

Benign and Time-Limited Visual Disturbances (Flashbacks) in Recent Abstinent High-Potency Heavy Cannabis Smokers: A Case Series Study

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ABSTRACT

Eight high-potency heavy cannabis smokers who fulfilled DSM-IV-TR criteria for cannabis dependence sought treatment for outpatient detoxification. During routine psychiatric interview they reported the presence of visual disturbances when intoxicated and no prior history of LSD use. They all communicated the persistence of visual disturbances after ceasing cannabis use. Seven categories of visual disturbances were described when staring at stationary and moving objects: visual distortions, distorted perception of distance, illusions of movement of stationary and moving objects, color intensification of objects, dimmed color, dimensional distortion and blending of patterns and objects. Patients reported having 2-5 different categories of flashbacks up to 3-6 months after cessation of cannabis use. The described phenomena may be interpreted as a time-limited benign side effect of high-potency cannabis use in some individuals. A combination of vulnerability and use of large amounts of high-potency cannabis seem to contribute to the appearance of this condition. Conclusions from uncontrolled case series should be taken with appropriate caution.

INTRODUCTION

Hallucinogens encompass a group of naturally-occurring substances from vegetable (1) and animal (2) origins as well as synthetic chemical agents (3) which

may induce a state of intoxication popularly referred to as a “trip” (4). These “trips” or substance-induced experiences are generally transient and reversible states that are typically accompanied by perceptual disturbances. The mind-altering effects are experienced in a clear sensory-conscious state, while awake and alert and generally in the absence of confusion (5-8). A well known, unique and intriguing side effect associated with the use of synthetic hallucinogens such as lysergic acid diethylamide-LSD and LSD-like substances is the partial or total recurrence of the perceptual disturbances which previously appeared during intoxication, in the absence of recent use (9-11). These experiences are accompanied by full insight and can be short or long-term (10, 11). The original intoxicating experience may be “good” (pleasant) or “bad” (unpleasant). In the same way, the perceptual recurrences recapitulate the prior “trip” or intoxication that was experienced as either “good” or “bad.” A previous “good” trip, however, does not always predict or ensure a “good” recurrence (10, 11). Common recurrent visual disturbances attributed to this complex syndrome are geometric hallucinations, false perception of movement in the peripheral visual fields, flashes of colors, intensified colors, trails of images of moving objects, positive afterimages, halos around objects, macropsia and micropsia (12).

At least two subtypes of this syndrome have been reported. The first is flashback. It is a short term, transient, recurrent, spontaneous, reversible and generally visual benign experience. Experienced LSD users generally look at these recurrences as a “free trip,” an aspect of the psychedelic dimension, and do not seek psychiatric assistance after experiencing these types of episodes. Certain individuals may experience the recurrence of

the same single flashback while other perhaps more suggestible subjects may have a variety of them. The second is hallucinogen persisting perception disorder (HPPD). This is long-term, spontaneous, intermittent or continuous, pervasive and either slowly reversible or irreversible. This disorder is entirely different from the benign flashback (10, 11). HPPD is a condition in which the re-experiencing of one or more perceptual symptoms causes significant distress or impairment in social, occupational or other important areas of functioning (12). HPPD often occurs in individuals with no prior psychopathology, and may be extremely debilitating. Hallucinogen users are usually aware of these severe, intruding and disabling consequences of LSD consumption and generally actively seek psychiatric help. HPPD seems to be part of a large spectrum of non-psychopathological and psychopathological experiences reported by hallucinogen users (10, 11).

Whether or not the use of cannabis alone can be associated with persisting perceptual abnormalities has been debated. Investigators tend to agree that cannabis can precipitate perceptual recurrences in subjects who had previously used LSD and that it is unlikely that cannabis alone can provoke recurrent perceptual disturbances (13-15). However, there are reports of depersonalization (16, 17), perceptual symptoms experienced during cannabis intoxication (18, 19) and short-term spontaneous recurrent visual disturbances (20) after the suspension of cannabis use alone. Reliability of recurrent cannabis associated visual experiences has been critically questioned. It should be noted that according to DSM-IV-TR the diagnostic criteria of cannabis intoxication allows for a diagnosis of "with perceptual disturbances" (12). If perceptual disturbances can be observed during intoxication by cannabis alone (12, 21), it is plausible that some predisposed and susceptible cannabis heavy smokers using high concentrated cannabis (22) may partially or totally recapitulate the previous perceptual experience in the absence of present cannabis use. We present the cases of eight high-potency heavy users of cannabis without a prior history of LSD use who reported the presence of benign persisting visual disturbances after stopping cannabis consumption.

