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ORIGINAL RESEARCH PAPER

Apophenia, absorption and anxiety: Evidence for individual differences in positive and negative experiences of Hallucinogen Persisting Perceptual Disorder

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ABSTRACT

Background and Aims: Little is known about individual differences in Hallucinogen Persisting Perceptual Disorder (HPPD). This study investigated visual processing style and personality across two HPPD types (HPPD I and HPPD II) and a Non-HPPD group. *Methods:* An online survey was delivered to participants sourced from online HPPD and psychedelic user groups and forums ($N = 117$). Using one-way ANOVA, respondents were compared across four measures of individual difference. Using logistic regression, a range of visual symptoms and experiences were investigated as potential predictors of group categorisation. *Results:* The HPPD I group had higher absorption and visual apophenia scores than the other groups and was predicted by higher drug use. The HPPD II group showed significantly higher trait anxiety than both other groups. Across the HPPD groups, HPPD II categorisation was also predicted by increased negative precipitating experiences, lack of prior knowledge and pre-existing anxiety diagnoses. *Conclusions:* Anxiety, negative precipitating experiences and lack of prior knowledge are associated with negative experiences of persistent visual symptoms following hallucinogen use, whilst higher absorption and visual apophenia are associated with positive or neutral experiences. Together these findings indicate that differences in personality may play a role in determining an individual's experience of HPPD, highlighting the role of individual difference research in expanding knowledge around HPPD.

KEYWORDS

hallucinogen persisting perceptual disorder, HPPD, psychedelics, anxiety, absorption, apophenia

INTRODUCTION

Hallucinogen persisting perceptual disorder (HPPD) is defined by a number of persistent visual and non-visual symptoms following hallucinogen use. HPPD incorporates a large number of visual symptoms such as increased awareness of entoptic phenomena (e.g., floaters– black/grey objects that follow eye movement) and various palinopsia (e.g., trails– normally coloured images that appear in the wake of moving objects. The recent resurgence of psychedelic research (Nutt & Carhart-Harris, 2020) has noted an absence of instances of HPPD arising in well-controlled research settings (Halpern & Pope, 2003; Johnson, Richards, & Griffiths, 2008) making causal inferences about the role hallucinogens play in HPPD problematic. The majority of HPPD presentations are reported to arise from recreational hallucinogen use. Surveys have proved an effective way of accessing those individuals reporting experiences of HPPD. The current research aims to benefit scientific understanding of the disorder through the use of a comprehensive survey exploring individual differences and collecting data around participant experiences of HPPD.

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Flashbacks and HPPD

The study of HPPD in scientific literature began with Sandison, Spencer, and Whitelaw (1954) noting prolonged effects in several participants undertaking an intense lysergic acid diethylamide (LSD) and psychotherapy program. Cooper (1955) also described protracted experiences resembling acute psychedelic (LSD) phenomena; however, neither of these initial reports were thorough. Later, through the continued research of the 1960s and 70s, these post-hallucinogenic experiences came to be termed *flashbacks*.

Flashbacks were generally considered to be a benign, transient re-experiencing of the acute psychedelic state, with a small percentage described as problematic (Matefy, Hayes, & Hirsch, 1978). This benign type of HPPD has come to be redefined as HPPD I (Lerner, Gelkopf, Skladman, & Oyffe, 2002; Lerner, Rudinski, & Bor, 2014; Lev-Ran, Feingold, Goodman, & Lerner, 2017) and is generally considered more consistent with the ICD-10 definition of HPPD (Halpern, Lerner, & Passie, 2016). The negative, long-term type, HPPD II, is more consistent with the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5; American Psychiatric Association, 2014) definition. There is considerable ambiguity in the diagnostic utility (Baggott, Coyle, Erowid, Erowid, & Robertson, 2011; Halpern et al., 2016; Martinotti et al., 2018) although they are considered distinct sub-types (Hermle, Ruchsow, & Täschner, 2015) with the latter forming the more clinically relevant diagnostic interpretation, despite only indicating likely prognosis (Martinotti et al., 2018). Lev-Ran et al. (2017) tentatively reported on differences among HPPD I and HPPD II as *positive vs negative experiences* of HPPD, pointing towards a more useful defining feature of the disorder.

Aetiology

LSD is the hallucinogen most commonly associated with HPPD onset (Martinotti et al., 2018); however, numerous drugs acting on disparate neurobiological systems (e.g, Halpern et al., 2016) are reported. Whilst other serotonergic hallucinogens (e.g., psilocybin) are often implicated, cannabis and phencyclidine (PCP), which interact with endocannabinoid and NMDA receptors respectively, have also been identified (for a review see Martinotti et al., 2018) alongside several other scheduled and non-scheduled drugs (Lauterbach, Abdelhamid, & Annandale, 2000). With lack of a clear definition surrounding the disorder and no single candidate for HPPD's aetiology, advancing research in this area is complex.

Neuroscience and neurophysiology

Recent neuroscience research investigating psychedelics has targeted understanding their actions more generally, elucidating the role of serotonin receptor agonists (i.e., classic psychedelics) on augmenting brain function (e.g., Muthukumaraswamy et al., 2013); however, no research has investigated differences in structural or functional differences with regards to HPPD. Abraham and Duffy (1996, 2001) undertook some early neurophysiological research looking at differences in visual processing. Their electroencephalogram studies proposed that hyper-synchrony in the visual system combines with cortical disinhibition to reduce top-down filtering of visual input amongst HPPD users; that is, more noise enters into conscious perception. Support for this hypothesis has been indicated, qualified by the suggestion that this overactive vision is a pre-existing factor, rather than a direct result of hallucinogen use (Halpern et al., 2016).

State-dependent learning

HPPD has historically been proposed as an example of state-dependent learning akin to post-traumatic stress disorder (McGee, 1984). In this way, HPPD might also be viewed as being an aspect of memory evoked by similar mental or environmental cues (see also, Heaton & Victor, 1976). Horowitz (1969) also encompassed some of this notion in his idea of a *deconditioning response*, where individuals having experienced these sensory changes, might more easily access them without volition. Deconditioning response theory and state-dependent learning are reliant on the re-experiencing of the psychedelic state, something that more recent HPPD research does not support. Hypnosis may enable psychedelic users to "relive the drug taking experience in their imagination" (Baumann, 1970, p. 20) with similar findings indicated more recently in a group of 3,4-Methylenedioxymethamphetamine (MDMA) users (Hastings, 2006) suggesting the re-accessing of psychedelic-type experiences is possible in some individuals.

It is thought that traumatic responses may have a role in the disorder (i.e., Halpern et al., 2016) suggesting prior experiences may, in some way, impart an influence on the disorder. Autobiographical memories are recalled more vividly in the acute psychedelic state (Carhart-Harris et al., 2012) and the intense, multi-modal aspects of a psychedelic experience may allow the formation of strong memories which could be confused with flashback experiences (Studerus, Kometer, Hasler, & Vollenweider, 2010). The idea of *stimulus generalization* proposed by Heaton and Victor (1976) may go some way towards incorporating a learned response from disparate stimuli.

Individual differences

The earlier work of Heaton (1975) also suggests that expectancy increases flashback response, irrespective of direct experience of flashbacks themselves. Similarly, Matefy's *role play* theory (1980) proposes individuals high in suggestibility, self-absorption and propensity for immersion in a role are primed for the experience of flashbacks. HPPD has also been proposed to be similar to somatoform disorders (Krebs & Johansen, 2013) as they share a focus on symptoms having causal attribution (Voigt et al., 2012). Together, these ideas suggest individual differences might influence an individual's propensity for flashback experiences. Going further, Cohen (1960) suggested that some hallucinogen users might also be more prone to report flashback symptoms when given a drug

alleged to elicit them. It is worth noting that most of this individual difference research was done under very different social circumstances, in cohorts commonly less debilitated by their experiences.

A developing disorder

The scientific understanding of HPPD is not fixed and the modern disorder bears little resemblance to initial accounts. Whether the symptoms of HPPD are evolving or not is unclear; however, Halpern et al. (2016) point out that a number of what we would now consider HPPD symptoms are absent from a historic review of psychedelic-assisted psychotherapy. Whether or not the disorder might be sensitive to socially or culturally imported factors (see Matefy et al., 1978) is beyond the scope of this investigation but combined with psychedelics' well-documented effects of increasing suggestibility (Carhart-Harris et al., 2014) it bears consideration. Both the scientific investigation of HPPD and accounts of the HPPD experience have undeniably changed.

RATIONALE

Purpose of the project

The search for predictors of HPPD has, to date, resulted in no supported findings. The lack of individual difference research in the last few decades (Halpern & Pope, 2003) has left a gap for investigation. Halpern et al. (2016) propose a model that includes a range of experiential triggers that are responsible for HPPD onset. Their trigger schematic incorporates several aspects of individual differences, which in some ways represent a look back to the work of the 1970s (e.g., Heaton & Victor, 1976; Naditch & Fenwick, 1977), indicating the continued value in researching aspects of personality in this field.

This project aims to broaden knowledge of potential factors that may determine or differentiate the HPPD–experience. Given the subjective nature of HPPD, it seems plausible that there may be individual differences in visual processing style and personality traits between HPPD and non-HPPD experiencing individuals.

Perception

It has been proposed that the visual content of flashbacks might be as imaginal as it is memory-based, allowing room for non-acute re-experiencing of visual content (Frankel, 1994) which might be investigated through the idea of mental imaging ability. Psychedelics have been shown to increase activation in the visual cortices (Carhart-Harris et al., 2016; de Araujo et al., 2011) and this, with concomitant reduction of frontal cortex inhibition, predicts both basic and complex hallucinations (Carhart-Harris et al., 2016). Vividness of imagery across multiple modalities (e.g., kinaesthetic, auditory) is suggested to be increased in flashback-experiencers (Matefy, 1980) but scientific understanding may benefit from more targeted measurement.

Vividness of visual imagery has been linked with a predisposition for anomalous perceptions (Salge, Pollmann, & Reeder, 2020) suggesting a potential role in the formation of imagery specific to HPPD experiences. It is possible then, that visual input perceived as ambiguous may impact judgement regarding veridical visual information. Pareidolia (proneness for seeing distinct objects within patterns) has long been noted in HPPD research (e.g., Abraham, 1983) and may be distinct from other symptoms such as trailing (Anderson & O'Malley, 1972). Independent measurement of proneness for false-positive associations has, to our knowledge, not been undertaken in the HPPD literature.

