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Brief Report: Comparing Triggers to Visual Disturbances Among Individuals With Positive Versus Negative Experiences of Hallucinogen-Persisting Perception Disorder (HPPD) Following LSD Use

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Background and Ojective: Exploring differences in visual disturbances and triggers between Hallucinogen-Persisting-Perceptual-Disorder (HPPD) Type I ("positive/benign") and II ("negative/distressing").
Methods: Forty individuals with HPPD and prior LSD use completed clinical questionnaires.
Results: The most common type of visual disturbances among individuals with HPPD I and II was slow movement of still objects and trailing phenomena, respectively. Those with HPPD I were more likely to report experiencing disturbances in dark environment, while looking at a still or moving object and during sexual intercourse.
Discussion And Conclusions: HPPD I and II differ in terms of visual disturbances and triggers, possibly representing different phenomena existing on the same spectrum.
Scientific Significance: Our study indicating differences in triggers to HPPD I and II adds to existing literature on differences in visual disturbances between the two subtypes. Further research elucidating additional differences between the subtypes of HPPD is needed. (Am J Addict 2017;XX:1–4)

INTRODUCTION

Hallucinogenic substances encompass a family of natural-occurring and synthetic agents which may trigger or precipitate states of usually short-term reversible intoxications principally characterized by the presence of visual disturbances popularly named "trips".[1] These may be manifested as pleasant "good trips" or unpleasant "bad trips", which may be followed by recurrent single-visual disturbances (ie, the appearance of the same visual disturbance when intoxicated) or recurrent multiple-visual disturbances (ie, the emergence of different visual disturbances when intoxicated).

An intriguing side effect linked to the use of synthetic hallucinogens such as lysergic acid diethylamide (LSD) is the partial or total reoccurrence of visual disturbances which previously emerged during intoxication, despite absence of recent use. These recurrent visual disturbances, referred to as Hallucinogen Persistent Perceptual Disorder (HPPD) are roughly divided into Flashback-Type (HPPD I) or HPPD-Type (HPPD II).[2] Flashback-Type visual disturbances are generally pleasant, short-term, reversible, non-intruding, non-distressing, non-disabling, and benign reoccurrences. while HPPD-Type visual disturbances are generally unpleasant, long-term, slowly reversible or irreversible, intruding, distressing, disabling, and pervasive reoccurrences.[3] Significant impairment in social, occupational, or other important areas of functioning is usually observed in HPPD II, but not HPPD I.[2]

While several types of triggers have been described for both HPPD Type I and II, including emotional (eg, tension and anxiety), environmental (eg, flickering lights), behavioral (eg, sexual activity) and biological (eg, use of other substances) triggers,[2] differences in types of triggers among those with the different sub-types of HPPD have never been explored. The aim of this study was to compare triggers associated with HPPD I and II following use of LSD.

MATERIALS AND METHODS

Subjects

Participants included 40 patients (men = 27) who sought out psychiatric consultation for substance use related problems and reported previous use of LSD. All subjects were diagnosed

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using the Structural Clinical Interview for DSM-IV-TR Axis I disorders (SCID-I). Diagnosis of HPPD was made according to DSM-IV-TR criteria. In accord with criteria C ("The symptoms ... are not accounted for by another mental condition"), diagnosis of HPPD was made only if the history of the patient included visual perceptual disturbances which were not accounted for by a psychotic disorder. None of the subjects included in the study received medications particularly targeted at treating HPPD.[2] The study was approved by the Institutional Review Board.

Measures

All subjects fulfilling the criteria for HPPD completed a questionnaire including the following three categories: sociodemographic/clinical, common visual disturabnces, and common triggeres for HPPD.

Data Analysis

Parametric data was compared using *t*-test analyses, additional chi-square analyses were used to compare non-parametric data. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 21.

RESULTS

The mean age among individuals in the HPPD I and HPPD II was 25.5 ± 3.7 and 22.1 ± 2.8, respectively ($t = 3.32$, $p = .002$). Comparing sociodemographic and clinical characteristics, individuals in the HPPD II group were significantly ($p < .05$) more likely to be men, and less likely to report any college education, employment, or participation in mandatory military service (Table 1).

