miller 2011; Faasse et al. 2015, 2018). In one study, participants reported more effects from placebo marijuana in a typical party environment than in a stark and sterile lab room (Simmons 1973). Further, drugs are often taken at night and may be confounded with the effects of sleep deprivation such as changes in mood or inhibition. Some of these effects may be misinterpreted as resulting from the drug itself (Barsky 2002), thereby promoting a contact high.

More broadly, the effects of psychedelic drugs result from three components: pharmacological factors, non-pharmacological (contextual) factors, and their interaction. Pharmacological factors involve the drug itself and its biological effects, which are usually studied by comparing psychedelic drugs to placebos. Non-pharmacological factors capture the context—"set and setting"—such as the user's mindset, expectations, and environment (Hartogsohn 2016, 2017). The environmental factors include the type of lighting or music (Kaelen et al. 2018), interactions with therapists or researchers (Hyde 1960), or the cultural views of psychedelic drugs (Carhart-Harris et al. 2018). Some studies have examined the interaction between the pharmacological and non-pharmacological factors by testing how different environments promote drug effects (Hartogsohn 2017; Carhart-Harris et al. 2018). Few studies, however, have explored the non-pharmacological factors alone by testing the effects of a placebo psychedelic in conducive or varied environments (Hartogsohn 2016, 2017).

Psychedelic studies generally find few effects in their placebo control groups. In the famous Good Friday experiment, 40% of the participants given psilocybin in a church setting reported having a complete mystical experience involving feelings of unity and sacredness, while none in the placebo group did (Pahnke 1970). In a therapeutic environment, Griffiths et al. (2006, 2011) found that the majority of participants in the psilocybin group had a mystical experience, compared with 11% in the methylphenidate (stimulant) group and none in the inactive (i.e. inert) placebo group. Other studies have also found minimal alterations in consciousness following the ingestion of placebo psilocybin (Studerus et al. 2010b; Grob et al. 2011; Griffiths et al. 2011) or placebo LSD (Liechti et al. 2017; Bershad et al. 2019).

We suspected that placebo psychedelic effects could be stronger than previously reported, as they may have been obscured by the lab setting, study design, or analysis decisions. Placebo effects are generally strongest when people believe they have taken the drug (Kirsch 2018). In randomised controlled trials, participants are told of the possibility that they may be in the placebo or low-dose control group; this knowledge alone can influence the magnitude of their placebo effects (Kirsch and Weixel 1988). Participants often vigilantly observe their experiences in an attempt to resolve the uncertainty over whether they are in the control group (Kaptchuk et al. 2009). After ingesting the drug and experiencing few effects, participants may infer that they have consumed a placebo (e.g. Doblin 1991; Pahnke 1970; Bershad et al. 2019). Indeed, due to the acute effects of psychedelic drugs, participants are generally aware when they have consumed one, making blinding difficult (Muthukumaraswamy et al. 2013; Hartogsohn 2017). Leary (1995, p. 311) even considered double-blind psychedelic studies "ridiculous" given that participants rapidly become aware of whether they are in the placebo group. This broken blind may reduce participant expectations in the control group and thereby weaken any placebo effects (Sneed et al. 2008; Kirsch 2018). Even if there are strong effects, the placebo group is often simply used as a comparator and not explored in detail. Furthermore, participants who experience no effects may pull down reported averages and thereby obscure potentially interesting individual experiences. All of these factors may inadvertently limit the magnitude of reported psychedelic placebo effects.

Still, some studies with individual-level metrics do occasionally report strong effects from placebo psychedelics. Abramson et al. (1955), for example, describe unexpected results after giving participants placebo LSD (i.e. tap water) in a typical experiment room. Many participants reported sweaty palms (35%), drowsiness (24%), headaches (20%), anxiety (13%), fatigue (11%), and a reduced appetite (11%). Some reported experiences more specific to psychedelics, including visual distortions, unusual sensations, and dream-like states. One participant "responded positively to almost half of the [symptom] items" for up to 10 h and required "considerable care … to maintain an experimental situation that was not traumatic" (p. 8). Further, Griffiths et al. (2011) report that of their 18 participants—almost all of whom were naïve to hallucinogens—2 considered their inactive placebo session to be in the top five most spiritually significant experiences of their lives, and 7 reported at least moderate increases in well-being or life satisfaction 1 month later. These kinds of effects indicate that there may be other placebo effects hidden within group averages.