METHOD

CLINICAL DATA

Eight patients were examined after seeking treatment for cessation of chronic cannabis use. Four of them

attempted to stop cannabis use in the past without professional assistance. Patients included in the report met the DSM-IV-TR criteria for cannabis dependence (12). They reported the need for markedly increased amounts of cannabis to achieve desired effect, cannabis was smoked over longer periods than was intended, there were unsuccessful efforts to stop or control its use, a great deal of time was spent to obtain cannabis and finally social, occupational and recreational activities were impaired (12). They communicated cannabis intoxication with perceptual disturbances (12), the intake of high concentrated cannabis (22) since starting cannabis use, a smoking period of at least five years and a daily consumption ("joints" and water pipes) of at least three times a day (i.e., morning, noon or afternoon and evening). They had no prior use of LSD or other hallucinogenic substances. All patients had previous compulsory military service, no prior police or criminal records, and were not married. Four of the patients reported smoking cannabis alone. The other four reported occasional use of cocaine, MDMA, and also fulfilled full criteria for nicotine dependence (12). Visual disturbances during intoxication were reported only after being interviewed for treatment and were not accurately recalled. Treatment was not sought due to visual disturbances. They associated the precipitation of visual disturbances only and strictly by cannabis smoking. Other consumed legal (nicotine and alcohol) and illegal (ecstasy and cocaine) substances were not associated with the perceptual disturbances. None of the patients had any co-morbid medical disease or co-occurring psychiatric disorders. Neurological and ophthalmologic examinations were intact. Two patients had a family history of schizophrenia.

DEMOGRAPHIC DATA

Mean age of patients was 29.25 years old (S.D.=2.25), mean education was 13.13 years (S.D.=1.55), mean duration of non-use was 82.25 days (S.D.=40.6), mean duration of cannabis use was seven years (S.D.=1.69), and mean number of previous attempts of cessation or detoxifications was 0.625 (S.D.=0.74). All patients were white males of Jewish Israeli descent, were currently employed, and had a middle class socioeconomic status.

DETOXIFICATION AND FOLLOW-UP

Tetrahydrocannabinol (THC) was present in urine samples prior to initiation of detoxification. No other psychoactive substances were identified. All patients

underwent uncomplicated outpatient cannabis detoxification using only minimal symptomatic medication like small doses of clonidine (23) and careful use of benzodiazepines. They continued working when undergoing treatment reflecting low severity or control of the detoxification process. After detoxification and follow-up, substances of abuse were not identified in random urine samples. Two out of eight patients relapsed after two months. One of the relapsing subjects reported having visual disturbances again when intoxicated. The remaining six abstinent patients reported flashbacks up to six months after stopping cannabis use. Interestingly, two patients who had a family history of schizophrenia reported longer duration of recurrences. None of the subjects were interested in pharmacological treatment for the flashbacks or psychotherapy. None of the six abstinent patients revealed the presence of flashbacks at the one-year follow-up visit.

FLASHBACKS

The term flashback is used instead of HPPD, due to the benign nature of the visual recurrences (9-11). Individuals reported the presence of flashbacks similar to those visual disturbances which appeared during intoxication. There was not a clear period of latency between the appearance of visual disturbances during intoxication and the continuation of flashbacks during detoxification and follow-up. The average time of persisting visual disturbances experienced by the participants following detoxification was 11.75 weeks (S.D.=5.80). Flashbacks were perceived as benign, generally short term (from a fraction of a second up to several minutes), spontaneous (without identified triggers), recurrent, non-distressing and entirely reversible. The accompanying affect was pleasant. Prodromal symptoms (aura) did not precede the flashbacks (11). Flashbacks started with a frequency of a few times a day (mean=11.75, S.D.=5.80) and their intensity was not experienced as disturbing or painful. After initial presentation, flashbacks usually decreased in frequency and intensity, with a tendency to slowly wear off. The accompanying affect usually disappeared along with the recurrence. Full insight, reality testing and judgement were always maintained. Users looked upon the flashback as a kind of "free trip" or curious experience. Patients reported having from two up to five different categories of flashbacks which appeared when staring at stationary and moving objects. Distortions were described as minimal, "almost imperceptible" and very slight in nature. Seven categories of visual disturbances were described

when staring at stationary and moving objects: visual distortion (slightly blurred object), distorted perception of distance (objects were slightly seen closer or distant), illusion of movement of stationary and moving objects (slow movement), color intensification of objects (slightly more intensified), dimmed color (slightly less intensified), dimensional distortion (objects were slightly seen smaller – micropsia, or larger – macropsia) and blending of patterns and objects. All eight of the patients experienced visual distortions of objects, six had distorted perception of distance from the object, five of the eight reported having illusions of movement of stationary and moving objects, two reported color intensification of objects, two reported dimmed color, two slight dimensional distortion of objects and two patients reported blending of patterns and objects. Number of flashbacks from each category and overall number were difficult to calculate. The most frequently reported type of flashback and the last to disappear was visual distortions of objects.

DISCUSSION

While the precise mechanisms underlying cannabis-associated perceptual disturbances are unknown, there is some knowledge indicating similarities with some proposed mechanisms related to LSD associated perceptual disturbances. Serotonin neurotransmission appears to be involved in the genesis of both acute and persisting LSD-induced perceptual disturbances. The acute effects of LSD seem to be mediated through a 5-HT₂ postsynaptic partial agonist activity (24). Similarly, the acute effects of cannabis appear to be related to serotonergic systems. Although the main acute pharmacological effects of cannabis are mediated through cannabinoid receptors, it is known to severely disrupt serotonergic neurotransmission. This disruption could be responsible for most of the cannabis effects on cognition and perception (25, 26) and could be associated with the ability of marijuana to produce perceptual disturbances such as depersonalization (16, 27). Moreover, marijuana smoking, but not placebo smoking, was able to produce depersonalization in healthy subjects (28). Therefore this mechanism could also attempt to explain acute cannabis associated visual disturbances.

