ARTICLE

When the trip doesn't end

Henry David Abraham describes his investigations into hallucinogen persisting perception disorder (HPPD), along with firsthand accounts

The nature of hallucinations has puzzled and fascinated us since the dawn of human consciousness. Where they come from, what they mean, and what they portend are questions that the psychological sciences have grappled with since Esquirol coined the term in 1817. Hallucinations are the stuff of dreams, drugs and diverse influences on the mind. Today it is possible to investigate the problem of hallucinations by taking advantage of tools that Esquirol never dreamt of.

questions

HPPD appears to be a continuous disorder of visual disinhibition. Are there other psychological disorders that have a similar mechanism?
Building on this theory, are there behavioural or pharmacological treatments for HPPD and other conditions that may rebuild the brain's inhibitory circuitry?

resources

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I began my psychiatric residency at the Massachusetts General Hospital in Boston in 1971. I was assigned to the Acute Psychiatric Service, at a time which coincided with the tail end of the international epidemic of use of LSD. Into my care came a steady stream of patients complaining of visual disturbances long after their last use of the drug. The idea that LSD could cause 'flashbacks' had appeared in the literature a few years before (Rosenthal, 1964; Shick & Smith, 1970). But these patients had the unique complaint of experiencing visual problems constantly. They described a number of pseudohallucinations devoid of emotional content. Auditory hallucinations were rare. The majority of these patients understood that what they were seeing was 'not real'. All of them attributed the onset of the disorder to their use of LSD.

Like any good bean counter I set about describing the phenomenology of this apparently new disorder (Abraham, 1983). Visual disturbances included prolonged afterimages, halos around objects, the false perception of movement in the peripheral visual fields, the illusion of trails behind objects as they moved, geometric shapes on surfaces and in the air, changes in the sizes and shapes of objects, and the perception of countless small dots in the air.

These symptoms persisted for approximately five years in half of my original sample. Over the next 40 years I observed that for some unlucky individuals these symptoms have persisted for a lifetime, and that other drugs with hallucinogenic activity, including psilocybin, MDMA and cannabis, could do the same thing.

These original observations formed the basis for including HPPD in the DSM-IV in 1984 and the DSM-5 in 2013. The stability of diagnostic criteria over 20 years may reflect the comparatively stereotyped symptom profile as well as the low frequency of the disorder among drug users.

Objectifying the symptoms

It seemed to me that it was one thing to write down what patients were telling me they saw, and quite another to somehow quantify the reports. In the clinic I set about testing the patients on a variety of visual tasks. One night I asked a patient to describe the colour of the setting sun on the cover of the 1972 South Boston telephone book. 'Yellow,' he said. To my eye it was white surrounded by a yellow aura. I brought the test object closer, and asked the patient to ignore the yellow aura and just describe the colour of the sun. 'Yellow,' he said again. Finally, I brought the object within inches of his face, and the patient said 'white'. I had found my test. I compared the next 67 patients reporting LSD use to a control group, measuring how close each group needed to get before saying the colour white. The LSD patients describing HPPD symptoms had to stand 89cm closer than drug-naive controls (Abraham, 1982).

Realising the unsophisticated metric I had used, I showed my results to Dr Ernst Wolf, Chief of Psychophysics at the Massachusetts Eye and Ear Infirmary. He proposed that we do a case-controlled series of patients who had used LSD in the past with a number of standardised psychophysical tests. The magnitude of the results startled both of us. For example, in order to see a test object in the dark, the LSD group required it to be much brighter than the controls did.

If you look at a fluorescent light it is likely to glow in a continuous, unbroken beam. But in reality, the light is flickering

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ANNA HEATH

'...a ghost image of the time is always present...'

Neon green patterns shaped like webs cover the screen of my computer monitor. This visual is not a psychedelic screensaver because when I look away towards my room's walls, which more than a decade ago I saw as a solid beige, I see these web pattern too. The negative afterimage of my computer monitor follows my visual attention and bright yellow horizontal bars replace the edges of the blue 'windows' from my screen. Looking down, I see the keyboard's letters bleed orange and pink halos just like they do on the screen. My entire room is edging back and forth but never goes anywhere; this is true of any space I occupy. The dark corner of the open closet prominently displays the visual static, like a projection from an old and disconnected TV screen layered over all of my vision. The blurred image of an LED clock form bright red streaks as I turn my head back to the screen.