Personality

Absorption describes the tendency of the individual to get mentally immersed in an experience and is also predictive of hallucination proneness (Glicksohn & Barrett, 2003). Research has shown trait absorption correlates with vividness of imagery within the acute psychedelic state (Carhart-Harris et al., 2012) as well as predicting visual effects (Studerus, Gamma, Kometer, & Vollenweider, 2012) and higher levels of mental imagery (Pekala, Wenger, & Levine, 1985) suggesting it may be a personality trait of interest with regards to HPPD.

State anxiety may be a prodromal trigger in HPPD II and anticipatory anxiety may precede visual episodes (Lerner et al., 2014). Anxiety was also identified as a potential risk factor for subsequent development of HPPD, based on findings of comorbidity in a sample of HPPD II sufferers (Halpern et al., 2016), predisposing individuals to a heightened awareness of ordinary visual phenomena (Halpern & Pope, 2003; Halpern et al., 2016; Martinotti et al., 2018). The inclusion of a trait anxiety measure is likely to be of value in investigating a role in HPPD. Combined these individual differences inform the basis of the research rationale and approach.

Research questions

This research will explore group differences between HPPD–type and also in comparison to hallucinogen-experienced controls (i.e., Non-HPPD). The proposed individual differences (vividness of visual imagery, visual apophenia, trait absorption and trait anxiety) are expected to vary across the three groups. There is a considerable gap between individuals' HPPD reports and the diagnostic criteria of both the ICD-10 and the DSM-5 which suggests HPPD-type experiences are varied and idiosyncratic. The presence of individual differences in visual processing style and anxiety across HPPD-type are unknown and this research seeks to help identify the differences across two proposed HPPD typologies and a non-HPPD psychedelic user group.

The primary research question, derived from a review of extant research, is: Are there significant differences between three groups (i.e., Non-HPPD, HPPD I and HPPD II) across our four dependent variables?

With reference to the existing literature in both HPPD and psychedelic research, we hypothesise that vividness of

mental imagery, absorption and apophenia will be higher in the HPPD groups as they relate to an individual's visual processing style (e.g., greater use of mental imagery, increased false-positive pattern recognition and propensity to become immersed in the visual imagery). Additionally, we expect those with persistent visual symptoms will report higher anxiety and this will be highest in our HPPD II group.

To further add to understanding of group differences, several additional questions are proposed. Firstly, across three groups we will ask: Do drug-use frequency, pre-existing diagnoses or prior knowledge of HPPD predict group categorisation? Given the gap in research looking at differences between HPPD types we also propose an investigation of the predictive ability of some HPPD-specific factors, informing our final research question: Do visual symptom severity, precipitating drug type or valence of precipitating experience predict HPPD-type categorisation? A large number of self-report data, in addition to the four psychometric measures, enable this analysis, providing an overall view of the cohorts and their relative context within existing research.

METHODS

Participants

Participants were sourced via several online HPPD forums (e.g., www.hppdonline.com) as well as HPPD-specific and psychedelic-community social media groups. This approach encouraged a mix of HPPD diagnosed and non-HPPD diagnosed participants to respond. Participants were sourced through a brief post explaining the premise of the survey.

From a total of 255 responses, there were 136 (53%) incomplete responses that provided insufficient data for analysis. A further 2 cases were removed due to questionable data identified during HPPD–type categorisation (see following section for details of process) retaining 117 participants for analysis.

Participant age (N = 116; 1 missing) ranged from 16 to 65 years old (M_{age} = 28.01, SD = 10.55). Seventy-four respondents identified as male (63.2%) with 38 female (32.5%), three gender non-conforming (2.6%), one transgender male (1%) and one transgender female (1%). The Non-HPPD (n = 36 [1 missing], M_{age} = 33.47, SD = 9.70) group was significantly older than both HPPD I (n = 33, M_{age} = 26.61, SD = 10.51, P = 0.014) and HPPD II (n = 47 M_{age} = 24.81, SD = 9.74, P < 0.001) groups. There was also a higher percentage of males in the HPPD I (69.7%) and HPPD II (68.1%) groups than in the Non-HPPD group (51.4%).

Categorisation

To categorise participants into their respective groups (i.e., Non–HPPD, HPPD I and HPPD II) a prior diagnosis of HPPD was requested. These diagnosis options were both for self-diagnosis and for an official diagnosis (i.e., made by a psychiatrist/clinical psychologist). Given the nature of the disorder, an official diagnosis is often problematic (Halpern & Pope, 2003) and a large number of those experiencing HPPD are self-diagnosed. Participant responses in this field were cross-reference with a number of other recorded factors to better determine likelihood of a valid HPPD diagnosis and subsequent assignation to HPPD group. Four participants indicating a self-diagnosis of HPPD did not provide responses indicating HPPD symptoms (i.e., post-hallucinogen use visual symptoms) and were included as non-HPPD.

The majority of HPPD research uses the DSM-5 definition of HPPD as a basis for diagnostic clarification and the ICD-10 classification offers no additional benefit (e.g. symptom specificity) and this extant research has informed our approach. DSM-5 definition proposes significant distress is a defining characteristic of an HPPD diagnosis; however, the HPPD literature further refines the disorder, identifying both negative and positive/neutral experiences. The negative experiences are generally understood as HPPD II with neutral/positive experiences consistent with a HPPD I typology. HPPD II is described as a 'severe, unpleasant and long-term condition' (Lerner et al., 2014, p. 297) although sustained symptoms can also be positively interpreted (Baggott et al., 2011; Lerner et al., 2014). HPPD I symptoms are generally understood to be more transient however this would require an arbitrary cutoff of symptom frequency; as a result neutral/positive and negative experiences (Lev-Ran et al., 2017) were determined to better differentiate HPPD-type.

Using Lerner et al.'s (2014) stricter definition we determined those individuals rating their experience of the disorder at 2 (*somewhat negative*) or 1 (*extremely negative*), and with reports of one or more visual symptoms at the score of 4 *(frequently - 1 to 3 times weekly*) or 5 (*very frequently - daily/continuously)* as meeting inclusion criteria for the HPPD II group (see also, Baggott et al., 2011 for interpretation of HPPD-type) and expressing neutral or positive experiences of visual symptoms were included in the HPPD I group. Where symptoms were reported at 2 (*rarely*) or 1 (*once*) to a maximum of three symptoms in any one participant, these participants were considered Non-HPPD. This cutoff was determined to be a valid reflection of the range of normal experiences reported in previous literature (Baggott et al., 2011; Halpern & Pope, 2003; Halpern et al., 2016).

Due to the majority of cases denoting pre-existing visual symptoms (see Figs 1–3) a visual symptom index was calculated to determine authentic change, this was calculated as an absolute score to account for presumably erroneous reductions in symptoms. There were six instances where only pre-existing visual symptoms were indicated but an existing diagnosis of HPPD (two official, two self-diagnosed) was also reported. Objectively, this data would indicate hallucinogens to have a curative effect, which seems unlikely given participants own diagnostic reporting and was determined to be likely erroneous response data.

Of these data, four were determined to be genuine HPPD cases due to the comprehensive nature of the diagnostic information reported in the subsequent free-text boxes. The

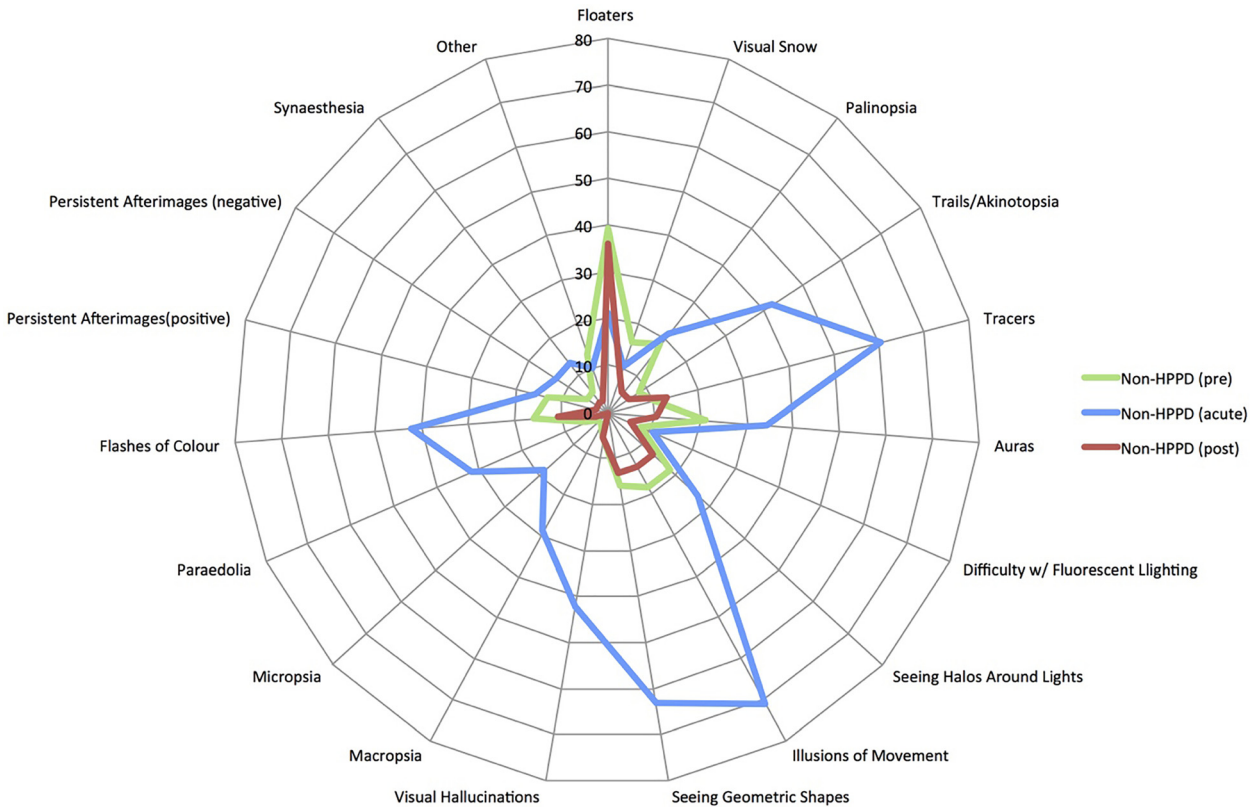

Fig. 1. Radar plot of percentage reported visual symptoms in Non–HPPD group experienced prior to hallucinogen use, in the acute experience and post hallucinogen use