The chronic and persisting effects of LSD, hallucinogen persisting perception disorder and flashbacks (10, 11), may closely resemble the previous hallucinogenic experience, implying that a mechanism related to the original one may be involved. The basic mechanism

underlying this syndrome appears to be a vulnerability or a predisposition of LSD users to continue the central process of visual imagery after the image has been removed from the visual field (29). An LSD-generated intense current (30) may provoke the destruction or dysfunction of cortical serotonergic inhibitory interneurons with GABA-ergic outputs and lead to the persistence of the visual imagery due to chronic disinhibition of visual processors (8). Thus, it is plausible that high-potency cannabis (22) that affects serotonergic neurotransmission (25, 26) could provoke a similar effect in some vulnerable and predisposed subjects.

There is more data indicating the possible serotonergic involvement in the genesis and perpetuation of visual disturbances. The appearance of visual phenomena resembling flashbacks (palinopsia) in patients without a previous history of cannabis or hallucinogen exposure after risperidone, nefazodone and trazodone administration (31-33) has been reported. These transient visual disturbances have been attributed to the 5HT_{2A} blocking properties of these agents. Heightened sensitivity to side effects and reduced 5HT_{2A} serotonin receptor stimulation rather than increased 5HT_{2c} stimulation have been proposed as explanations for these intriguing phenomena (31).

Medications shown to be beneficial in the treatment of persisting visual disturbances may provide additional support for serotonergic involvement. Alleviation of persisting visual disturbances after administration of sertraline was attributed to the down regulation of 5-HT₂ receptors (29). Reboxetine also appears to be helpful in the treatment of some subjects complaining of persisting visual recurrences with depressive features (34). Reboxetine may have an α_2 adrenoreceptor modulating effect on both noradrenaline and serotonin release (35). Reboxetine may also affect the reuptake of serotonin and lead to down regulation of 5-HT₂ receptors resembling the improvement of persisting visual disturbances after administration of SSRIs (29, 34). Benzodiazepines' effectiveness in the treatment of persisting visual disturbances may be related to benzodiazepine activity at cortical serotonergic inhibitory interneurons with GABA-ergic outputs (5, 6). Clonazepam which may improve persisting visual occurrences (10), HPPD with anxious features (11) and depersonalization (36) may also affect serotonergic system and enhance serotonergic transmission (37). This effect may secondarily lead to down regulation of 5-HT₂ receptors, which may contribute to the HPPD symptoms remission (29). This amelioration

may also support the estimation that persistent visual disturbances may be related to disinhibition of visual processors via impairment of GABA transmission by inhibitory interneurons. It is still unclear how serotonin systems are involved in the phenomena.

Cannabis-related compounds and the anandamidergic system seem to be involved in areas of visual information processing (38). Impairment of visual sensory data has also been suggested (38). The physiological and pathophysiological roles of the central nervous endogenous cannabinoid system are not completely understood (39). The suspected influence and participation of psychoactive cannabinoids on acute and persistent visual perception and central information processing need to be elucidated.

High-potency cannabis may have some influence in the development of the presented visual side effects. The THC content varies between different sources and preparations of cannabis (22). Sophisticated cultivation such as hydroponic farming and plant-breeding techniques have greatly increased the potency of cannabis products (22). In the 1960s and 1970s an average joint contained about 10 mg of THC. Now a joint made out of potent subspecies may contain around 150 mg of THC or 300 mg if laced with hashish oil (22). Given the fact that the effects of THC are dose related (25) and most of the research on cannabis was carried out in the 1970s using doses of 5-26 mg of THC (40), modern predisposed and vulnerable cannabis smokers may be exposed to doses of THC greater than in the past and risks and consequences might be greater (41).

Cannabis-induced flashbacks appear to be a benign side effect. It remains unclear if it is an uncommon and infrequent associated feature or if it has been underreported by patients due to its benign nature or underdiagnosed by clinicians. A combination of vulnerability and use of large amounts of high-potency cannabis seem to contribute to the appearance of this condition. Additionally, those predisposed individuals seem to present a returning pattern of visual disturbances whenever cannabis is smoked. The return of visual disturbances in relapsing subjects and the continuation of visual disturbances in those who suspended cannabis intake for short periods in the past and during treatment may support the existence of this suggested pattern. It should be reiterated that patients only applied for cannabis detoxification treatment. Information regarding the presence of visual disturbances was identified and collected during routine clinical interview.

We suggest that clinicians actively investigate the presence of visual disturbances in cannabis users. Clinical psychiatrists should be aware of this persisting visual side effect. Due to the fact that these phenomena may be also attributable to misinformation or unreliable self reports, conclusions from uncontrolled case series should be taken with appropriate caution.

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