My vision was measured perfect 20/20 before I ingested an adulterated pill sold to me as Ecstasy. Today, a doctor has yet to feel they have an accurate measurement of my vision. Lenses are unable to correct the ghosting and doubling of vision, but taking a benzodiazepine helps reduce the symptoms and improve my vision. Now, my LED clock is blurry and a ghost image of the time is always present. The same ghosting appears on every word I see on the printed page or on a computer screen.

I am only giving a fraction of the total changes in my perception that were altered that day in 1998, which have remained with me 24 hours a day without remission. I know my perception does not match the stimuli, but for me it is part of my perceptual experience and affects whether I can drive a car at night and if I am able to see the dancers on a stage in a lowly lit theater. I can close my eyes and enter a pitch-black room and watch the coloured patterns dance knowing no light creates their form. I am lucky that I have learned to cope with these images and have received proper treatment, but for those who have not I hope they find the educated clinician to be a partner in accepting this condition.

David Kozin

at a rate too great to see, courtesy of the miracle of a 50- or 60-cycle per second alternating current through the bulb. But if the rate of the flicker is slowly lowered, there will come a point when you say, 'Now! I see the flicker'. This is the test that Ernst Wolf and I did, comparing LSD users to drug-naive controls. Again we were taken aback. LSD users needed to have the flicker reduced by as much as 7 cycles per second more than the controls in order to see the flicker. This was especially marked in the peripheral visual fields (Abraham & Wolf, 1988).

These observations, along with what the patients described to me (see boxes), led to the hypothesis that HPPD was a disorder of the disinhibition of visual information processing. In the phone book study the LSD patients could not inhibit the yellow aura from contaminating the white sun until the size of the sun itself created a large enough signal. Similarly, subjects were preconditioned by a bright environmental light before dark adaptation testing. It was plausible that the light created uninhibited visual noise that prevented the LSD participants from seeing the small test object in a timely manner. During flicker testing the LSD group apparently could not see flickering as well, either, because the off-phase of light was being contaminated by the on-phase.

The neurophysiology of HPPD

At this point the question of whether HPPD occurred in the eye or the brain was not answered. An occasional patient would exhibit the Ladd-Franklin manoeuvre, in which digital pressure on one eye would generate imagery in the other. This suggested that HPPD was not simply an ocular problem. I was able to interest Dr Frank Duffy at the Children's Hospital of Boston in this problem. Duffy had developed technology that permitted mapping of the brain's electrical activity in real time (Duffy, 1989). Together we began to map electrical activity in the cerebral cortex of HPPD patients and

