25 years of Hallucinogen Persisting Perception Disorder- A diagnostic challenge

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Abstract
We present an interesting case of a forty eight year old man who took LSD in his early twenties. He continued to experience visual perceptual disturbances for 25 years following cessation of the hallucinogen. This is a unique case, where symptoms of hallucinogen persisting perception disorder have persisted for over two decades after the cessation of Lysergic acid diethylamide. He was treated with clonazepam 1 mg four times a day with good effect. There is a need for raising awareness about this condition to prevent misdiagnosis and delay in appropriate treatment.

Keywords: LSD- Lysergic acid diethylamide
Abbreviations: EEG- electroencephalogram, MRI- magnetic resonance imaging, LSD- Lysergic acid diethylamide, DSM- Diagnostic and statistical manual, HPPD: Hallucinogen persisting perceptual disorder, SSRI- selective serotonin reuptake inhibitors.

Case report
A forty-eight year old man presented with unusual and distressing visual experiences with varying degrees of severity for over twenty years. Some of these included the following; red objects having a green shimmer around them like 3-D glasses, altered sense for distance estimation, people’s faces seeming to change shape when looked at, alteration of own reflection, anything patterned appearing to move all the time, words moving about while reading, things appearing to be multi-layered, bright lights throwing up shadows, vehicles appearing to stretch as they drive past, flying birds looking like animation and difficulty in focussing.

When present, his symptoms interfered markedly with his functioning. For example, he could not cross the road, could not read, and had to dim his lights. He struggled with knowing which visual perceptions were real and which were not. The patient felt his visual experiences were related to his past LSD use twenty-five years ago. He felt the drug had put him “in a coma” and he was “dreaming all of this”.

He specifically remembered a party with friends where he took a cocktail of illicit drugs, including LSD and marijuana, with alcohol. He said he would usually take drugs and alcohol in a binge pattern. The ‘trips’ would usually last twelve hours. He felt he experienced some memory loss of that particular night. When he woke up the next morning he was still experiencing the effects of LSD and said he has felt these effects ever since. He tried to explain that it was like drinking alcohol, waking up drunk and being drunk from that point on. After this incident he did not use illicit drugs again.

Prior to this particular night he said he may have used LSD about fifteen times, as Microdot tablets, usually one at a time, with cannabis. He said it was “like having a tripping switch in your brain”. When you took LSD, “the switch turned the tripping on and after a while it turned off”. He said his switch “was broken” and he therefore continued to re-experience the effects of the drug.

His other complaint was that of feeling he was “not real”; to the extent he even thought he should harm his family members so he could prove he was real.

He also complained of low mood, decreased concentration, anxiety and an inability to cope.

His first contact with mental health services was at the age twenty two years. He presented with symptoms of anxiety but it was not felt he had a mental illness. He was referred again a year later and was diagnosed to have Primary Depersonalization syndrome.

The patient himself reported that all his symptoms started after he had used LSD about fifteen times in six months. At the time he had described having undergone a complete personality change due to his experiences. He felt objects and experiences had a dream-like quality. His visual experiences caused so much distress he felt suicidal.

Over the next twenty-five years he has had various other diagnoses; LSD induced Depersonalisation Syndrome, Depersonalisation-Derealisation Syndrome, LSD induced Simple schizophrenia, depressive disorder and anxiety disorders. His visual disturbances had been interpreted as visual hallucinations. He had received treatment with antidepressants (Imipramine, Amitriptyline, and Venlafaxine); antipsychotics (Trifluperazine, Promazine); Benzodiazepines (Diazepam);
### Table 1: Change in symptoms with Clonazepam

<table>
<thead>
<tr>
<th>DSM IV/V Symptom Checklist</th>
<th>Prior to treatment with Clonazepam</th>
<th>3 months after initiation of Clonazepam treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geometric hallucinations</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>False perception of movement in peripheral fields</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Flashes of colour</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Intensified colours</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Trails of images of moving objects</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Positive after images</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Halos around objects</td>
<td>Present</td>
<td>Present but reduced in intensity and frequency</td>
</tr>
<tr>
<td>Macropsia</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Micropsia</td>
<td>Present</td>
<td>Absent</td>
</tr>
</tbody>
</table>

Propranolol; and Fentazine. He was also prescribed Hydergine (which helped reduce symptoms briefly) at one point.

Investigations: EEG, MRI Brain, and Carotid ultrasound were normal.