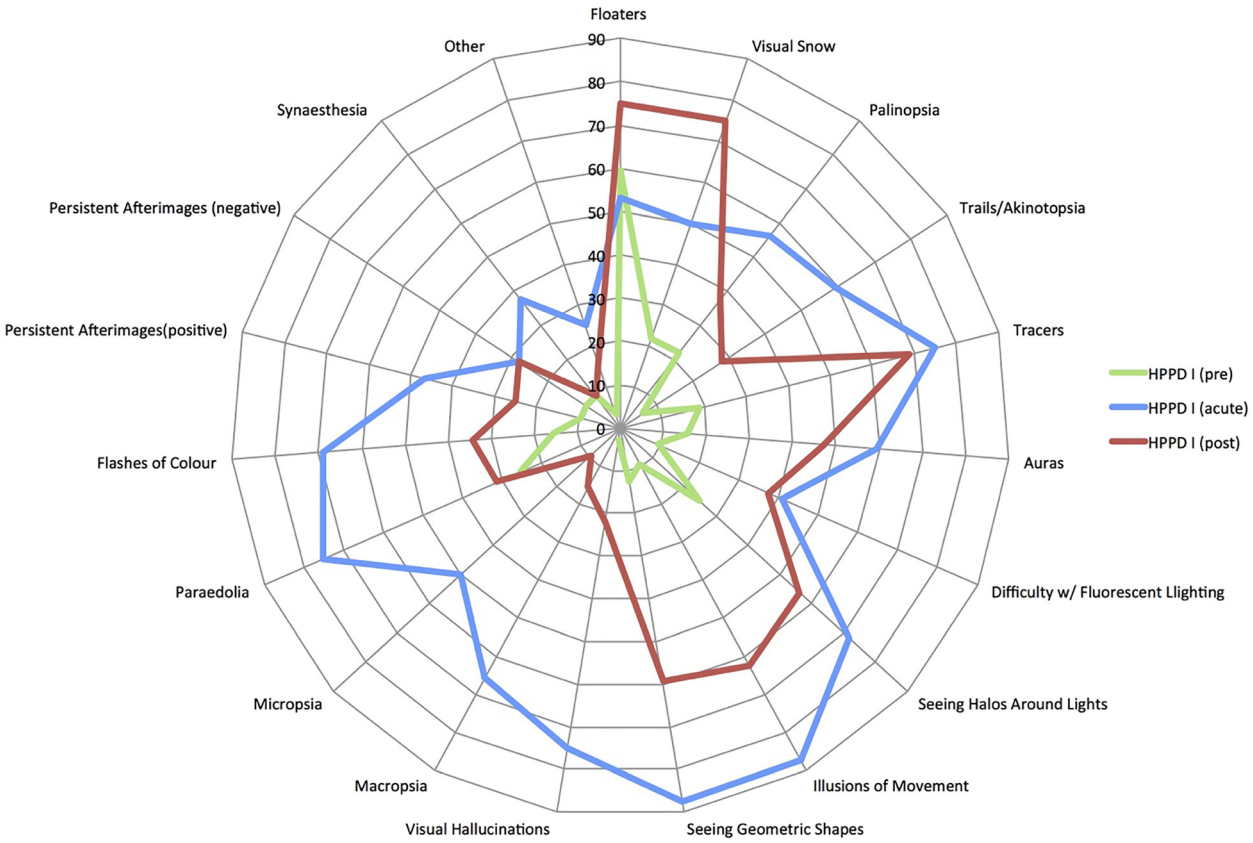

Fig. 2. Radar plot of percentage reported visual symptoms in HPPD I group experienced prior to hallucinogen use, in the acute experience and post hallucinogen use

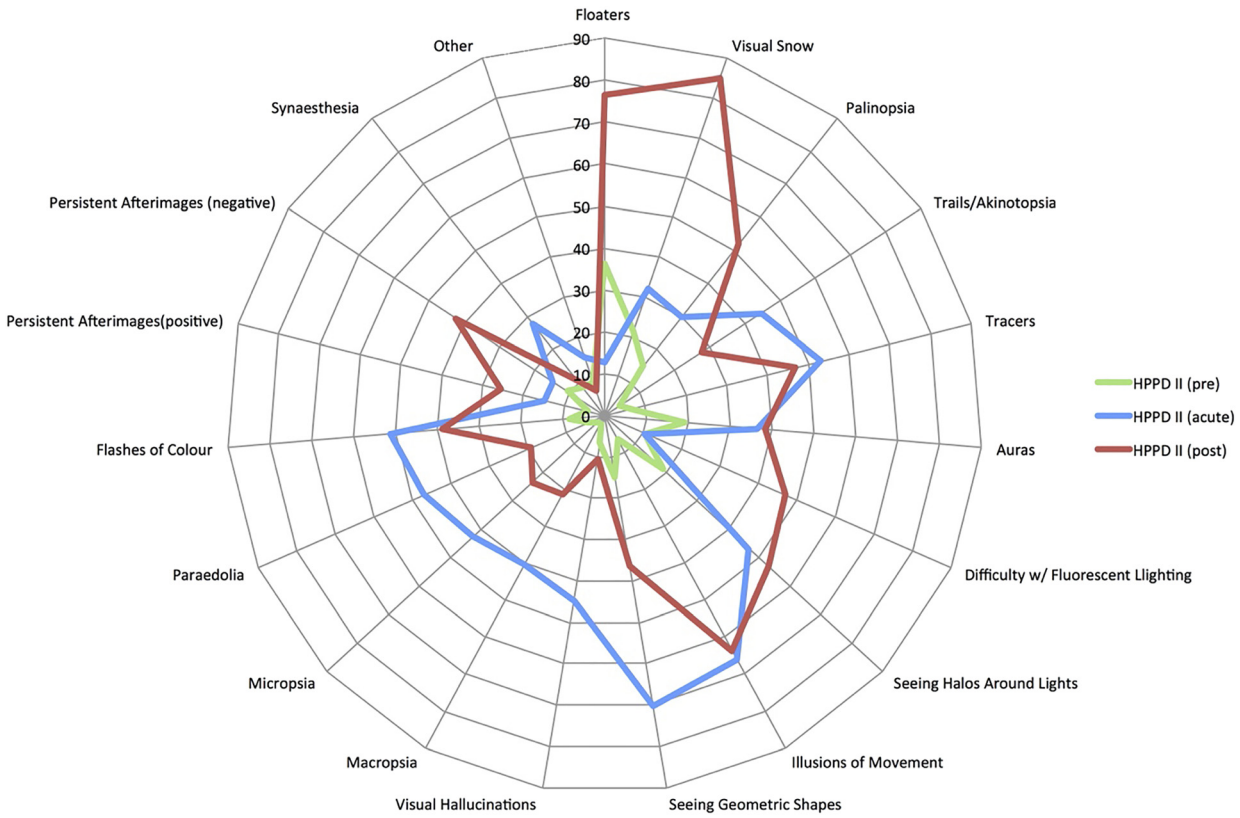

Fig. 3. Radar plot of percentage reported visual symptoms in HPPD II group experienced prior to hallucinogen use, in the acute experience and post hallucinogen use

remaining two cases could not be satisfactorily resolved due to lack of supporting evidence and were therefore removed from analysis. Four respondents indicated pre-existing diagnoses of visual snow syndrome (VSS) which were might better explain their symptoms; however, three responses reported only post-hallucinogen use visual snow and the remaining participant had increase in visual symptom severity consistent with HPPD, all four cases were therefore retained for analysis.

Materials

Following written consent, participants completed a survey asking a range of questions related to pre-existing conditions that might better explain HPPD, their drug use history and experiences (where relevant) of HPPD. Following this, participants were issued four questionnaires delivered in a random block.

The Vividness of Visual Imagery Questionnaire (VVIQ; Marks, 1973) is a scale consisting of 16 items requesting self-report responses to a variety of statements intended to investigate vividness of mental imagery such as, "Visualize a rising sun. Consider carefully the picture that comes before your mind's eye. The sun is rising above the horizon into a hazy sky". Responses are scored between 1 (*perfectly clear and as vivid as normal vision)* and 5 (*No image at all, you only 'know' that you are thinking of an object*). These scores are then reversed to calculate the total VVIQ score (Marks, 1973). Respondents at the extreme responses are considered aphantasic if their score falls between 16–23 and hyperphantasic if it exceeds 75 out of a possible total score of 80 (Milton et al., 2020). Marks' original work (1973) reported test-retest reliability of 0.74, with higher split-half reliability ranging from 0.85 (Marks, 1973) to 0.95 (see Campos, 2011) and internal consistency ranging from 0.88 to 0.91 (Campos, 2011).

The Modified Tellegen Absorption Scale (MODTAS; Jamieson, 2005) is a 34-item measure developed to measure absorption, self-altering experience and hypnotic susceptibility through statements such as "I imagine some things so vividly they hold my attention as a good movie or story does". The scores are measured on a 5-point frequency scale from 1 (*never)* to 5 (*very often*), with higher scores on this scale representing higher levels of absorption. Recent studies indicate good internal consistency (e.g., Cronbach's α 0.96 [Terhune et al., 2016] and 0.94–0.95 [Andrei, Vessely, & Siegling, 2016])

Apophenia describes the propensity for individuals to perceive patterns in apparently random information; that is, a propensity for false pattern recognition. Our study employed the Visual Apophenia Luke Irvine Scale (VALIS; Luke & Irvine, 2020), an instrument designed to investigate participant propensity for apophenia in the visual modality. The VALIS is a five-item measure consisting of a series of

images of clouds (devoid of additional content). These images are presented sequentially and information about the content of any imagery seen in the clouds is requested. A rating between 1 (*not clear at all*) to 5 (*very clear*) of the clarity of each percept is also recorded. Higher scores represent greater clarity of percept and increased apophenia.