Thus, the present feasibility study explores individual variation in responses to placebo psychedelics. We used

a naturalistic context that may promote contact highs and placebo effects—a party setting in which we led participants to believe that there was no placebo control group. We predicted that at least some participants would report psychedelic-like experiences from a placebo alone.

Methods

Participants

We recruited participants through social media advertisements for a study testing the "effect of a psychoactive drug on creativity". The advertisement stated that the drug "has been shown to induce positive mood, creative thinking, personal insight, and spiritual experience". We screened participants by phone to ensure that they were university students with no physical or mental health issues. We excluded those in psychology-related fields at McGill University who may know that our lab studies placebos. Thirty-five people passed the screening and were eligible and available at the time of the study; 33 showed up to participate ($M = 21.7$ years old, SD = 3.4; 18 men). They studied in a variety of disciplines, most commonly engineering ($n = 6$) and visual arts ($n = 4$). In each sample, we also had 6 to 7 confederates in a similar age range, described below.

We ran two samples of participants ($n_1 = 16$, $n_2 = 17$), each with students from a different university, to reduce information leaking about the placebo component of the study. In our first sample, we attempted to exclude participants with previous psychedelic drug use, but several of them later revealed to us that they had hidden their previous experience for fear of being ineligible for the study. Thus, in our second sample, we removed this criterion from the screening. The protocol was approved by the McGill University Faculty of Medicine Institutional Review Board (A08-B02-17A).

Procedure

Screening

During the phone screening, the researcher explained that participants would consume a small dose of the psychedelic drug *iprocin*—a homologue of psilocybin, the active ingredient in psychedelic mushrooms. We expected that none of the participants would have heard of this little-known drug, so we could better control their expectations. Drawing on the common effects of psilocybin, the researcher listed the effects of iprocin as:

> improved mood, heightened cognition, emotional sensitivity, light sensitivity, hallucinations, sleepiness, tingling sensation of the skin, vivid recall of memories, increased perspiration, slurred speech, mild anxiety, slower reflex response, and dizziness.

Participants were asked to avoid drugs or alcohol for 24 h and to avoid caffeine or tobacco for 1 h before the beginning of the study. This screening procedure helped improve credibility by matching what participants would likely expect from a typical drug study (Bernstein et al. 2016).

Setting

We used an elaborate procedure to mask the fact that we were studying placebos and to plant the expectation that there was no placebo control group. Both samples of the study were run on weekend evenings from 19:00 to 23:00. The participants (and confederates) met a researcher in the lobby of the Montreal Neurological Institute of McGill University to leverage institutional credibility. The researcher asked for government-issued photo identification to make the procedure appear more official. Participants received a hospital wristband and a name tag both showing an identification number, ostensibly to maintain confidentiality throughout the study. To build anticipation, the group waited in the lobby for 20 min as some confederates casually planted statements to boost expectations (e.g. "My friend did this study last week and had a blast"; cf. Bernstein et al. 2016).

Another researcher then led the participants through the hallways of the institute where numerous other researchers held doors open. A security guard stood outside the experiment room. We intentionally used excessive personnel to make the study appear more legitimate. The participants removed their shoes and left their belongings in an adjacent room.

The experiment room had a naturalistic atmosphere, resembling a party (Fig. 1). Psychedelic paintings with subtle visual illusions adorned the walls. Changing-colour lights illuminated the paintings and red light-therapy lamps lit the rest of the room. A DJ played ambient music on a turntable. Gym mats, bean bags, and meditation cushions covered the carpet. A few books describing psychedelics were placed on the cushions (Masters and Houston 1966; Leary 2000), along with paper and pencil crayons for drawing. A projector played the non-verbal films *Baraka* (1992) and *Samsara* (2011), known for their stunning visuals, without sound. Snacks and water were available. Discreet cameras placed around the room and in each researcher's lab coat pocket recorded the experiment. An official-looking sign on the room door displayed hospital logos, names of professors, and emergency contacts. In short, the environment was relaxed yet credible.

To make the study appear more scientific, all 7 (first sample) to 11 (second sample) researchers wore white lab coats

Fig. 1 Setting. The study was set up like a psychedelic party with lights, paintings, projections, and music

and held identical clipboards and pens. The main experimenter played the role of a post-doctoral researcher leading a multi-site study across several universities. Periodically throughout the study, the principal investigator would enter the room to scribble notes and give confirmatory nods to the researchers. A psychiatrist was on site to increase credibility and in case participants were anxious or had (placebo) emergencies (cf. Johnson et al. 2008; Reeves et al. 2007).