He was admitted to a psychiatric hospital at the age of forty-eight years old where the admitting doctor described his symptoms as visual hallucinations and started him on Risperidone, which increased the intensity of his symptoms. He was also treated with Citalopram for his low mood. It was noted that his symptoms were different from common psychotic illnesses. Detailed history taking and assessment of his perceptual abnormalities over the following few weeks in hospital confirmed the diagnosis of hallucinogen persisting perception disorder (HPPD).

He was treated with Clonazepam 1 mg four times a day with good effect; as seen by the reduction of symptoms - see Table 1.

After discharge he had a depressive episode and was treated with Escitalopram. This was later changed to Reboxetine.

**Discussion:**

This is the first case that we are aware of where symptoms of HPPD have persisted for over two decades after the cessation of the use of Lysergic acid diethylamide. There is a need for raising awareness about this condition to prevent misdiagnosis and delay in appropriate treatment.

This patient presented to psychiatric services over twenty-five years ago and at that time he felt his symptoms were related to his use of LSD. He was given a variety of different diagnoses before the correct diagnosis was established and treatment initiated with good outcome.

The patient had also experienced migraines and used alcohol excessively on occasions in the past. Although we are not aware of any connection between this disorder and these factors, future reports and studies may help provide further knowledge in these areas.

HPPD is a recognised condition described in DSM V and DSM IV with a diagnostic code 292.89. In DSM III it was referred to as post hallucinogen perception disorder (PHPD). It is described in ICD 10 under the code F16.983.

LSD has been known to alter perception and mood in the presence of an unaltered sensorium. HPPD was first described by Eisner and Cohen, who observed spontaneous recurrences of LSD like states in subjects, days to weeks following cessation of drug use.

Other authors have described more or less the same clinical picture; for example, Rosenthal described patients suffering from post-drug visual hallucinations lasting as long as five months from the time of drug use.

In a survey of sixty five users of LSD, Holsten found fifty users who described post LSD disturbances eighteen months to four years later.

Flashbacks have been suggested to be a misnomer as patients described cases of continuous rather than paroxysmal visual disturbances from LSD.

It is not clear what made our patient re-experience these visual disturbances however the literature suggests that emerging into a dark environment can precipitate or exacerbate post LSD visual symptoms. Among other precipitating factors are intentional inductions, marijuana use, medications like: neuroleptics (phenothiazine), amphetamines, cold remedies, anti-Parkinson’s agents and SSRI’s.
The patient mentioned that he had ingested LSD approximately fifteen times before he developed this condition. The data suggests that peak incidence occurs with fifteen exposures and second smaller peaks at around forty to fifty exposures.

A number of hypotheses have been formulated in order to understand the underlying aetiology. HPPD is related to the recreation of symptoms experienced in intoxication. LSD has been shown to be excito-toxic to neurons. It is also known to be a partial agonist at post synaptic 5HT2 receptors and enhances glutaminergic transmission.

The patient had suffered from these rather distressing visual disturbances for more than two decades, which have had considerable impact on his daily living. He was given different diagnoses which included induced depersonalisation, depersonalisation-derealisation syndrome, LSD induced simple schizophrenia, depressive disorder and anxiety disorders.

The patient had been treated with different psychotropic medications including antidepressants, antipsychotics, benzodiazepines, propranolol, fentazine and hydergine. Some had little effect like hydergine, whilst others worsened symptoms, in particular antipsychotic medications.

A case series of three HPPD patients treated with Risperidone reported an exacerbation of LSD-like panic and visual symptoms. Thus from these reports and our case report Risperidone could be contraindicated in patients with HPPD.

There have been some published case reports on treatment of HPPD, including the use of Reboxetine, which suggest it is beneficial in the treatment of the visual disturbances and depressive features associated with HPPD. This is possibly due to its alpha 2 adrenoceptor modulating effect on both Noradrenaline and Serotonin release. Another case report suggested the use of a combination of Fluoxetine and Olanzapine in the treatment of HPPD.

Benzodiazepines seem to be the most beneficial treatment so far and Clonazepam is the most effective due to its high potency compared to low potency Benzos and its long action at the GABA receptors.

Conclusion:

Hallucinogen Persisting Perception Disorder is one of the outcomes associated with the ingestion of LSD. Symptoms can be present for years as demonstrated by different case reports, and for over two decades as reported in this report. The effect could be devastating to the person experiencing extremely distressing and disturbing perceptual phenomenon. It can last up to twenty five years after the cessation of the hallucinogenic drug. Early diagnosis and appropriate treatment can significantly help improve the quality of life of patients with this condition.

Competing Interests
None declared

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