A brief measure of trait anxiety was undertaken using the Spielberger State–Trait Anxiety Inventory Trait– 5 (STAIT–5; Zsido, Teleki, Csokasi, Rozsa, & Bandi, 2020) The STAIT–5 is a highly correlated, modified version of the original 20-item scale that retains good reliability (i.e., Cronbach's α 0.86; Zsido et al., 2020). Participants are requested to answer five statements such as "I take disappointments so keenly that I can't put them out of my mind" scored on a scale of 1 (*not at all*) to 4 (*very much so*). Higher scores represent higher levels of anxiety, with a score greater than 14 proposed to represent clinically significant anxiety (Zsido et al., 2020). Cronbach's α for all measures employed in this sample can be found in Table 1.

Design

The research undertaken was an exploratory investigation of group differences between psychedelic users (Non–HPPD, HPPD I and HPPD II) across four variables. The four questionnaires (VALIS, VVIQ, STAIT–5 and MODTAS) comprised the dependent variables used in four separate one-way Analysis of Variance tests (ANOVA) with group categorisation (three levels) as the independent variable. The other response data was collated and used as predictor variables in multinomial logistic regression when the model utilised three groups (i.e., Non–HPPD, HPPD I and HPPD II) and in binary logistic regression when analysis was specific to a dichotomous dependent variable (i.e., across only HPPD groups).

Procedure

Participants completed the survey using the Qualtrics survey tool. Average survey completion time was 49.36 min (SD = 224.49 min, median = 21.72 min), length of survey was determined by participant responses. No personal identifying data was recorded to ensure anonymity was maintained. Data were stored as per GDPR requirements. Participants confirmed their participation via a consent form detailing the research and were also delivered a debrief form upon completion. Data were analysed using SPSS version 25.0. Ethical approval for this study was granted by the Psychology and Counselling Research Ethics Panel of the University of Greenwich.

Table 1. Correlations matrix with Cronbach's alpha indicated on the diagonal

Variable	*M*	SD	1	2	3	4
1. MODTAS	55.48	24.07	(0.93)			
2. STAIT-5	13.33	4.35	−0.15	(0.86)		
3. VALIS	6.51	5.71	0.32**	−0.02	(0.76)	
4. VVIQ	39.60	16.83	−0.29**	0.21*	−0.05	(0.97)

Note. MODTAS = modified Tellegen absorption scale, STAIT-5 = Spielberger state-trait anxiety inventory (trait) – 5, VALIS = visual apophenia Luke Irvine scale, VVIQ = vividness of visual imagery questionnaire.
* $P < 0.05$. ** $P < 0.01$. ** $P < 0.01$.

Data processing

Main analysis (ANOVA). No outliers were statistically determined (i.e. all studentised residuals <2.5). STAIT-5 scores were found to be significantly heterogeneous (F (2,114) = 3.28, $P = 0.041$) the remainder of IVs satisfied the assumption of homogeneity (all $P > 0.05$). A series of F-tests was undertaken for the homogeneous variables (i.e., VVIQ, VALIS, & MODTAS) and a Welch's ANOVA was performed on the STAIT-5 measure. Tukey-Kramer HSD post-hoc tests were used for post hoc testing (unless otherwise stated).

Low rates of missing data were indicated in the VVIQ responses were assessed by expectation maximisation and determined to be random, as assessed by Little's MCAR (Little, 1988), X^2 (37) = 15.0, $P = 1.00$). Data were replaced using *missing values analysis* (SPSS 25.0).

Secondary analyses (logistic regression). Box-Tidwell (Box & Tidwell, 1962) transformation was not significant for either Logistic Regression, indicating linearity of the logit for all continuous predictor variables.

The area under the curve discrimination in the binomial model (AUC = 0.76) was acceptable (Hosmer, Lemeshow, & Sturdivant, 2013, p. 177).

RESULTS

Descriptive statistics

Participants were distinguished into one of three groups based on their visual symptoms following hallucinogen use for group comparisons. Radar plots spanning stages of hallucinogen experience (pre, acute and post) show lifetime experiencing of visual symptoms across the three groups (see Figs 1–3).

On average HPPD II participants reported an increase of 2.91 novel visual symptoms (out of a possible 19) following hallucinogen use and a mean increase of visual symptom frequency score of 24.78 on a scale of 1 (*once*) to 5 (*daily/continuously*) over 19 visual symptoms (see Table 2 for additional group means). Cannabis was the most commonly used drug and had the highest reported frequency of use across all three groups. Taken together 90.6% of the total participants reported lifetime use of cannabis.

Lifetime drug use across groups was largely comparable; however, use of cannabis was significantly higher in the HPPD I group than the Non-HPPD and HPPD II groups. Ketamine and LSD use was significantly higher in the HPPD I group than the Non-HPPD group and MDMA use was higher in the HPPDI group than the HPPII group (see

Table 2. Mean increase in number of novel visual symptoms and frequency of symptoms (visual symptom index) following hallucinogen use by group

Variable	Non-HPPD		HPPD I		HPPD II	
	n	*M*	*n*	*M*	*n*	*M*
Novel visual symptoms	3	0.08	15	2.18	20	2.91
N (Missing)	37 (34)		33 (18)		47 (27)	
Symptom frequency increase	19	1.63[a]	33	21.18[a]	47	24.79[a]
N (Missing)	37 (18)		33 (0)		47 (0)	

Note. Measured across 19 visual symptoms.
[a] Calculated from visual symptom index.

Fig. 4). Uncorrected *t*-tests comparing constant/near-constant symptom score across HPPD groups indicated visual snow ($P = 0.005$) and negative afterimages ($P = 0.022$) were significantly higher in the HPPD II group (see Table 3)

Primary research questions

ANOVAs were performed using Tukey-Kramer post hoc tests unless otherwise stated. For all means and model fit data see Table 4. Correlations of the four dependent variables and their overall means can be found in Table 1.

A one-way ANOVA indicated significant differences in absorption scores. Absorption scores were significantly higher in the HPPD I group than in both the Non–HPPD group ($M_{diff} = 18.72$, 95% CI [5.73, 31.71], $P = 0.002$, $d = 0.82$) and the HPPD II group ($M_{diff} = 17.42$, 95% CI [5.09, 29.74], $P = 0.003$, $d = 0.76$) indicating increased absorption is significantly higher in HPPD I. No significant differences between HPPII and Non–HPPD groups.

One-way ANOVA also indicated significant differences in VALIS scores. HPPD I group scores were significantly higher than both the Non–HPPD group ($M_{diff} = 3.61$, 95% CI [0.45, 6.77], $P = 0.021$, $d = 0.65$) and the HPPD II ($M_{diff} = 3.05$, 95% CI [0.05, 6.04], $P = 0.045$, $d = 0.54$). No significant differences were identified between HPPD II and Non–HPPD groups suggesting high levels of visual apophenia are associated specifically with HPPD I group categorisation.

Significant differences in anxiety scores were also indicated across the three groups. The HPPD II group scored significantly higher in trait anxiety than both the HPPD I group ($M_{diff} = 3.09$, 95% CI [0.85, 5.33], $P = 0.005$, $d = 0.76$) and the Non–HPPD group ($M_{diff} = 3.46$, 95% CI [1.35, 5.57], $P = 0.001$, $d = 0.85$). No significant differences were indicated between Non–HPPD and HPPD I groups suggesting increased anxiety is particular to the HPPD II group.

No significant differences were found between the means of the three groups on their VVIQ scores suggesting

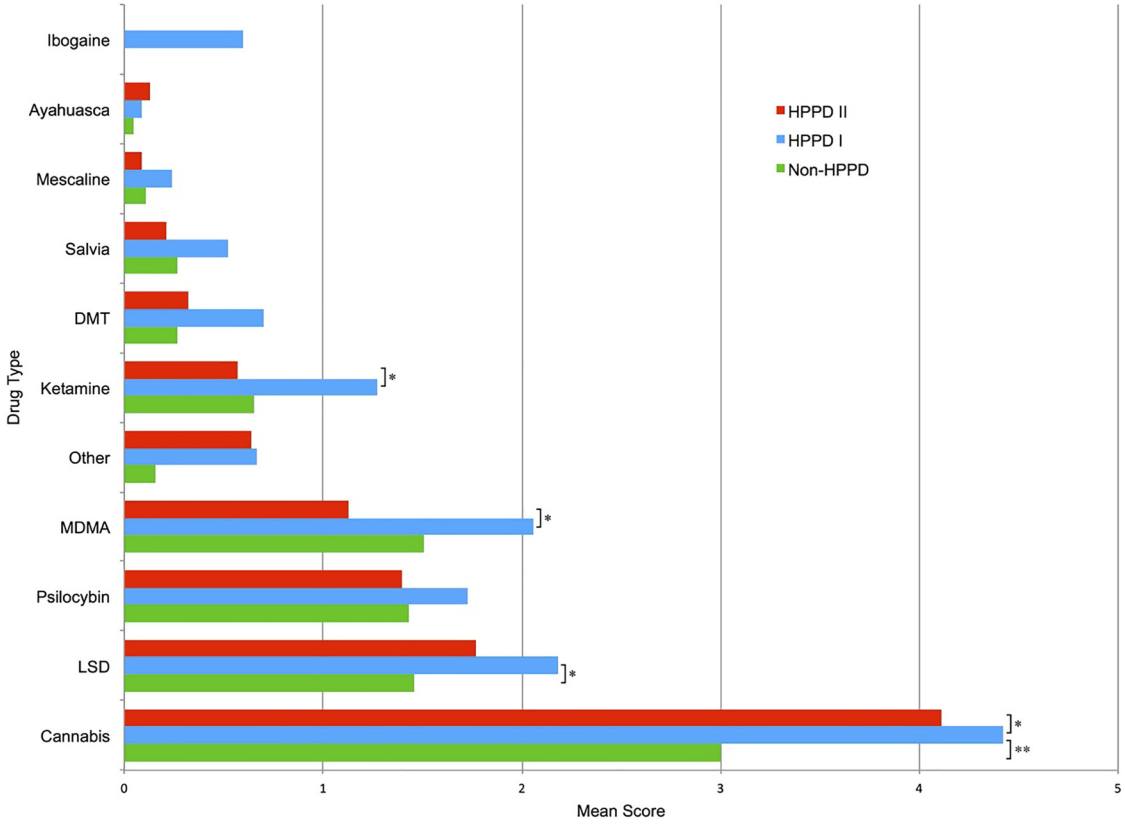

Fig. 4. Mean reported drug use frequencies by group.
Note. Scale: 0 = *Never*, 1 = *Once*, 2 = *Occasionally*, 3 = *Often*, 4 = *Regularly*, 5 = *Extensively*, 6 = *Excessively*.
Significance calculated using Tukey Kramer post hoc test. $^{*}P < 0.05$ $^{**}P < 0.01$