Briefing

As the participants entered the room, the experimenter told them to sit in a semi-circle arranged by participant number. This distributed the confederates across the room and promoted interaction with them, preparing the eventual emotional contagion and social modelling.

As a cover story, the experimenter stated that the study investigated the interaction between a drug and the environment on creativity. Most studies, he explained, take place in sterile rooms and give little opportunity for participants to express their creativity. To reduce suspicion about the possibility of a placebo control group, the experimenter stated that this was a feasibility study aimed at resolving logistical issues before starting the more controlled trial. No part of the briefing mentioned placebos.

The experimenter explained that iprocin was a fast-acting and legal drug similar to psychedelic mushrooms. Its effects start quickly, within 15 min, peak in 1 to 2 h, then quickly fade. We told participants that they would stay in the room until the effects had worn off, but that these would unlikely persist beyond the 4-h study. An official-looking information sheet listed the dose (4 mg) and the effects described during the phone screening.[1] We described the dose as small to ensure participants would have realistic expectations about the effects (Kirsch and Weixel 1988; Kirsch 2018).

The participants did not appear sceptical about the study procedure. This may seem surprising, given that some of the students were knowledgeable about drugs and may have known that the institution has done little psychedelic research since the 1960s (Lee and Shlain 1992). However, we had several factors working in our favour. We followed a principle of deception to use an excessive amount of preparation and effort (Teller 2012) to conceal the true purpose of the study. We hoped that participants would not expect phone screenings, health certifications, hospital wristbands, 11 researchers, a psychiatrist, and a security guard for a mere placebo study. Further, unbeknownst to the participants, the main experimenter had training in deception (as a former professional magician) and was ready to offer deceptive explanations if the cover story was threatened. In previous studies, we have used such elaborate procedures to make students (and researchers) believe even less plausible ideas, such as that a neuro-imaging machine was controlling their thoughts (Olson et al. 2016; Olson 2019). Given these previous findings, it is less surprising that participants appeared to believe our drug cover story here.

Baseline measurements

After signing the consent form, participants completed three questionnaires measuring personality, mood, and subjective experience (see "Measures" section). Another researcher then took each participant's heart rate and blood pressure (Physio Logic LuminA device, AMG Medical Inc., Montreal, QC). The researcher read out both values as 10 units lower than they actually were. This false feedback helped ensure that the next reading (after consuming the drug) would be higher, making it appear as if the drug was having a physiological effect.

[1] The sheet resembled Health Canada's "Quality Overall Summary — Chemical Entities (Clinical Trial Applications — Phase III)" form containing sensible-looking but bogus information.

Placebo

The participants then individually met with the experimenter at a corner of the room to receive the placebo pill. The pill was a size 0 (2-cm long) capsule filled with an inert powder (microcrystalline cellulose), purchased from a local pharmacy. The pills were pink, since they have been shown to promote more stimulant effects than placebos of other colours such as blue (Blackwell et al. 1972). To help participants believe that everyone was in the same condition (i.e. that there was no separate control group), we casually offered participants to select any pill cup from the tray, paying little attention to which one they took, to imply that they were all identical. Participants took the capsule with water, then the experimenter shined a flashlight in their mouth to ensure that they had swallowed it.

The participants then had 30 min to mingle, ostensibly to wait for the drug to take effect. Approximately 15 min after ingestion, the confederates started to act out the effects of the drug in subtle ways. They were previously instructed to *pace and lead* (cf. Nash and Barnier 2012)—that is, to match and then magnify the effects shown by other participants. For example, if participants seemed to show an improvement in mood, the confederates would match this increase and then act even happier. Indeed, watching confederates experience effects of a placebo makes participants more likely to experience them (Colloca and Miller 2011; Faasse et al. 2015, 2018). To make it appear as if the drug was having a physiological effect, one confederate with naturally large pupils told some participants individually, "Your pupils are huge! Are mine like that?" The room contained no mirrors (nor did the bathroom) or phone cameras for participants to verify this statement, and the dark room with red lights naturally dilated their pupils.

The environment was upbeat and social. Many participants watched the films, others swayed to the music, some played cards, and a few threw paper airplanes into popcorn bowls. The researchers periodically probed individual participants about their experience.