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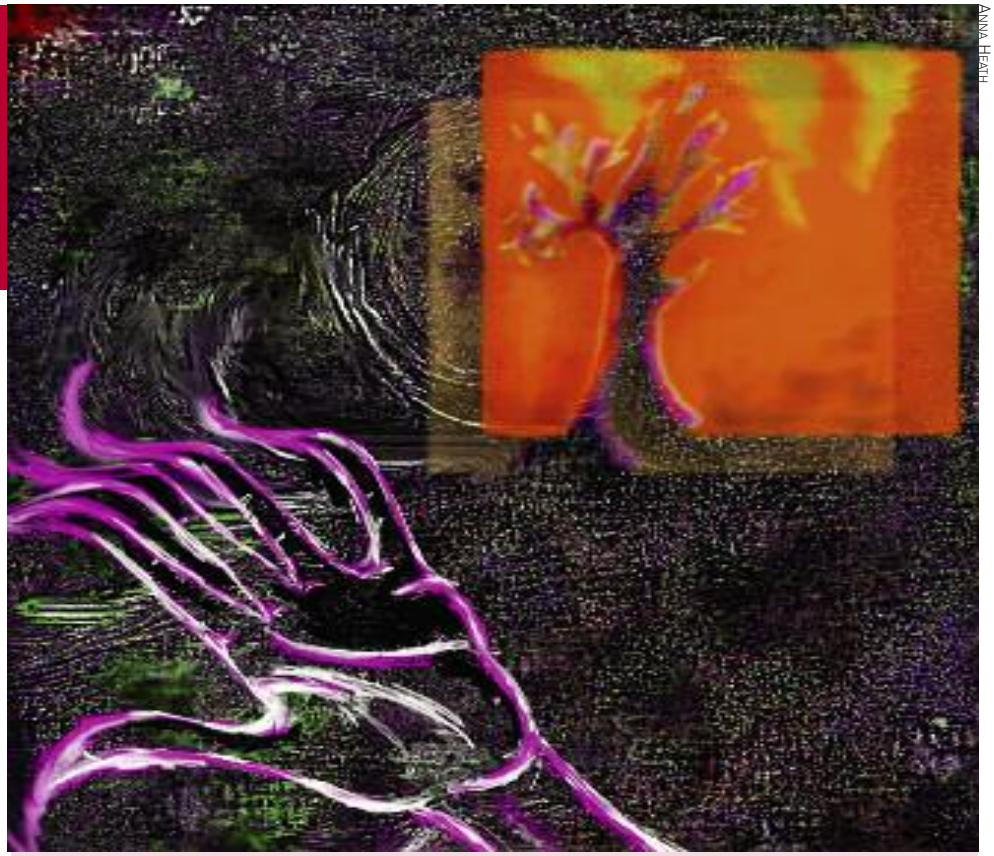

ANNA HEATH

‘I was going to be all alone on an acid trip forever’

In 1974, two weeks after an anxiety-filled LSD trip, I fell into a black hole of panic, crushing depression, terror, horror, and hell. Everything sparkled and glinted with dots like a noisy TV screen. My hand looked like it didn’t belong to me. When I moved it, long streaks trailed behind. After looking at the window, when I looked away the lingering afterimage remained for seconds. I was tripping all over again. Now we categorise these as classic symptoms of HPPD, but at that time, I just knew I was alone in one of those ‘mythical’ never-ending acid trips we always thought were bullshit scare stories. I came to the terrifying realisation that it was not stopping, and I was going to be all alone on an acid trip for ever.

I called my doctor, who with derision brusquely told me to ‘go see a psychiatrist’. The psychiatrist only parroted the conventional wisdom: hallucinogens created psychosis, so the treatment was an antipsychotic drug. These did not help any of the symptoms I was experiencing, but suppressed my personality, slurred my speech, and created more depersonalisation.

Soon after that I went on a trip, hitchhiking several hundred miles, refusing to cave in to the terror. I walked around with a stone where my heart used to be, everything looked and felt like I was on an acid trip, yet I was still somehow able to function. But as I hiked I could not stop my mind chanting nonsense words endlessly. I stumbled and tripped along a riverbed, then lay down amongst the rocks sobbing over the devastation I had brought down on myself.

Later, when the psychiatrist told me ‘you are sicker than you think you are’, I’d had enough. I stopped the antipsychotics and created my own treatment protocols alone by trial and error: nutrition, rest, exercise, no drugs, keep engaged, and never give up. But there was no formal diagnosis and I was all alone.

I was indelibly stamped with HPPD and am not who I might have been, but over decades I have overcome it. Medications, plus electroshock for a severe depression, may have helped. I still see artefacts, feel some depersonalisation, but I have had a very successful career, raised a family, and am not alone any more.

Greg W

controls. Electrophysiological variables were able to successfully identify LSD participants 87 per cent of the time using discriminant analysis. Visual and evoked potentials were significantly different in the temporal and left parietal regions of the brain, posterior regions of the cortex known to be involved in a visual information processing. Finally, the latencies of visually evoked potentials in the cerebral cortex were shortened in the LSD group compared to controls, further evidence of visual disinhibition (Abraham & Duffy, 1996).