Table 3. Collated table of percentage of lifetime experience and constant experience of HPPD visual symptoms reported in previous research

	Abraham (1983)	Baggot et al., (2011)		Lewis (2020)		Puledda et al., (2020)		Current Study			
								HPPD I		HPPD II	
Visual symptom	Lifetime %	Lifetime %	Constant %	Lifetime %	Constant %	Lifetime %	Constant %	Lifetime %	Constant %	Lifetime %	Constant %
Visual snow	–	–	–	96.2	65.4	100	100	72.7	54.4	85.1	83**
Floaters	–	–	–	96.2	57.7	77	–	75.8	42.4	76.6	57.4
Trails	49.2	22.1	9.2	96.2	57.7	64	–	30.3	18.2	27.7	19.1
Fluorescent	–	22.4	–	88.5	42.3	–	–	36.4	30.3	46.8	36.2
Halos	30.2	20.5	7.3	88.5	50	–	–	54.5	39.4	53.2	46.8
Breathing walls	–	33.9	8.6	88.5	34.6	–	–	60.6	33.3	63.8	36.2
Flashes	49.2	–	–	84.6	38.5	60	–	33.3	18.2	38.3	29.8
Auras	–	–	–	80.8	46.2		–	45.5	21.2	38.3	34
Positive afterimage	31.7	–	–	76.9	30.8	83	–	24.2	18.2	25.5	23.2
Geometric	65.1	24.2	8.8	69.2	19.2	–	–	60.6	36.4	36.2	25.5
Negative afterimage	17.5	–	–	65.4	19.2	–	–	27.3	18.2	42.6	23.4*
Pareidolia	20.6	–	–	50	11.5	–	–	33.3	18.2	19.1	12.8
Macropsia	23.8	–	–	46.2	3.8	–	–	15.2	9.1	21.3	6.4
Micropsia	19	–	–	46.2	3.8	–	–	9.1	3	23.4	8.5
Visual hallucinations	47.6	6.3	1.2	42.3	3.8	–	–	21.2	9.1	10.6	6.4
Synaesthesia	–	–	–	–	–	–	–	9.1	9.1	10.6	6.4
Tracers	–	7.6	1.5	–	–	–	–	69.7	36.4	46.8	38.3
Palinopsia	–	–	–	–	–	–	–	39.4	27.3	51.1	46.8

Note. Lifetime % = ever experienced.

Visual Snow = TV static-like overlay on vision. Floaters = black/grey objects that move with eye movement. Trails = normally coloured still images that appear in the wake of moving objects (i.e., akinotopsia). Fluorescent = difficulty being under fluorescent lights. Halos = seeing halos around lights. Breathing walls = illusions of seeing objects moving. Flashes = flashes of coloured light. Auras = zig-zag lines of colour and growing blind spots. Positive afterimage = persistent after images of a normal colour. Geometric = seeing geometric shapes (eyes open and/or eyes closed). Negative afterimage = persistent after images of the opposite colour. Pareidolia = seeing distinct objects within objects (e.g., false positive of seeing a defined face in a pattern). Macropsia = seeing objects as larger than they actually are. Micropsia = seeing objects as smaller than they actually are. Visual Hallucinations = seeing objects that are not really there (i.e., pseudo-hallucinations). Synaesthesia = combined sensory perceptions (e.g., colours being associated with sounds or letters). Tracers = objects leaving trails behind them as they move– like long exposure photography. Palinopsia = objects that persist in vision after the object is no longer present.

Abraham (1983) (N = 63, flashbackers, self-reporting clinical population, severity of symptoms not reported). Baggott et al. (2011) (N = 2,455, self-reporting abnormal visual experiences following hallucinogen use,(104 HPPD II participants). Lewis (2020) (N = 26, HPPD diagnosis). Puledda et al. (2020) (visual snow, self-reporting, classified as suspected HPPD, N = 70).

* $P < 0.05$ (two-tailed).

** $P < 0.01$ (two-tailed).

Table 4. Means, standard deviations, and one-way analyses of variance of dependent variables

	Non-HPPD		HPPD I		HPPD II			
	M	SD	M	SD	M	SD	*F* (2,114)	Estimated Effect Size (ω2)
MODTAS	49.68	23.40	68.39	24.97	50.98	20.78	7.38**	0.10
STAIT-5	11.84	4.40	12.21	4.53	15.30	3.41	10.13***[a]	0.12
VALIS	5.27	4.86	8.88	6.25	5.83	5.54	4.28*	0.05
VVIQ	40.89	17.37	38.88	17.34	39.08	16.34	0.16	−0.01

Note. MODTAS = modified Tellegen absorption scale, STAIT-5 = Spielberger state-trait anxiety inventory (trait) – 5, VALIS = visual apophenia Luke Irvine scale, VVIQ = vividness of visual imagery questionnaire.
[a] Welch *F* (2, 67.39).
* $P < 0.05$. ** $P < 0.01$. *** $P < 0.001$.

vividness of visual imagery was homogenous across all three groups.

Additional research questions

Given the exploratory nature of the data analyses a forward stepwise multinomial logistic regression was undertaken (Osborne, 2015; Tabachnick & Fidell, 2014) to determine if any pre-existing diagnosis present across the three groups (i.e. visual snow, anxiety disorder and other), prior knowledge of HPPD (collapsed into a binary variable, 0 = *no prior knowledge*, 1 = *prior knowledge*) or total drug use score predicted group categorisation.

Table 5. Multinomial logistic regression predicting HPPD – type based on pre-existing diagnosis, prior awareness and total drug score

			95% Confidence Interval for Odds Ratio		
Variable	*B* (SE)	Wald X^2	Lower	Odds Ratio	Upper
HPPD I vs. Non–HPPD					
Intercept	−0.45 (1.47)	0.11	–	–	–
Anxiety Diagnosis	−1.77 (1.14)	2.42	0.17	0.17	1.58
HPPD Awareness	0.98 (0.72)	1.86	0.65	2.65	10.78
Total Drug Score	0.19 (0.07)**	7.83	1.06	1.21	1.38
HPPD II vs. Non–HPPD					
Intercept	1.01 (1.27)	0.64	–	–	–
Anxiety Diagnosis	−2.18 (1.09)*	4.00	0.01	0.11	0.96
HPPD Awareness	1.66 (0.65)**	6.48	1.47	5.27	18.98
Total Drug Score	0.10 (0.07)	2.26	0.97	1.10	1.25

Note. Nagelkerke Pseudo-R^2 = 0.27. Model: $X^2(6) = 26.93$, $P < 0.001$. Anxiety Diagnosis = Pre-HPPD anxiety diagnosis (coded 0 = *no diagnosis*, 1 = *diagnosis*), HPPD Awareness = prior awareness of HPPD (coded 0 = *none*, 1 = *aware*), Total Drug Score = sum of drug use frequencies reported.
* $P < 0.05$. ** $P < 0.01$.

Participants reporting pre-existing anxiety diagnoses were 8.85 times more likely to be in the HPPD II group than the Non–HPPD group. Lack of prior knowledge of HPPD significantly predicted HPPD II group categorisation, with the HPPD II group 5.27 times more likely to indicate a lack of prior knowledge than the Non–HPPD group. HPPD I group categorisation was also significantly predicted by higher drug use scores than the Non–HPPD group. Details of the model can be found in Table 5.

A binary logistic regression was also undertaken to explore predictors of HPPD group categorisation. Due to sample size, the model was limited to three predictors (Peduzzi, Concato, Kemper, Holford, & Feinstein, 1996). The variables chosen were, LSD as a precipitating drug, constant symptom score (i.e., number of constant/near-constant symptoms reported) — suspected to better define negative experience of HPPD (Halpern et al., 2016) and valence of precipitating experience, with higher scores indicating a more negative experience, where 1 = *extremely positive* and 5 = *extremely negative*.

Participants reporting negative precipitating experience were 1.8 times more likely to be in the HPPD II group than the HPPD I ($P = 0.001$). None of the other variables significantly predicted HPPD group categorisation (see Table 6).

Table 6. Binary logistic regression of valence of precipitating experience, constant symptom score and LSD as precipitating drug

			95% Confidence interval for odds ratio		
Variable	*B* (SE)	Wald X^2	Lower	Odds ratio	Upper
Valence of precipitating experience	0.59 (0.17)*	11.74	1.29	1.81	2.53
Constant Symptom Score	0.07 (0.07)	1.02	0.94	1.07	1.23
LSD Precipitating Drug	0.72 (0.53)	1.85	0.73	2.05	5.80
Constant	−2.20 (0.70)*	9.82	–	0.11	–

Note. Nagelkerke R^2 = 0.27, Model = $X^2(3) = 17.96$, $P < 0.001$. Constant Symptom Score = sum of participant constant & near constant responses.
* $P < 0.01$.

DISCUSSION

The present study set out to determine the primary research question, investigating differences between three groups of hallucinogen users across vividness of visual imagery, absorption, visual apophenia and trait anxiety. Additionally, the predictive ability of prior knowledge, drug use and pre-existing diagnoses were investigated across three groups. Potential predictors of HPPD–type were also explored across two HPPD groups. There was partial support for our hypothesis that absorption, apophenia and vividness of visual imagery would be higher in the HPPD groups. Significant group differences were found, with HPPD I scoring higher than the other groups on both absorption and apophenia and with the HPPD II group scoring higher on measures of trait anxiety. Trait anxiety was comparable in Non-HPPD and HPPD I groups, indicating it may be specific to HPPD II–type and VVIQ scores did not differ across the three groups indicating partial support for our main hypothesis. These results are interpreted in relation to the findings from our additional research questions and with reference to existing HPPD research.

Our HPPD cohorts were comparable in age but had a lower proportion of male participants than that found in previous HPPD research (e.g., Baggott et al., 2011; Halpern et al., 2016; Lewis, 2020). Both our HPPD groups were younger and predominantly more male than the Non-HPPD group. Considerable homogeneity of visual symptoms was apparent across the two HPPD groups, with only the symptoms of constant visual snow and negative afterimage differing significantly between the two groups, most strongly linking constant visual snow with negative experiences of HPPD.