Filler creativity measures

To maintain our cover story, we next collected data on creativity. We told participants to move to a new area of the room; this gave them a chance to interact with other confederates. They then completed verbal and visual creativity tasks (see "Filler measures" section). These tasks also gave participants different contexts to notice any placebo effects.

Experience measurements

After another 45 min of mingling, the participants regrouped to complete the same mood and experience questionnaires as the ones completed prior to ingesting the placebo. We also took another measure of heart rate and blood pressure. This time, the researcher increased the values by 10 units. Several participants asked about this increase; the researcher stated that the value was higher than before, but that this was normal. The participants then met with the experimenter at a corner of the room who asked them about any effects they had noticed since the study began. We used this open-ended wording to avoid inflating the reporting of side effects, as can sometimes occur when asking specific questions (Rief et al. 2009). The responses were tape-recorded and later transcribed. Combined with their verbal reports to the researchers throughout the study, these responses gave a qualitative measure of the participants' experience.

Debriefing

At 3.5 h into the study, the participants regrouped for a debriefing. In the second sample, we asked them to write down whether they had used any of the classical psychedelic drugs before, which we specified as LSD, magic mushrooms, mescaline, or DMT. We also asked whether they believed they had ingested a psychedelic drug or a placebo. In both samples, the experimenter then revealed that the drug was a placebo and explained the true purpose of the study. The participants then signed another consent form allowing us to use their data now that they were aware of the deception. Participants were compensated $40 for their participation.

Measures

5-dimensional altered states of consciousness rating scale (5D-ASC)

The 5D-ASC measures changes in subjective experience (Dittrich 1998) and is commonly used in psychedelic studies. Each item uses a visual analogue scale ranging from "No, not more than usually" (0) to "Yes, much more than usually" (100). The measure has 11 subscales (Studerus et al. 2010a):

- anxiety (e.g. "I was scared without knowing exactly why"),
- spiritual experience ("My experience had religious aspects to it"),

- insightfulness ("I felt very profound"),
- impaired control and cognition ("I felt incapable of making even the smallest decision"),
- disembodiment ("I felt as if I no longer had a body"),
- experience of unity ("Everything seemed to unify into a oneness"),
- blissful state ("I experienced boundless pleasure"),
- changed meaning of percepts ("Some everyday things acquired special meaning"),
- complex imagery ("I saw whole scenes roll by with closed eyes or in complete darkness"),
- audio-visual synaesthesia ("The colours of things seemed to be altered by sounds or noises"), and
- elementary imagery ("I saw colours with closed eyes or in complete darkness").

Participants completed this measure before and after ingesting the pill, in order to assess any effects of the setting itself independent from the placebo. Two participants had unexpectedly high scores on the scale before consuming the pill (with some subscale averages above 15 and corresponding z scores above 4), so we excluded these participants from the entire scale.

Positive and negative affect schedule (PANAS)

The PANAS is a 20-item questionnaire (Watson et al. 1988) measuring how much participants feel various emotions, such as "Enthusiastic" or "Distressed". Each item uses a 5-point Likert scale ranging from "Very slightly or not at all" (1) to "Extremely" (5). The ten positive and ten negative items are summed to give two separate affect scores. At baseline, the internal consistency was good for positive affect (Cronbach's $\alpha = .87$) but lower for negative affect ($\alpha = .61$), likely due to a floor effect.

Filler measures

The rest of the measures served to maintain the cover story and to meet participants' expectations of a drug study. Participants completed the Big Five Inventory, Remote Associates Task, Divergent Association Task, and the House Tree Person Test.

Big five inventory (BFI) The 44-item BFI measures five broad personality traits (John et al. 2008). An example item is: "I am someone who talks a lot". Each item uses a 5-point Likert scale ranging from "Disagree strongly" (1) to "Agree strongly" (5). None of its subscales predicted alterations in consciousness in our participants ($|r|$ values $\leq .13$).

Remote associates test (RAT) In the RAT (Mednick 1968), participants hear three words (e.g. cream, skate, cube) and have to find a fourth word (e.g. ice) that forms a compound word when combined with each of the others (e.g. ice-cream). After two practice trials, participants had 30 s to find the matching word for each of the 10 (second sample) or 20 (first sample) trials.

Divergent association task In the second sample, participants additionally completed a creativity measure in which they generated 10 words as different from each other as possible in meaning and usage. We developed this task in an attempt to capture the divergent associations that are commonly reported in altered states of consciousness (Kuypers et al. 2016; Prochazkova et al. 2018). The task is currently being validated (Olson and Webb, in progress).[2]

House tree person test Finally, participants were instructed to draw a house, tree, and person; they were given 1 min to draw each item and then another minute to add any details to the drawings (Buck 1948).