A second brain-mapping study revealed that HPPD patients had an increase in electrical coherence, a measure of cortical coupling, located in the occipital scalp region (Abraham & Duffy, 2001) This, too, suggested an increased excitability in a part of the brain involved in vision. What excited Frank Duffy and me was the fact that the patients being studied were also experiencing the visual symptoms of HPPD at the same time as brain-wave data were being acquired – quantitative EEG data had shown us pictures of the brain experiencing visual pseudohallucinations in real time.

Treatment

The neurotransmitter gamma-aminobutyric acid (GABA) is a major inhibitory agent in the human brain. Medications such as the benzodiazepines are agonists at this site, and so would be expected to reduce the symptoms of HPPD if the disinhibition hypothesis were correct. Indeed, this seems to be the case, but unfortunately only partially so. One possible explanation for an incomplete treatment response may be pharmacokinetic, that is, too little drug reaching its destination in the brain. Indeed, when treating six patients with a short-acting benzodiazepine, the volunteer (a psychologist) excitedly said, ‘I can see normally for the first time in years.’ Similar strong responses were observed in the other volunteers. But the excitement was misplaced, since midazolam must be administered intravenously, and has a half-life of two hours. Clinical studies by my colleague Dr Lerner and his group in Israel have shown that clonazepam appears to be the benzodiazepine drug of choice for HPPD (Lerner et al., 2003)

There is an axiom in clinical medicine that the more mysterious the ailment, the more multitudinous the treatments. That is certainly the case with HPPD. In addition to the benzodiazepines, a long list of other agents have been tried, including antipsychotics, antidepressants,

antiepileptics, alpha-two adrenergic agonists, and antiparkinsonian drugs. Levetiracetam was reported helpful in one study (Casa & Bosio, 2005). Some patients report that the use of psychostimulants improved the symptoms, leading me to try a study of tolcapone supplemented with carbidopa and l-DOPA in HPPD. The combination of medications reduced symptoms significantly in about a third of the sample (Abraham, 2012). While this may be a biological effect, it is equally consistent with a placebo response, since the study was an open-label one.

Certain agents make HPPD worse. These include cannabis, infectious disease, emotional stress, alcohol and opiate withdrawal, fatigue, over-exercise in certain drugs that block the serotonin-2A receptor, such as risperidone (Abraham & Mamen, 1996). Given the effectiveness of benzodiazepines to reduce symptoms, it was not surprising to observe on a number of occasions patients who used alcohol for the same purpose only to become dependent on that drug.

One psychological treatment has been observed to be helpful in multiple cases, namely, the use of inattention. Patients frequently report that by attending to the visual requirements of the moment, they are temporarily and even chronically able to push the visual intrusions of HPPD to the periphery of consciousness. Thus, talking about the symptoms tends to increase them. Focusing on the work of everyday life tends to decrease them. Thus, patients who do best with HPPD over the years are the ones who can commit themselves to the productive lifetime activities of love and career. Among my successful cases are physicians, attorneys, psychologists and writers.

Patients new to HPPD are usually burdened by guilt, confusion and misdiagnosis. Mental health clinicians often suspect that the patient is psychotic. The use of antipsychotic drugs is more often a liability than benefit in such cases. The presence of other mental health conditions is common: in the tolcapone study it was striking that 55 per cent of the subjects suffered current panic disorder, and 35 per cent major depression. On an optimistic note the tools that the psychological sciences have in the treatment of such conditions are quite good, even as the specific treatment of HPPD symptoms is not yet at hand. Nearly all HPPD patients can benefit from supportive psychotherapy, and cognitive behavioural therapy for depression and anxiety disorders.

In summary, HPPD is an uncommon but vexatious disorder arising from the use of hallucinogens. Sufferers describe a consistent and constant pattern of visual disturbances that persist from months to a lifetime (see boxes). Studies of the brain in these patients suggest that the disorder is caused by an inability of the visual system to filter out useless information. Medications for anxiety such as the benzodiazepines can reduce, but not cure, this problem. Psychological approaches that reduce the patient's attention to such visual noise, and address the issues of guilt, anxiety and depression, appear to be more effective than drugs at this time.

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