Overall our HPPD II group was statistically no more likely to report a greater number of constant symptoms, suggesting the presence of constant/near-constant symptoms may not best define the HPPD II experience. Taken together, these findings indicate our HPPD cohorts were largely comparable to recent literature (see Table 3) and contests the assumption that non-negative HPPD experiences are best defined by transient symptoms (e.g., Halpern et al., 2016) and that constancy of visual symptoms plays a primary role in determining the HPPD experience.

LSD was the most common drug implicated with HPPD onset, a finding consistent with the majority of recent research (Baggott et al., 2011; Halpern et al., 2016; Lev-Ran et al., 2017); and there was no significant difference between our HPPD groups. Poly-substance onset was commonly reported — a relatively novel finding within the HPPD literature (e.g., Halpern et al., 2016). A review of free-text responses (not published here) indicates that both single-event and long-term poly-substance use might be implicated with HPPD onset, further reducing evidence of a single precipitating drug type. Case reports of substituted phenethylamines (Stanciu & Penders, 2016). and THC-analogue cannabinoids (Orsolini et al., 2017) in the subsequent development of HPPD symptoms seem to point towards an increasing divergence of aetiology.

The primary serotonergic hypothesis of HPPD proposed by Abraham and Aldridge (1993) suggests that LSD disrupts the inhibitory function of 5HT2 interneurons, with chronicity occurring as the result of neurotoxic effect of LSD (Abraham & Duffy, 1996). This occipital disinhibition (Abraham & Duffy, 2001) is effectively a proposition that disruption of the top-down control over visual input is at play. This idea of chronic "liberated bottom-up information flow" (Carhart-Harris & Friston, 2019, p. 317) is also proposed to underlie HPPD within the *relaxed beliefs under psychedelics* (REBUS) model. Other research suggests a potential role of the 5-HT2A receptor in a wide range of visual disorders (Ffytch, 2007); however, given the aetiological diversity associated with HPPD onset, this hypothesis seems unlikely to provide a complete explanation.

The number of participants reporting visual symptoms prior to hallucinogen use was comparable across the three groups (see Figs 1–3) lending support to the idea that HPPD might represent some degree of increased sensitivity to pre-existing visual experiences— as suggested in previous research (Halpern et al., 2016). Halpern and colleagues also suggest that increased anxiety may constitute a risk factor that interacts with this predisposition, resulting in persistent visual symptoms. Only our HPPD II group was predicted by both prior diagnoses of anxiety disorders and higher trait anxiety scores lending partial support to this theory.

Pre-existing anxiety might influence the acute psychedelic experience, with state-based factors (i.e., set and setting) predicting challenging psychedelic experiences; however, trait anxiety has also been shown to predict reduced long-term well-being (Haijen et al., 2018). Lack of prior knowledge and the valence of the precipitating experience also predicted HPPD II group categorization, these unexpected, negative experiences might further increase anxiety and lead to concern around persistent visual phenomena. Increased stress has also been shown to trigger episodic visual symptoms at a higher rate in HPPD II compared to HPPD I participants (Lev-Ran et al., 2017) suggesting a differentiating role across HPPD–type. The relationship between anxiety and stress is complex (Wiggert, Wilhelm, Nakajima, & al'Absi, 2016) but invites the idea of a psychobiological response in HPPD.

Similar HPPD symptoms can originate independently of increased anxiety, suggesting pre-existing anxiety may be better understood as a potential risk factor in the development of HPPD II. Halpern et al. (2016) suggestion that HPPD might be, in itself, a type of traumatic anxiety disorder seems a good fit with our findings; however, this remains only a partial explanation of the HPPD experience. Taken together this suggests that trait anxiety might be better understood to influence the HPPD experience more generally (e.g., as a negative response to persistent visual stimuli), with individuals high in anxiety experiencing the same symptoms as more severe, something that itself could affect prognosis (Rief, Mewes, Martin, Glaesmer, & Braehler, 2010). The partial efficacy of benzodiazepines in the reduction HPPD symptoms (Abraham, 2014) also points towards anxiety as a candidate for the worsening of HPPD experience or exacerbating symptoms and not underlying development *in toto*.

Absorption in an experience reflects readiness for experiential engagement (Wild, Kuiken, & Schopflocher, 1995) and may increase propensity for *cognitive bizarreness* (Kraehenmann et al., 2017, p. 2031). Matefy (1980) also suggested that flashback experiencers (i.e., HPPD I) are more prone to immersion in an experience which appears to fit the findings with our HPPD I cohort. Absorption may also be more effective at reducing anxiety response than vividness of visual imagery (Kwekkeboom, Huseby-Moore, & Ward, 1998). Using guided imagery interventions Kwekkeboom et al. (1998) showed that an increased ability to become immersed in the mental imagery generated, over and above its vividness, may promote anxiety reduction potentially explaining some of our findings.

Absorption is also correlated with trait openness (Wild et al., 1995), a personality construct associated with less stringent filtering of preconscious information and increasing associations between irrelevant stimuli (i.e., apophenia; Christensen, 2020). This offers some aid in interpretation of our findings that both absorption and apophenia were increased in our HPPD I group. The measures of apophenia used in research vary considerably. Incorporation of non-visual apophenia measures in future investigations would help clarify apophenia's relationship with absorption and its role in positive/neutral experiences of HPPD. In light of our findings, it is conceivable that an increased propensity to become absorbed in the HPPD experience indicates a distinct response to persistent visual imagery, whilst also accounting for the similar VVIQ scores.

The finding that vividness of mental imagery was homogeneous across all the groups is contra to both our expectations and the findings of Matefy (1980). Vividness of mental imagery has shown to increase with psychedelic use (Carhart-Harris et al., 2012) and psychedelics have even implicated in the reversal of aphantasia (Dos Santos, Enyart, Carlos Bouso, Pares, & Hallak, 2018; however this may not be true of congenital aphantasia, see, Luke, 2018). Our sample displayed considerably lower VVIQ scores than normal populations (see Milton et al., 2020) suggesting the cohort may have had a lower baseline of vividness of visual imagery, which may also account for the difference in findings with Matefy's work (1980).

Combined, these findings indicate that individual differences within HPPD might play a role in determining the resultant experience of the disorder, rather than predicting onset of HPPD per se. Negative experiences of HPPD are typified by heightened anxiety, lack of prior knowledge and negative precipitating experiences; whilst increased drug use, propensity for higher visual apophenia and absorption are associated with positive/neutral experiences of HPPD.

Limitations

HPPD is little understood and poorly defined, making accurate diagnosis problematic (Halpern & Pope, 2003; Lewis, 2020). The group categorisation procedure was based on existing theory; however, our findings must be interpreted in the context of researchers with no direct clinical experience of HPPD. Without clear delineating criteria (e.g., exact number of symptoms or defined latency period) any attempt at effective group categorisation risks being somewhat arbitrary. The approach of Lev-Ran et al. (2017) in distinguishing positive versus negative HPPD is somewhat supportive of our approach, in that an individual's experience of HPPD is a defining factor of HPPD categorisation.

The VVIQ measure used is proposed to have both eyes open and eyes closed subscales (Marks, 1973) however in the interests of study design this was limited to an eyes open subscale only, potentially reducing the sensitivity of the measure. However, similar approaches have been employed in recent aphantasia/hyperphantasia research (e.g. Milton et al., 2020).

Despite the attention paid to study design (e.g., the brevity of measures employed), those participants who experienced HPPD were presented with a longer survey. This was investigated as a reason for the high rates of attrition; however, this was deemed unlikely as the majority of incomplete responses were filed ahead of reaching the HPPD-specific items. It is possible that the relative length of the survey offered some protection against the inclusion of unserious response data. Given the additional mental health issues present in the sample, the researchers might also have considered controlling for additional psychotropic drugs (e.g., prescription antipsychotics).

Perhaps the biggest limitation, as with all survey-based research, was the reliance on self-report data. Our sample was opportunistic and therefore risks inaccurate representation of HPPD and other psychedelic-using populations; however, our findings indicate a good fit with the existing literature. Individuals using online forums represent an accessible cohort of HPPD experiencers that, due to the estimated low prevalence rates (Baggott et al., 2011), would otherwise be difficult to obtain.

Future research

The 5HT2-A receptor enables the experiencing of the abstract aspects (e.g., mental imagery) of serotonergic hallucinogens (Kraehenmann et al., 2017). Increased sensitivity at the receptor via 5HT2-A polymorphism (Ott, Reuter, Hennig, & Vaitl, 2005) appears to contribute to the response to psychedelic experiences (Preller & Vollenweider, 2016) and is linked with increased absorption (Ott et al., 2005). A potential mediating role for 5HT2–A polymorphism in determining an HPPD I response to persistent visual stimuli may be a question of scientific value.

The finding that visual snow was the most common and most severe symptom reported across both HPPD groups is of interest as it has only recently been identified as an associated symptom of HPPD. Comparison with findings of recent VSS and HPPD research indicates a large overlap in symptomology and severity of the two conditions (see Table 3). Recent VSS literature has also proposed HPPD might be understood as a subtype of VSS (Puledda, Schankin, & Goadsby, 2020). A comparative

brain imaging study, using VSS findings (e.g., Aldusary et al., 2020; Schankin et al., 2020) as a roadmap to explore the two disorders' functional and structural similarities would be of scientific interest.

CONCLUSIONS

Our findings point towards a potential role of individual differences in determining the experience of HPPD. The increased absorption and visual apophenia characteristic of HPPD I, suggests immersion in the HPPD experience and propensity for pattern finding might represent a particular way of responding to a persistent visual experience. Similarly, the increased anxiety associated with HPPD II may determine an individual's response to persistent visual symptoms— a heightened awareness, typified by concern over symptoms. Those with a negative experience of HPPD (i.e., HPPD II) are potentially at higher risk of developing this response through pre-existing anxiety, a lack of prior knowledge and potential for negative precipitating experiences. The increased trait anxiety in the HPPD II group could be in response to the severity of the symptoms or it could be driving the negative experience — which would explain participants' increased pre-existing anxiety diagnoses— however, this relationship might also be reciprocal. Until a more advanced, comprehensive understanding of the potential aetiologies is sought, treatment of anxiety may constitute the only treatment options available for improving quality of life.