Analysis

We explored the subscales of the 5D-ASC and PANAS to see how experience and mood changed throughout the study. We focused on individual variation rather than group averages in order to prevent the placebo non-responders from diluting any effects. As a result, we did not perform any statistical tests.

Results

Alterations in consciousness

There was considerable individual variation in placebo effects. Figure 2 shows the individual responses to the 5D-ASC subscales after ingestion, compared with the average effects reported after consuming psilocybin (Studerus et al. 2010b). If there were no placebo effects, we would expect most of the values to be around 0, indicating no alterations in consciousness. Instead, on some of the subscales, several participants reported changes in experience greater than those associated with ingesting moderate or high doses of psilocybin (Studerus et al. 2010b) or moderate doses of LSD (Liechti et al. 2017; Bershad et al. 2019). Other participants showed little changes from the placebo, and thus average values were low ($M_{pre} = 1.25\,[0.62, 2.08]$; $M_{post} = 3.77\,[2.33, 5.54]$).[3] Tables S1 and S2 show the average scores for each subscale and item.

[2] See https://www.datcreativity.com.

[3] Square brackets throughout denote bootstrapped 95% confidence intervals.

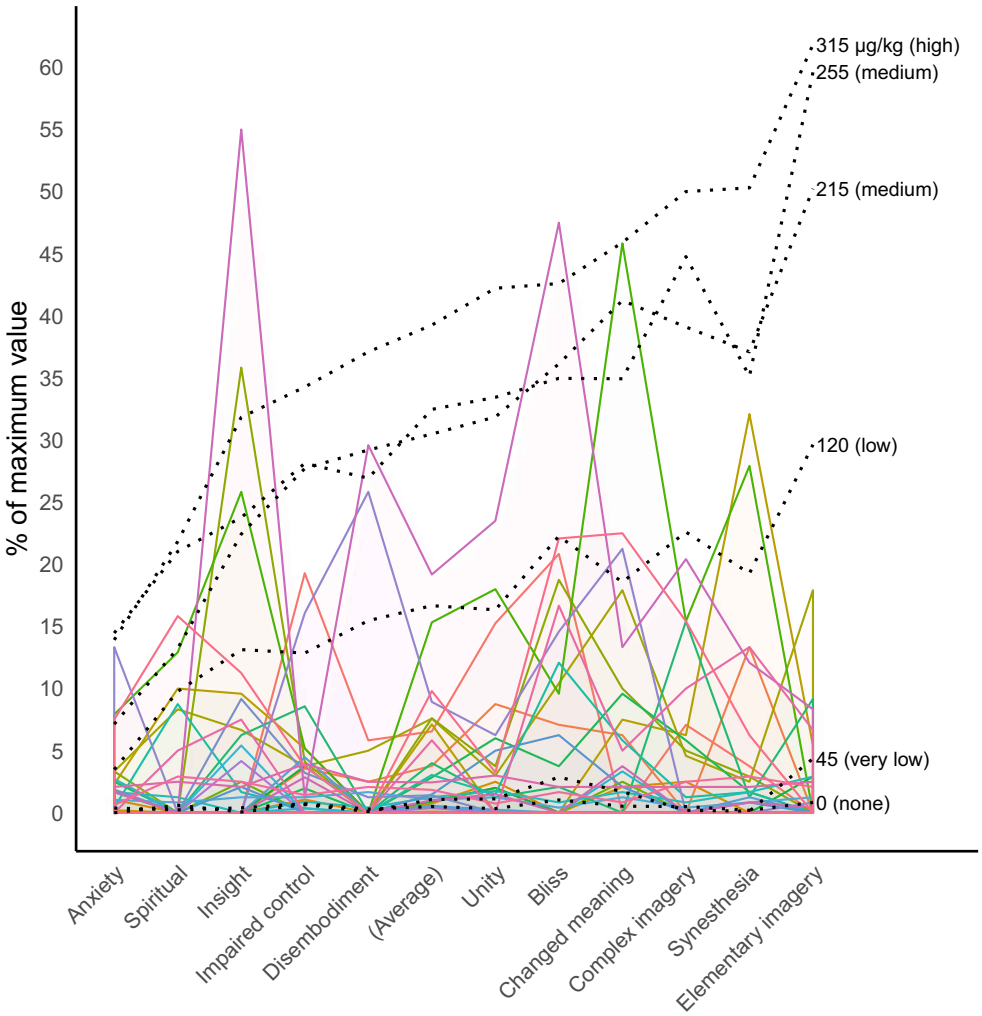

Fig. 2 Changes in experience after consuming the placebo, as measured by the 5-Dimensional Altered States of Consciousness Rating Scale. Higher values (up to 100) indicate greater alterations from usual consciousness. Coloured lines show individual scores. As a comparison, dotted lines show effects from 0 to 315 μg/kg of psilocybin (Studerus et al. 2010b)