The mean age of onset of LSD use was 21 ± 2.4 and 19.4 ± 1.8 among the HPPD I and HPPD II groups, respectively ($t = 2.26$, $p = .029$). Individuals in the HPPD II group reported using LSD more times than those in the HPPD II group ($\bar{x} = 24.6 \pm 1.4$ and $\bar{x} = 7.1 \pm 4.3$, respectively; $t = 18.36$, $p < .0001$). All subjects in both groups reported lifetime use of cannabis. Individuals in the HPPD II group were significantly more likely to report lifetime use of synthetic cannabinoids, stimulants, and inhalants ($p < .0001$), whereas individuals in the HPPD I group were more likely to report lifetime use of alcohol ($p = .007$) (Table 1).

The average duration (in days) of visual disturbance was significantly higher among individuals in the HPPD I group ($\bar{x} = 1{,}717 \pm 882$) compared to those in the HPPD II group ($\bar{x} = 809 \pm 539$; $t = 4.03$, $p < .0001$). Individuals in the HPPD I group were more likely than those in the HPPD II group to report experiencing disturbances in dark environment ($p < .05$), while looking at a still or moving object ($p < .0001$) and during sexual intercourse ($p < .05$). Among those in the HPPD II group, 95.7% reported that they had intentionally experienced visual disturbances in the past (meaning voluntarily concentrated and triggered a flashback),[4] compared to 58.8% among those in the HPPD I group ($p < .001$).

DISCUSSION

This study sought to explore differences in triggers between individuals with HPPD I (Flashback type) and HPPD II (HPPD type) perceptual disturbances following LSD use. Individuals in the HPPD II group were found to initiate LSD use at an earlier age and report a higher number of overall incidents of use compare to those in the HPPD I group. Significant differences were found in the type of perceptual disorders between the groups. Regarding the primary outcome measures, significant differences were found in common triggers to perceptual disturbances, with individuals in the HPPD II group more likely to report intentionally triggering perceptual disturbances and individuals in the HPPD I group more likely to report experiencing perceptual disorders triggered by sexual intercourse, dark environment and looking at a still or moving objects.

Though younger age of exposure to several substances as well as increased overall use has been found to be associated with higher rates of a spectrum of psychiatric disorders,[5] this has not been previously reported regarding HPPD. Our findings suggest that individuals diagnosed with the more distressing form of perceptual disturbances (HPPD II) initiate LSD use earlier and use it more frequently than those with HPPD I. Furthermore the ean age of subjects with HPPD II in our sample was younger than among those with HPPD I. The association between age of onset, of drug use and intensity of use and subsequent onset of several psychiatric disorders has been attributed to disruption of natural neurobiological processes due to early-onset drug and alcohol use, which in turn may disrupt maturation of behaviors. Adolescence is characterized by periods of marked changes in neurogenesis, cortical synaptic remodeling, neurotransmitter receptors, and transporters, as well as major changes in hormones. Development of the visual cortex is characterized by a critical period of plasticity during early adolescence, involved in establishing visual acuity in adulthood. Animal studies indicated that disruption of these processes during the critical period by intensive use of drugs might affect relevant normal visual processes.[6] These factors and others may partially explain the reported association between earlier onset of LSD use and higher frequency of use among individuals in the HPPD II group.

Individuals in the HPPD I group reported longer overall persistence of perceptual disorders. This may be partially due to postponing psychiatric treatment, as flashback-type perceptual disorders commonly do not cause psychological distress and impaired function. This is in line with research from other fields of drug use and mental health in which increased level of impairment and distress were associated with higher rates of treatment utilization.[7] As flashback-type perceptual disturbances are not associated with high levels of distress, this may have postponed utilizing treatment.