In summary, it is proposed that our findings are best understood as distinguishing two personality profiles in response to experiencing HPPD. Our findings indicate support for a dual taxonomy of HPPD; however, a dimensional approach to investigation of the disorder may prove fruitful. Further investigations are warranted and greater clarification of what constitutes HPPD is essential for advancing scientific understanding.

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REFERENCES

Abraham, H. D. (1983). Visual phenomenology of the LSD flashback. *Archives of General Psychiatry*, *40*(8), 884. https://doi.org/10.1001/archpsyc.1983.01790070074009.

Abraham, H. D. (2014). When the trip doesn't end. *Psychologist*, *27*(9), 670–673.

Abraham, H. D., & Aldridge, A. M. (1993). Adverse consequences of lysergic acid diethylamide. *Addiction*, *88*(10), 1327–1334. https://doi.org/10.1111/j.1360-0443.1993.tb02018.x.

Abraham, H. D., & Duffy, F. H. (1996). Stable quantitative EEG difference in post- LSD visual disorder by split-half analysis: Evidence for disinhibition. *Psychiatry Research: Neuroimaging*, *67*(3), 173–187. https://doi.org/10.1016/0925-4927(96)02833-8.

Abraham, H. D., & Duffy, F. H. (2001). EEG coherence in post-LSD visual hallucinations. *Psychiatry Research: Neuroimaging*, *107*(3), 151–163. https://doi.org/10.1016/s0925-4927(01)00098-1.

Aldusary, N., Traber, G. L., Freund, P., Fierz, F. C., Weber, K. P., Baeshen, A., et al. (2020). Abnormal connectivity and brain structure in patients with visual snow. *Frontiers in Human Neuroscience*, *14*, 582031. https://doi.org/10.3389/fnhum.2020.582031.

American Psychiatric Association (2014). *Diagnostic and statistical manual of mental disorders (DSM-5®)* (5th ed.). American Psychiatric Publishing.

Anderson, W. H., & O'Malley, J. E. (1972). Trifluoperazine for the "trailing" phenomenon. *JAMA*, *220*(9), 1244–1245. https://doi.org/10.1001/jama.1972.03200090066017.

Andrei, F., Vesely, A., & Siegling, A. B. (2016). An examination of concurrent and incremental validity of four mindfulness scales. *Journal of Psychopathology and Behavioral Assessment*, *38*(4), 559–571. https://doi.org/10.1007/s10862-016-9546-x.

Baggott, M. J., Coyle, J. R., Erowid, E., Erowid, F., & Robertson, L. C. (2011). Abnormal visual experiences in individuals with histories of hallucinogen use: A web- based questionnaire. *Drug and Alcohol Dependence*, *114*(1), 61–67. https://doi.org/10.1016/j.drugalcdep.2010.09.006.

Baumann, F. (1970). Hypnosis and the adolescent drug abuser. *American Journal of Clinical Hypnosis*, *13*(1), 17–21. https://doi.org/10.1080/00029157.1970.10402074.

Box, G. E., & Tidwell, P. W. (1962). Transformation of the independent variables. *Technometrics*, *4*(4), 531–550. https://doi.org/10.2307/1266288.

Campos, A. (2011). Internal consistency and construct validity of two versions of the revised vividness of visual imagery questionnaire. *Perceptual and Motor Skills*, *113*(2), 454–460. https://doi.org/10.2466/04.22.PMS.113.5.454-460.

Carhart-Harris, R. L., & Friston, K. (2019). REBUS and the anarchic brain: Toward a unified model of the brain action of psychedelics. *Pharmacological Reviews*, *71*(3), 316–344. https://doi.org/10.1124/pr.118.017160.

Carhart-Harris, R. L., Kaelen, M., Whalley, M. G., Bolstridge, M., Feilding, A., & Nutt, D. J. (2014). LSD enhances suggestibility in healthy volunteers. *Psychopharmacology*, *232*(4), 785–794. https://doi.org/10.1007/s00213-014-3714-z.

Carhart-Harris, R. L., Leech, R., Williams, T. M., Erritzoe, D., Abbasi, N., Bargiotas, T., et al. (2012). Implications for psychedelic-assisted psychotherapy: Functional magnetic resonance imaging study with psilocybin. *British Journal of Psychiatry*, *200*(03), 238–244. https://doi.org/10.1192/bjp.bp.111.103309.

Carhart-Harris, R. L., Muthukumaraswamy, S., Roseman, L., Kaelen, M., Droog, W., Murphy, K., et al. (2016). Neural correlates of the LSD experience revealed by multimodal

neuroimaging. *Proceedings of the National Academy of Sciences*, *113*(17), 4853–4858. https://doi.org/10.1073/pnas.1518377113.

Christensen, A. P. (2020). Openness to experience. In V. Glăveanu (Ed.), *The palgrave encyclopedia of the possible*. Palgrave Macmillan. https://doi.org/10.1007/978-3-319-98390-5_113-1.

Cohen, S. (1960). Lysergic acid diethylamide: Side effects and complications. *Journal of Nervous and Mental Disease*, *130*(1), 30–40. https://doi.org/10.1097/00005053-196001000-00005.

Cooper, H. A. (1955). Hallucinogenic drugs. *The Lancet*, *265*(6873), 1078–1079. https://doi.org/10.1016/s0140-6736(55)91156-9.

de Araujo, D. B., Ribeiro, S., Cecchi, G. A., Carvalho, F. M., Sanchez, T. A., Pinto, J. P., et al. (2011). Seeing with the eyes shut: Neural basis of enhanced imagery following ayahuasca ingestion. *Human Brain Mapping*, *33*(11), 2550–2560. https://doi.org/10.1002/hbm.21381.

Dos Santos, R. G., Enyart, S., Carlos Bouso, J., Pares, O., & Hallak, J. E. C. (2018). "Ayahuasca turned on my mind's eye": Enhanced visual imagery after ayahuasca intake in a man with "blind imagination" (aphantasia). *Journal of Psychedelic Studies*, *2*(2), 1–4. https://doi.org/10.1556/2054.2018.008.

Ffytche, D. H. (2007). Visual hallucinatory syndromes: Past, present, and future. *Dialogues in Clinical Neuroscience*, *9*(2), 173–189. https://doi.org/10.31887/DCNS.2007.9.2/dffytche.

Frankel, F. H. (1994). The concept of flashbacks in historical perspective. *International Journal of Clinical and Experimental Hypnosis*, *42*(4), 321–336. https://doi.org/10.1080/00207149408409362.

Glicksohn, J., & Barrett, T. R. (2003). Absorption and hallucinatory experience. *Applied Cognitive Psychology: The Official Journal of the Society for Applied Research in Memory and Cognition*, *17*(7), 833–849. https://doi.org/10.1002/acp.913.

Haijen, E. C. H. M., Kaelen, M., Roseman, L., Timmermann, C., Kettner, H., Russ, S., et al. (2018). Predicting responses to psychedelics: A prospective study. *Frontiers in Pharmacology*, *9*, 897–897. https://doi.org/10.3389/fphar.2018.00897.

Halpern, J. H., Lerner, A. G., & Passie, T. (2016). A review of hallucinogen persisting perception disorder (HPPD) and an exploratory study of subjects claiming symptoms of HPPD. In A. L. Halberstadt, F. X. Vollenweider, & D. E. Nichols (Eds.), *Behavioral neurobiology of psychedelic drugs. Current topics in behavioral neurosciences* (Vol. *36*, pp. 333–360). Springer.

Halpern, J., & Pope, H. G. (2003). Hallucinogen persisting perception disorder – What do we know after 50 years? *Drug and Alcohol Dependence*, *69*(2), 109–119. https://doi.org/10.1016/s0376-8716(02)00306-x.

Hastings, A. (2006). An extended nondrug MDMA-like experience evoked through posthypnotic suggestion. *Journal of Psychoactive Drugs*, *38*(3), 273–283. https://doi.org/10.1080/02791072.2006.10399853.

Heaton, R. K. (1975). Subject expectancy and environmental factors as determinants of psychedelic flashback experiences. *The Journal of Nervous and Mental Disease*, *161*(3), 157–165. https://doi.org/10.1097/00005053-197509000-00002.

Heaton, R. K., & Victor, R. G. (1976). Personality characteristics associated with psychedelic flashbacks in natural and experimental settings. *Journal of Abnormal Psychology*, *85*(1), 83–90. https://doi.org/10.1037/0021-843x.85.1.83.

Hermle, L., Ruchsow, M., & Täschner, K. L. (2015). Hallucinogen-Induced persistent perception disorder (HPPD) and flashback phenomena: Differential diagnosis and explanatory models. *Advances in Neurology Psychiatry*, *83*(9), 506–515. https://doi.org/10.1055/s-0035-1553717.

Horowitz, M. J. (1969). Flashbacks: Recurrent intrusive images after the use of LSD. *American Journal of Psychiatry*, *126*(4), 565–569. https://doi.org/10.1176/ajp.126.4.565.

Hosmer, D. W., Jr, Lemeshow, S., & Sturdivant, R. X. (2013). *Applied logistic regression* (Vol. *398*). John Wiley & Sons.

Jamieson, G. A. (2005). The modified Tellegen absorption scale: A clearer window on the structure and meaning of absorption. *Australian Journal of Clinical & Experimental Hypnosis*, *33*(2), 119–139.

Johnson, M., Richards, W., & Griffiths, R. (2008). Human hallucinogen research – Guidelines for safety. *Journal of Psychopharmacology*, *22*(6), 603–620. https://doi.org/10.1177/0269881108093587.

Kraehenmann, R., Pokorny, D., Vollenweider, L., Preller, K. H., Pokorny, T., Seifritz, E., et al. (2017). Dreamlike effects of LSD on waking imagery in humans depend on serotonin 2A receptor activation. *Psychopharmacology*, *234*(13), 2031–2046. https://doi.org/10.1007/s00213-017-4610-0.

Krebs, T. S., & Johansen, P. Ø. (2013). Psychedelics and mental health: A population study. *Plos One*, *8*(8), e63972. https://doi.org/10.1371/journal.pone.0063972.