Verbal reports

When asked by the experimenter, most of the participants (61%) reported some effect of the drug, which we list approximately ordered by magnitude.

Thirty minutes after ingestion, one participant reported feeling light-headed and experiencing less effort when trying to move her head. An hour later, she reported watching the colours shift on the paintings and feeling "very, very relaxed". Near the end of the study, she reported still feeling heavy, relaxed, and warm. She said that during the tasks, she was distracted and "just wanted to look at the painting [on the wall] and stare at it". She sometimes "did not feel like [she] could talk to anyone else". In the middle of the study she felt "sober for a while"—she "had a come-down"—and then was able to "bring it upon [herself] again" and felt another "wave" hitting her. She could make herself "sober" if she wanted to, but instead she was "trying to make [herself] feel it" to enjoy the experience. After the debriefing, she mentioned she was "very surprised it was a placebo" and that she "definitely felt [she] was high on something". Before leaving, she added that people thought that she was a confederate who was acting out the effects. She then asked where she could get the placebo drug again.

Another participant had a similarly positive experience. She initially reported feeling tense, then later talkative, friendly, and open to sharing her ideas with others. She reported heightened senses, with sounds and colours being more vibrant. She also later reported feeling certain that she had taken a psychedelic.

Other participants experienced nocebo (negative placebo) effects. One reported feeling nauseated throughout the study. She felt hot with sweaty palms, and her arms and legs felt heavier. Another had a similar experience:

> I didn't feel anything until we were doing the drawings. And everything kind of dropped a little bit and maybe I had a headache… maybe, low energy… I think it was a sinking feeling. Like gravity [had] a

> stronger hold on me or something… mostly [in] my head. Specifically in the back of my head.

One other participant also reported perceptual changes:

> I had not been feeling anything until looking at this [painting]. It's moving. The colours aren't just changing, it's moving. It's reshaping itself.

One participant reported that he had trouble understanding what people were saying for approximately 20 min during the study, as if their words did not register.

Other participants reported feeling energetic, uninhibited, warm, relaxed, mild, mellow, or dulled. Two participants reported that thoughts "came easier" and "without effort". Two others mentioned time passing faster or slower; one of them reflected, "The way we live is too active… too fast for me". Twenty minutes after ingestion, one reported feeling a "chemical tingling" in his torso, as if he had taken a drug or drank coffee. Others reported zoning out more than usual, minor headaches, seeing the lines on the paintings move, or feeling more inventive during the drawing task. One participant reported that for several minutes he felt "very much like laughing".

The rest of the participants (39%) reported feeling nothing out of the ordinary.

Previous drug use

In our second sample, we asked participants at the end of the study whether they had previously used any of the classical psychedelic drugs. Overall, 6 participants reported that they had, 10 that they had not, and 1 did not answer. This sample is too small to draw strong conclusions, but there did not appear to be a clear relationship between participants' drug use and their experience. Among those who had used psychedelic drugs, 50% [19%, 81%] verbally reported effects; among those who had not, 70% [35%, 92%] reported effects. There also seemed to be no major difference in alterations of consciousness, with average 5D-ASC scores of 3.82 [1.36, 6.82] in the experienced users and 3.59 [0.69, 7.37] in the naïve ones.

Mood

Participants reduced in both positive and negative affect throughout the study. At baseline, participants reported an average positive affect of 32.18 [29.61, 34.49]; by the end of the study, it was at 26.23 [22.70, 29.82]. Negative affect similarly dropped from 14.39 [13.33, 15.46] to 11.27 [10.67, 12.00]. The "excited" and "nervous" items dropped the most on each subscale, suggesting that this change in mood may have simply reflected participants adapting to the lab setting as the excited and nervous anticipation dissipated.