TABLE 1. Sociodemographic and clinical characteristics of individuals with HPPD I ("Flashback Type") and HPPD II ("HPPD Type") following lysergic acid diethylamide (LSD) use

	HPPD-1		HPPD-2			
	n	%	*n*	%	Chi-square	*p*-value
Gender						
Male	14	82.4	23	100		
Female	3	17.6	0	0	4.39	.036
Any college education						
Yes	6	35.3	2	8.7		
No	11	64.7	21	91.3	4.32	.038
Ever employed						
Yes	17	100	17	73.9		
No	0	0	6	26.1	5.22	.022
Military service						
Yes	12	70.6	4	17.4		
No	5	29.4	19	82.6	11.53	.001
Criminal record						
Yes	0	0	2	8.7		
No	17	100	21	91.3	1.56	.212
Latent period after perceptual disturbance						
Less than 1 Year	1	5.9	0	0		
1–2 Years	3	17.6	1	4.3		
3–4 Years	10	34.5	19	82.6		
More than 4 Years	3	17.6	3	13	3.98	.263
Lifetime use: alcohol						
Yes	17	100	15	65.2		
No	0	0	8	34.8	7.39	.007
Lifetime use: synthetic cannabis						
Yes	0	0	23	100		
No	17	100	0	0	40	<.0001
Lifetime use: stimulants						
Yes	1	5.9	22	95.7		
No	16	94.1	1	4.3	32.23	<.0001
Lifetime use: opioids						
Yes	4	23.5	2	8.7		
No	13	76.5	21	91.3	1.69	.194
Lifetime use: inhalants						
Yes	0	0	8	34.8		
No	17	100	15	65.2	17.74	<.0001
Lifetime use: MDMA						
Yes	15	88.2	23	100		
No	2	11.8	0	0	2.45	.091
Lifetime use: other hallucinogens						
Yes	9	52.9	8	34.8		
No	8	27.1	15	65.2	1.32	.251
Most common type of visual disturbance					36.23	<.0001
Visual distortions of still objects	2	11.8	1	4.3		
Slow movement of still objects	8	47.1	0	0		
Halos around objects	2	11.8	0	0		
RCD	1	5.9	1	4.3		
Geometric shapes	2	11.8	0	0		

(*Continued*)

Individuals in the HPPD II group reported significantly higher rates of lifetime use of synthetic cannabinoids, inhalants, and stimulants. As synthetic cannabinoids vary widely in terms of content and potency,[8] it is difficult to account for the effects of these diverse compounds. Notwithstanding, there have been previous reports of HPPD following synthetic cannabis use,[9] which may have contributed to a portion of the HPPD in our sample as well. Since all subjects in both groups reported previous cannabis use, it is possible this increases the risk of developing both subtypes of HPPD, though the mechanism for this is unclear. Though patterns of use of cannabis and potency of cannabis used may play a role in substance-related disorders (see for example Roncero et al),[10] this was not directly explored in our study.

Though visual disturbances are considered more distressing in HPPD II, individuals in this group reported intentionally triggering perceptual disturbances more commonly compared to those in the HPPD I group. They were also five-fold more likely to report experiencing perceptual disturbances following stress compared to those in the HPPD I group. It is possible that individuals in the HPPD II group tend to intentionally trigger perceptual disturbances in response to negative feelings, perhaps in an effort to attenuate these feelings, though this was not directly explored in our study.

Limitations of this study should be noted. Drug use was assessed by self-report, which increases risk of recall or report bias. This may particularly true regarding age of onset of use and number of incidents of use. In addition, co-occurring psychiatric disorders were not routinely assessed in this study. This may also influence the type of perceptual disorder and associated experience.

To the best of our knowledge, this is the first study comparing triggers associated with benign flashback HPPD I and unpleasant HPPD II. Though HPPD has been generally well described, investigation of this phenomenon is usually not included in the general psychiatric assessment, even in cases assessed for Dual Disorders (psychiatric disorders with co-occurring substance use disorders). Exploring triggers for perceptual disorders may be an important aspect in further setting the ground for much-needed clinical research in this field.

Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

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