Kwekkeboom, K., Huseby-Moore, K., & Ward, S. (1998). Imaging ability and effective use of guided imagery. *Research in Nursing & Health*, *21*(3), 189–198. https://doi.org/10.1002/(sici)1098-240x(199806)21:3<189::aid-nur2>3.0.co;2-d.

Lauterbach, E., Abdelhamid, A., & Annandale, J. B. (2000). Posthallucinogen-like visual illusions (palinopsia) with risperidone in a patient without previous hallucinogen exposure: Possible relation to serotonin 5HT2a receptor blockade. *Pharmacopsychiatry*, *33*(01), 38–41. https://doi.org/10.1055/s-2000-8452.

Lerner, A. G., Gelkopf, M., Skladman, I., & Oyffe, I. (2002). Flashback and hallucinogen persisting perception disorder: Clinical aspects and pharmacological treatment approach. *The Israel Journal of Psychiatry and Related Sciences*, *39*(2), 92–99.

Lerner, A. G., Rudinski, D., & Bor, O. (2014). Flashbacks and HPPD: A clinical-oriented concise review. *The Israel Journal of Psychiatry and Related Sciences*, *51*(4), 296–301.

Lev-Ran, S., Feingold, D., Goodman, C., & Lerner, A. G. (2017). Comparing triggers to visual disturbances among individuals with positive versus negative experiences of hallucinogen-persisting perception disorder (HPPD) following LSD use. *The American Journal on Addictions*, *26*(6), 568–571. https://doi.org/10.1111/ajad.12577.

Lewis, D. M. (2020). Faces of HPPD: Hallucinogen persisting perception disorder patient survey results and a descriptive analysis of patient demographics, medical background, drug use history, symptoms, and treatments. *Addictive Disorders & Their Treatment*, *19*(1), 36–51. https://doi.org/10.1097/ADT.0000000000000178.

Little, R. J. (1988). A test of missing completely at random for multivariate data with missing values. *Journal of the American*

Statistical Association, *83*(404), 1198–1202. https://doi.org/10.1080/01621459.1988.10478722.

Luke, D. (2018). Reply to "ayahuasca turned on my mind's eye" – A case of acquired versus congenital aphantasia, as evidenced with DMT use? *Journal of Psychedelic Studies*, *2*(2), 97–98. https://doi.org/10.1556/2054.2018.014.

Luke, D., & Irvine, A. (2020). *Visual Apophenia Luke Irvine scale*. Unpublished instrument, University of Greenwich, UK.

Marks, D. F. (1973). Visual imagery differences in the recall of pictures. *British Journal of Psychology*, *64*(1), 17–24. https://doi.org/10.1111/j.2044-8295.1973.tb01322.x.

Martinotti, G., Santacroce, R., Pettorruso, M., Montemitro, C., Spano, M., Lorusso, M., et al. (2018). Hallucinogen persisting perception disorder: Etiology, clinical features, and therapeutic perspectives. *Brain Sciences*, *8*(3), 47. https://doi.org/10.3390/brainsci8030047.

Matefy, R. E. (1980). Role-play theory of psychedelic drug flashbacks. *Journal of Consulting and Clinical Psychology*, *48*(4), 551–553. https://doi.org/10.1037/0022-006x.48.4.551.

Matefy, R. E., Hayes, C., & Hirsch, J. (1978). Psychedelic drug flashbacks– Subjective reports and biographical data. *Addictive Behaviors*, *3*(3–4), 165–178. https://doi.org/10.1016/0306-4603(78)90015-1.

McGee, R. (1984). Flashbacks and memory phenomena. *The Journal of Nervous and Mental Disease*, *172*(5), 273–278. https://doi.org/10.1097/00005053-198405000-00004.

Milton, F., Fulford, J., Dance, C., Gaddum, J., Heuerman-Williamson, B., Jones, K., et al. (2020). Behavioral and neural signatures of visual imagery vividness extremes: Aphantasia vs. hyperphantasia. *PsyArXiv*. https://doi.org/10.31234/osf.io/j2zpn.

Muthukumaraswamy, S. D., Carhart-Harris, R. L., Moran, R. J., Brookes, M. J., Williams, T. M., Errtizoe, D., et al. (2013). Broadband cortical desynchronization underlies the human psychedelic state. *Journal of Neuroscience*, *33*(38), 15171–15183. https://doi.org/10.1523/JNEUROSCI.2063-13.2013.

Naditch, M. P., & Fenwick, S. (1977). LSD flashbacks and ego functioning. *Journal of Abnormal Psychology*, *86*(4), 352–359. https://doi.org/10.1037/0021-843x.86.4.352.

Nutt, D. J., & Carhart-Harris, R. L. (2020). The current status of psychedelics in psychiatry. *JAMA Psychiatry*. https://doi.org/10.1001/jamapsychiatry.2020.2171.

Orsolini, L., Papanti, G. D., De Berardis, D., Guirguis, A., Corkery, J. M., & Schifano, F. (2017). The "Endless Trip" among the NPS users: Psychopathology and psychopharmacology in the hallucinogen-persisting perception disorder. A systematic review. *Frontiers in Psychiatry*, *8*, 240. https://doi.org/10.3389/fpsyt.2017.00240.

Osborne, J. (2015). *Best practices in logistic regression*. SAGE Publications Ltd. https://www.doi.org/10.4135/9781483399041.

Ott, U., Reuter, M., Hennig, J., & Vaitl, D. (2005). Evidence for a common biological basis of the absorption trait, hallucinogen effects, and positive symptoms: Epistasis between 5-HT2a and COMT polymorphisms. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*, *137*(1), 29–32. https://www.doi.org/10.1002/ajmg.b.30197.

Peduzzi, P., Concato, J., Kemper, E., Holford, T. R., & Feinstein, A. R. (1996). A simulation study of the number of events per variable in logistic regression analysis. *Journal of Clinical Epidemiology*, *49*(12), 1373–1379. https://doi.org/10.1016/S0895-4356(96)00236-3.

Pekala, R. J., Wenger, C. F., & Levine, R. L. (1985). Individual differences in phenomenological experience: States of consciousness as a function of absorption. *Journal of Personality and Social Psychology*, *48*(1), 125–132. https://doi.org/10.1037//0022-3514.48.1.125.

Preller, K. H., & Vollenweider, F. X. (2016). Phenomenology, structure, and dynamic of psychedelic states. In A. L. Halberstadt, F. X. Vollenweider, & D. E. Nichols (Eds.), *Behavioral neurobiology of psychedelic drugs. Current topics in behavioral neurosciences* (Vol. *36*, pp. 221–256). Springer.

Puledda, F., Schankin, C., & Goadsby, P. J. (2020). Visual snow syndrome: A clinical and phenotypical description of 1,100 cases. *Neurology*, *94*(6), e564–e574. https://doi.org/10.1212/WNL.0000000000008909.

Rief, W., Mewes, R., Martin, A., Glaesmer, H., & Braehler, E. (2010). Are psychological features useful in classifying patients with somatic symptoms? *Psychosomatic Medicine*, *72*(7), 648–655. https://doi.org/10.1097/PSY.0b013e3181d73fce.

Salge, J. H., Pollmann, S., & Reeder, R. R. (2020). Anomalous visual experience is linked to perceptual uncertainty and visual imagery vividness. *Psychological Research*, 1–18. https://doi.org/10.1007/s00426-020-01364-7.

Sandison, R. A., Spencer, A. M., & Whitelaw, J. D. A. (1954). The therapeutic value of lysergic acid diethylamide in mental illness. *Journal of Mental Science*, *100*(419), 491–507. https://doi.org/10.1192/bjp.100.419.491.

Schankin, C. J., Maniyar, F. H., Chou, D. E., Eller, M., Sprenger, T., & Goadsby, P. J. (2020). Structural and functional footprint of visual snow syndrome. *Brain*, *143*(4), 1106–1113. https://doi.org/10.1093/brain/awu050.

Stanciu, N. C., & Penders, M. T. (2016). Hallucinogen persistent perception disorder induced by new psychoactive substituted phenethylamines; A review with illustrative case. *Current Psychiatry Reviews*, *12*(2), 221–223. https://doi.org/10.2174/1573400512666160216234850.

Studerus, E., Gamma, A., Kometer, M., & Vollenweider, F. X. (2012). Prediction of psilocybin response in healthy volunteers. *Plos One*, *7*(2), e30800. https://doi.org/10.5167/uzh-59652.

Studerus, E., Kometer, M., Hasler, F., & Vollenweider, F. X. (2010). Acute, subacute and long-term subjective effects of psilocybin in healthy humans: A pooled analysis of experimental studies. *Journal of Psychopharmacology*, *25*(11), 1434–1452. https://doi.org/10.1177/0269881110382466.

Tabachnick, B. G., & Fidell, L. S. (2014). *Using multivariate statistics*. Pearson Education Limited.

Terhune, D. B., Luke, D. P., Kaelen, M., Bolstridge, M., Feilding, A., Nutt, D., et al. (2016). A placebo-controlled investigation of synaesthesia-like experiences under LSD. *Neuropsychologia*, *88*, 28–34. https://doi.org/10.1016/j.neuropsychologia.2016.04.005.

Voigt, K., Wollburg, E., Weinmann, N., Herzog, A., Meyer, B., Langs, G., et al. (2012). Predictive validity and clinical utility of DSM-5 somatic symptom disorder – Comparison with DSM-IV somatoform disorders and additional criteria for consideration. *Journal of Psychosomatic Research*, *73*(5), 345–350. https://doi.org/10.1016/j.jpsychores.2012.08.020.

Wiggert, N., Wilhelm, F. H., Nakajima, M., & al'Absi, M. (2016). Chronic smoking, trait anxiety, and the physiological response to stress. *Substance Use & Misuse*, *51*(12), 1619–1628. https://doi.org/10.1080/10826084.2016.1191511.

Wild, T., Kuiken, D., & Schopflocher, D. (1995). The role of absorption in experiential involvement. *Journal of Personality and Social Psychology*, *69*(3), 569–579. https://doi.org/10.1037/0022-3514.69.3.569.

Zsido, A. N., Teleki, S. A., Csokasi, K., Rozsa, S., & Bandi, S. A. (2020). Development of the short version of the Spielberger state—trait anxiety inventory. *Psychiatry Research*, *291*, 113223. https://doi.org/10.1016/j.psychres.2020.113223.