Physiology

There were no major changes in physiology. Heart rate averages went from 82 [77, 87] to 78 [74, 82] bpm. Systolic blood pressure went from 134 [129, 139] to 128 [123, 133] mm Hg; diastolic blood pressure went from 81 [77, 85] to 80 [75, 84].

Scepticism

In the second sample, before the debriefing, we asked participants to guess whether they had taken a psychedelic, a placebo, or whether they were uncertain. Overall, 35% reported being certain they had taken a placebo, 12% were certain that they had taken a psychedelic, and the rest (53%) were uncertain. In the first sample, we did not ask this question, but the same number of people spontaneously reported being certain that they had taken a psychedelic drug.

During the debriefing, when we revealed the placebo nature of the study, many participants appeared shocked. Several gasped and started laughing. One stated, "It's very funny!", and another replied, "It's sad!" One of the participants who had sat with a group near the paintings throughout the study asked, "So we were all sober and just watching these paintings for 45 minutes?!"

Discussion

In this study, we explored placebo effects and contact highs in a naturalistic setting. By carefully controlling contextual factors, social interactions, and participants' expectations, we investigated whether we could induce psychedelic-like experiences from a placebo alone. There was considerable variation in both quantitative and qualitative results: many participants reported nothing unusual while others reported effects typically associated with moderate or high doses of psychedelic drugs. To our knowledge, these are the strongest alterations in consciousness reported in the literature following an inactive placebo psychedelic (e.g. Bershad et al. 2019; Studerus et al. 2010b; Griffiths et al. 2011; Liechti et al. 2017).

These findings prompt the question: what role does expectation play in the psychedelic experience? This question may be particularly relevant for microdosing, in which there are many open questions about the role of context and expectation (Carhart-Harris et al. 2018; Polito and Stevenson 2019). In our study, some of our participants

Table 1 In balanced placebo designs, what participants expect to receive is fully crossed with what they actually receive

	Receive psychedelic (or high dose)	Receive placebo (or low dose)
Expect psychedelic (or high dose)	Common	Tested here
Expect placebo (or low dose)	Untested?	Common (in open-label studies)

reported alterations in consciousness stronger than the usual effects of microdosing either psilocybin (Figure 2; Studerus et al. 2010b) or LSD (Bershad et al. 2019). We thus agree with Carhart-Harris et al. (2018) that expectations and context likely remain important even when microdosing.

One way to isolate the role of expectation would be to use a *balanced placebo design* (Rohsenow and Marlatt 1981; Studerus et al. 2012). In this 2 × 2 design, what participants are told they will receive (e.g. a placebo or psychedelic) is fully crossed with what they receive in reality (Table 1). This creates four experimental conditions, two of which require deception: expecting to receive a psychedelic but receiving a placebo (as tested here), and expecting to receive a placebo but receiving a psychedelic. The latter seems plausible at least at lower doses of the drug. Balanced placebo designs would be ideal for microdosing studies, in which it is more difficult to differentiate a placebo from the drug (Bershad et al. 2019). This would allow researchers to isolate how expectations interact with the drug to create psychedelic (or placebo) effects. To be clear, the elaborate procedure used in our study is unnecessary to create the basic expectation that participants will receive a psychedelic drug; here we were also interested in maximising placebo effects based on the context. One additional way to boost expectations would be to use an active placebo which has some physiological effects, such as niacin (which causes facial flushing). By leading participants to believe that the control group will receive an inactive placebo (as in Pahnke 1970), experiencing any kind of effect may be misinterpreted as evidence of a psychedelic drug. In our study, using an active placebo would have likely promoted stronger effects, making more participants feel certain that they had consumed a psychedelic.

Better understanding expectation and context may help explain the mystery of contact highs. Here, having confederates act out the effects of the drug may have promoted a "placebo contact high". We hypothesise that both contact highs and placebo psychedelics work through similar mechanisms, such as classical conditioning, positive expectations, emotional contagion, and social modelling (Carlin et al. 1972; Hatfield et al. 1993; Colloca and Miller 2011; Faasse et al. 2015). We would therefore predict, for example, that the more confederates act out the drug effects and the more the environment resembles naturalistic drug settings, the greater the placebo effects and contact highs will be. The mere knowledge of contact highs may even strengthen their effect by boosting expectations and making people more sensitive to potential changes in their conscious experience (cf. Kaptchuk et al. 2009). Contact highs may thus be self-reinforcing: after experiencing one once, people may expect them in the future, making them more likely to occur (Kirsch 2018). We hope our study helps break the decades-long hiatus on contact high research in order to test these kinds of predictions.

