A persisting perception disorder after cannabis use

Zoë Ellison-Wright *MBBS, MSc, MRCPsych,* **Ben Sessa** *MBBS, BSc, MRCPsych*

Hallucinogen persisting perception disorder is a disorder of uncertain aetiology occurring mainly after 'classical' hallucinogen use (*ie* mescaline, psilocybin, dimethyltryptamine and LSD) use. Here, the authors describe the case of a boy with similar symptoms developing after he reported using cannabis seven times.

Cannabis use may lead to acute intoxication, dependence or psychosis but some reports suggest that it may be associated with the type of perceptual disorder usually described after hallucinogen use.[1] Hallucinogen persisting perception disorder (HPPD) is an uncommon or rare consequence of 'classical' hallucinogen misuse. Patients experience persistent and distressing perceptual changes, such as visual distortions, auras or halos.[2] We describe the case of a boy with similar symptoms after minimal cannabis use.

Presentation

A 15-year-old white British male was referred by the Early Intervention in Psychosis Service with possible psychotic symptoms. He said he had been well until four weeks previously. He had no past medical or psychiatric history. However, he said he had always had a tendency to worry about things.

He was studying for his GCSEs and hoped to study graphic design in the future. He had good peer relationships. He lived with his parents and two younger siblings. His mother described herself as very anxious. A paternal uncle suffered from epilepsy.

Symptoms

The patient said he had used cannabis with his friends on one occasion four weeks previously. The following day he felt different and said that his perceptions were altered. He gave some examples, *eg* when he looked at things, they seemed closer or further away than they should or appeared distorted or 'wave about as though made of jelly'. He occasionally saw strange colours and lights. When he wrote, his sentences appeared distorted. If he focused on things for too long then the colours changed and the objects appeared to turn into other things.

He also said that when he heard sounds, they sometimes echoed or continued for a long period in his head. He said that when he touched things, there was a delay before he actually felt them and he also described sensations going through his body such as tingling, heat or cold. Sometimes he felt that he was taller than normal.

As well as these perceptual disturbances, he said his thoughts were 'all over the place'. He sometimes had thoughts in his head that he could not control that seemed like someone else's thinking and were 'gibberish'.

He did not describe auditory hallucinations or unusual tastes or smells. His mother noticed that he was withdrawn, and 'lost his spark and his mischievousness'. He also seemed tired, irritable and anxious. Subsequently, he said that he had smoked cannabis on several occasions (prior to four weeks ago), and recalled being told that the cannabis may have had other things mixed in with it, possibly LSD.

Initial management

It was considered that he may be developing psychosis. He was prescribed risperidone 0.5mg per day. He became increasingly agitated. The risperidone dose was increased over the next two weeks to 4mg and he was also prescribed lorazepam 1mg up to three times daily as needed.

Despite the increase in risperidone, his symptoms continued to worsen. His mother thought his anxiety had increased while taking it, so four weeks after starting it risperidone was reduced and stopped. Psychiatric inpatient admission was considered, but the family preferred intensive community support. He was referred for a paediatric opinion to exclude an organic cause for his symptoms. He was admitted as a day patient for investigations. He had a neurology assessment, a brain CT which was normal and later an EEG, also normal.

No organic cause for his psychiatric symptoms was discovered, but he described painless haematuria for the last year; he had not told anyone until the paediatrician

interviewed him because he was not concerned about it. A bladder tumour was found on ultrasound. He underwent transurethral resection of bladder. Results confirmed a complete resection of transitional cell carcinoma with a very good prognosis.

Progress

Within five days of stopping risperidone his anxiety symptoms had greatly reduced, although he continued to describe constant perceptual abnormalities – in particular, grainy vision and a dream-like state. His functioning began to improve and two weeks later he was able to go out and visit his friends. He gradually returned to school, but found concentration difficult.

He took his GCSE exams, and despite continuing to experience symptoms he coped well and achieved good results. Following his exams, lorazepam was gradually stopped and he started in the Sixth Form. He continued to experience perceptual abnormalities, which were worse when he was tired or stressed, and increased after starting his A-Level courses. He had also become preoccupied about cannabis, feeling very anxious that he might inhale cannabis that someone else was smoking. He even felt anxious if he saw a picture of cannabis on a computer screen. He knew that this was an irrational fear.

Six months later, following a second opinion, he decided to try cognitive behavioural therapy (CBT) and sertraline 25mg per day was started, increasing to 50mg after a week. Three weeks later he complained of tiredness and nose bleeds. It was postulated that sertraline may be contributing to nose bleeds[3] because SSRIs may increase the risk of bleeding by blocking the uptake of serotonin into platelets, impairing the platelet haemostatic response.[4] Sertraline was reduced to 25mg per day.

One year later his anxiety symptoms had resolved and the perceptual symptoms, though still present to some degree, were not impairing. He had coped well with A-Level exams. Sertraline was discontinued. He said he was not using drugs and remained scared of them. He was discharged from the service.