Several aspects of our procedure may also be useful for placebo drug or alcohol studies looking to create credible experiments. For example, the use of numerous research personnel, confederates acting out the drug effects, implied physiological changes, or the apparent lack of a control group may be useful to strengthen deception and placebo effects. Indeed, even 3 h after ingesting the inert pill, some participants thought it was a psychedelic, the majority were uncertain, and only a third thought it was a placebo. This may be an inflated estimate of scepticism, since some participants may not have considered the idea of a placebo until they were asked (Bernstein et al. 2016). As a comparison, in one study of LSD microdosing, nobody in the placebo group thought they had received a psychedelic; all guessed it was a placebo or a different drug (Bershad et al. 2019).

Beyond its research implications, understanding the optimal context for placebos and psychedelics may also be useful for clinicians. Since drug effects result from a combination of pharmacological and non-pharmacological factors, carefully controlling the context may promote therapeutic outcomes (Blasi et al. 2001; Zion and Crum 2018). The same factors that may have promoted psychedelic-like effects in our participants could have magnified actual psychedelic effects had they consumed a real drug. Some of these factors could be translated into clinical contexts. For example, rather than using confederates, clinicians could show videos of previous patients discussing the positive effects they experienced from the drug in order to boost expectations and promote social modelling (Colloca and Miller 2011; Faasse et al. 2015). In doing so, clinicians may be able to obtain similar therapeutic experiences from lower doses of the drug; in a sense, some of the pharmacological components could be replaced with or enhanced by non-pharmacological ones. Lower therapeutic doses are more safe, which is important given the re-emergence of psychedelic therapy and the numerous clinical trials underway (Tupper et al. 2015).

One limitation of our study is that we cannot identify which factors promoted the effects without a separate control group. The control could be an *open-label placebo* group (Charlesworth et al. 2017), in which participants are aware they are receiving a placebo (bottom right cell of Table 1). Alternatively, the control group could receive a different list of expected drug effects (Barsky 2002; Colagiuri et al. 2012), vary the number of confederates (Faasse et al. 2015), or take place in a traditional lab environment versus a more naturalistic one (Simmons 1973). Isolating and controlling the relevant contextual factors could help improve psychedelic study designs and explain replication differences across sites (Liechti et al. 2017).

Another limitation is that some of the participants in our sample unexpectedly reported alterations in consciousness even before consuming the drug. These changes may have been due to the environment itself. The individual items with the highest pre-drug averages seemed reasonable given the time and setting (e.g. being sleepy or feeling like one was in a "wonderful other world"). After removing the two participants with outlying scores, these baseline alterations were relatively small compared with after consuming the drug. In any case, completing a pre-drug measure may have changed participants' expectations in some way, so it may be better to avoid this in the future as in most psychedelic studies. Future research could also include more behavioural or objective measures in order to assess whether these placebo effects are limited to subjective alterations in consciousness. An additional subjective measure that would also be relevant is the Mystical Experience Questionnaire (Barrett et al. 2015) which correlates strongly with 5D-ASC scores ($r = .87$; Liechti et al. 2017). A final limitation was that our sample size was constrained: after the first session, word of the placebo aspect of the study quickly spread across the campus, so we had to recruit our next sample from a different university.

Overall, our study highlights the importance of the placebo component of psychedelic drugs. Given our results, we suggest that psychedelic researchers explore and report individual effects found in their placebo (or very low dose) control groups (e.g. Abramson et al. 1955). This could involve reporting maximum values or using graphs that show individual variation (e.g. as in Figure 2 or with violin plots, Hintze and Nelson 1998) rather than focusing only on group averages. We also suggest that researchers describe the setting in more detail—ideally with photographs—and mention the behaviour of clinicians or experimenters (Hyde 1960). In particular, it would be helpful to describe the list of drug effects given to participants, which can influence their expectations and experiences (Planès et al. 2016). This level of reporting will be useful to help explain differences in psychedelic effects across sites (Liechti et al. 2017). Indeed, understanding the psychedelic experience means isolating which parts are due to the drug itself and which are due to the contextual factors (Carhart-Harris et al. 2018). We hope that our results help shift the view of placebo effects from a necessary nuisance to a demonstration of the power of context in both modulating and creating the psychedelic experience.

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Data availability The full data set (including the filler measures) is available online at https://osf.io/xqtnh/.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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