Discussion

The symptoms experienced by the boy, as noted by his mother, shared similarities to those described in HPPD. This is a disorder of uncertain pathophysiology, first recognisable in reports of drug use in the late 19th century,[2] defined in the American Diagnostic and Statistical Manual DSM-4 and updated in DSM-5 (see Box 1).[5] It typically occurs after use of classical hallucinogens, although there is also some contemporary emerging evidence that other drugs with mild psychedelic properties, *ie* MDMA (3,4-methylenedioxy-methamphetamine), may also rarely produce a similar HPPD-like syndrome.[6]

The classical hallucinogens include LSD (lysergic acid diethylamide), DMT (N,N-dimethyltryptamine), DOB (dimethoxybromoamphetamine), psilocybin and mescaline. They act by binding to the 5-HT_2 serotonin receptor.[7] Although cannabis can cause some hallucinogenic effects, it is not considered a classical hallucinogen. The main psycho-active ingredient is tetrahydrocannabinol (THC) which acts in the brain on the cannabinoid receptors, CB_1 and CB_2.[8]

According to DSM-5, the disorder follows cessation of hallucinogen use and is associated with re-experiencing some of the perceptual symptoms which occurred during intoxication. The main perceptual changes described are visual hallucinations, *eg* flashes of colour or moving images, halos around objects, macropsia (objects appear larger than normal which may cause the person to feel smaller) or micropsia (objects appear smaller than normal which may cause the person to feel larger). For diagnosis the symptoms need to cause significant distress or impairment. Other diagnoses need to be excluded, *eg* brain lesions, visual epilepsies, delirium, schizophrenia or hypnopompic hallucinations (hallucinations which occur when waking from sleep). The symptoms may last for last for weeks, months, or years.

DSM-5 notes that HPPD occurs primarily after LSD use, but not exclusively, and some instances may be triggered by use of other substances, *eg* cannabis.[5]

Diagnostic criteria

- **A** Following cessation of use of a hallucinogen, the re-experiencing of one or more of the perceptual symptoms that were experienced while intoxicated with the hallucinogen (eg geometric hallucinations, false perceptions of movement in the peripheral visual fields, flashes of colour, intensified colours, trails of images of moving objects, positive afterimages, halos around objects, macropsia and micropsia)
- **B** The symptoms in Criterion A cause clinically significant distress or impairment in social, occupational, or other important areas of functioning
- **C** The symptoms are not attributable to another medical condition (eg anatomical lesions and infections of the brain, visual epilepsies) and are not better explained by another mental disorder (eg delirium, major neurocognitive disorder, schizophrenia) or hypnopompic hallucinations

Table 1. Hallucinogen persisting perception disorder: DSM-5 diagnostic criteria

Prevalence

A series of reports of subjects with HPPD-like symptoms were systematically reviewed by Halpern and Pope in 2003.[2] They concluded that there was considerable variability in

the reports. For example, in a follow-up study of 247 subjects who had received LSD in conjunction with psychotherapy or in research protocols in the 1960s, only 2% of subjects described symptoms suggestive of HPPD.[9] Overall, studies reported that between 0–77% subjects suffered HPPD after LSD use with the higher rates in studies where LSD was used illicitly rather than therapeutically, there was ongoing illicit drug use, or subjects had premorbid psychiatric illness.

Differential diagnosis

As well as the differential diagnoses noted in DSM-5, they suggested that others to consider were normal visual experience (*eg* seeing floaters), migraine, continued drug intoxication, affective disorders, malingering, hypochondriasis, anxiety disorders with depersonalisation/derealisation or post-traumatic stress disorder.

Pathophysiology

The cause of HPPD remains uncertain but three possibilities have been suggested.[2] Firstly, individuals might have a heightened awareness to normal visual phenomena. Secondly, the perceptual symptoms might represent memories of the acute intoxication experience accompanied by a high level of emotional distress. Thirdly, the symptoms could be due to some neurological change induced by the drug exposure, *eg* disinhibition of visual processing related to loss of serotonin receptors on inhibitory inter-neurons. With regard to this last hypothesis, Halpern and Pope comment that if HPPD was due to some 'kindling' phenomenon then one might expect that it would be more common in individuals with a large number of LSD exposures rather than just a few – however, this does not appear to be the case.[2]

Treatment

HPPD can cause considerable distress for some individuals for a prolonged period. A large number of treatments have been tried but have mainly been described in case series rather than controlled trials. According to these reports, some cases have benefitted from using sunglasses, psychotherapy, behavioural modification or pharmacological agents.[2] The latter have included antipsychotics (haloperidol, trifluoperazine, olanzapine), antiepileptics (carbamazepine), clonidine, benzodiazepines, or SSRIs (sertraline).[2] Conversely, some reports have described worsening of symptoms with antipsychotics (including risperidone) or SSRIs.[2] More recent reports have suggested beneficial treatment with the antiepileptic lamotrigine or tolcapone, a catechol-O-methyltransferase (COMT) enzyme inhibitor used in the treatment of Parkinson's disease.[10]

Clinical case

The boy described in this case experienced perceptual symptoms similar to those reported in HPPD. His symptoms were persistent, lasting months, distressing and impairing (to the extent that psychiatric inpatient admission was considered at one stage). Although he was initially suspected to have a prodromal psychotic illness (such as schizophrenia), he did not experience auditory hallucinations or first-rank symptoms, he retained insight into his visual experiences and he did not benefit significantly from taking risperidone.

This raises the possibility he might have developed an HPPD-like disorder induced by minimal cannabis use, perhaps in common with the very small number of cases described in the literature of HPPD in subjects who reported previous cannabis but not hallucinogen use. Some strains of cannabis are now very rich in THC and can produce marked psychedelic experiences.

The boy said that he recalled being told that the cannabis he had taken may have had other things mixed in with it, possibly LSD. If this was the case, then his symptoms might have been due to HPPD after minimal LSD use. Although a wide variety of contaminants have been described in cannabis (*eg* sand, sugar, glass bead, industrial chemicals and phencyclidine),[11] it has been suggested that hallucinogens are more likely to be added by users rather than dealers. There is the possibility that the boy's friends adulterated the cannabis; however, given the very volatile nature of LSD crystals, the likelihood of it being effectively administered via smoking in a joint is very low indeed. Nevertheless, it is possible that he was spiked with LSD some other way, *eg* in food or a drink.

In this case, the patient's symptoms worsened while he was prescribed risperidone. This is consistent with reports of risperidone exacerbating HPPD, although it may also have worsened his symptoms through its side effects of agitation and akathisia.

Second opinion

During the course of the illness, the boy was referred for a second opinion. At that time he said he experienced permanent 'visual snow' and he frequently saw 'floaters' which looked like two-dimensional bubbles. At times the walls appeared distorted or 'breathing'. He described depersonalisation and derealisation at times. These symptoms were worse when his eyes were closed or when feeling stressed, *eg* when 'bogged down by school work'.

He said prior to the onset of the illness he had smoked cannabis

seven times. The first five times he smoked a joint with friends, it was a relatively low dose and not an unpleasant experience. The next two times he smoked cannabis at high dose in a water pipe, without tobacco, and he and his friends experienced a very intense reaction. He felt highly depersonalised, detached, dissociated and paranoid, and was hallucinating.

The opinion was that a few exposures to cannabis would be very unlikely to result in these symptoms. It was thought likely that the experience was a psychologically frightening one and that he had subsequently focused on it and concentrated on the potential negative outcomes which had therefore persisted. Therefore his diagnosis was considered to be an anxiety disorder, similar to post-traumatic stress triggered by a traumatic psychological event. It was considered that a genetic risk factor was his mother's anxious temperament. Treatment with CBT and an SSRI was recommended.

In support of this diagnosis, the boy became more preoccupied that he might be inadvertently exposed to cannabis, which he recognised as an irrational fear. His symptoms also improved with sertraline treatment.

During the course of his psychiatric treatment, he was diagnosed with an apparently incidental bladder carcinoma and he underwent surgery for this with remarkable stoicism. However, in a teenager, the effects of persistent haematuria, a cancer diagnosis and the surgical treatment must have been considerable, despite the good prognosis. This may have resulted in displaced and projected anxiety exacerbating his symptoms.

Conclusion

In patients presenting with visual hallucinations or perceptual distortions, HPPD should be considered in the differential diagnosis and a careful history of substance use should be taken. Treatment options remain empirical but if the symptoms are regarded as anxiety-related then CBT approaches or SSRIs may be considered. Alternatively, if the symptoms are viewed as neurological due to cerebral receptor changes then other pharmacological treatments include antipsychotics, antiepileptics or benzodiazepines.

HPPD has been described mainly after use of the classical hallucinogens such as LSD. There are a few reports of symptoms starting after cannabis use, although a causative role remains speculative. In this case, the patient may have smoked a strain of cannabis very rich in THC producing a marked psychedelic experience, or he was in some other way spiked with LSD. It is possible that his symptoms were exacerbated by anxiety associated with an erroneous and overly risk-aversive attitude to the dangers of classical hallucinogens.

However, the relative low risk of clinically significant and functionally impairing HPPD, even with prolonged classical hallucinogen use, must be considered in the contemporary context of the potential therapeutic benefits for psychedelic-drug therapy.[12]

A number of studies worldwide are investigating the role for using drugs such as psilocybin, LSD and other psychedelic drugs, as well as cannabis, as agents to facilitate psychotherapy for patients with a wide range of mental disorders, which show that psychedelic drugs can be safely administered in the medical setting.[12] Emerging evidence shows that even when used in the recreational context, the majority of users of psychedelic drugs do not demonstrate clinically significant mental health problems.[13]

Dr Ellison-Wright is a Consultant Child and Adolescent Psychiatrist, Dorset HealthCare University Foundation Trust, and Dr Sessa is a Consultant Child and Adolescent Psychiatrist, Addiction Substance Misuse Services, Weston-Super-Mare

Declaration of interests

There are no conflicts of interest declared.

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