What is Hallucinogen persisting perception disorder (HPPD)

An edit. Since writing this the site HPPDonline.com has sadly been shut down after being up for nearly two decades.

HPPD is a non-psychotic neurological disorder that primarily causes visual disturbances, but in many cases also non-visual symptoms. The spectrum of severity is big, so some might just get one or a few persistent visuals, while others get it moderate to real severe and pretty much every known visual and non-visual symptom that it can cause.

There's two different types of HPPD, type 1 and type 2. Type 1 has a good prognosis and is usually pretty benign, some even find it pleasurable (usually hallucinogen fanatics), and the symptoms of it are so called "flashbacks" were the person randomly and usually briefly re-experience visuals that he or she had during the intoxication of the hallucinogen. Type 1 goes away by itself with abstinence, but it can take months to years, it can even be cured with the antiepileptic Keppra, as can be seen in the study in the forum thread on HPPDonline under "treatments".

Type 2 HPPD does however not have a good prognosis. It causes the person constant symptoms and a significant impairment in daily and occupational functioning, or atleast for those that end up getting it moderate to severe on the spectrum.

As from what we know so far, type 2 seems to be chronic in it's nature, but can wax and wane in intensity, but from anecdotes on forums and after being in contact with the now retired Dr. Henry Abraham and Dr. Steven Locke *(top HPPD experts in the world)* some symptoms can go away or decrease in intensity, but if it fully can go away remains to be answered, and if so, it seems to be very rare. I also guess that the severity of it plays a role in if it can. If we look at the literature there's case reports were HPPD has gone away, but every single one of them seem to be cases of type 1, since none of them mention anything about constant symptoms, rather "occasional" or "re-experiencing" of visual disturbances, which as said is what type 1 causes.

There is anecdotes on forums were people claim that their HPPD has gone away, but then the question is if they've actually had type 2 HPPD or just regular psychedelic 'after effects' that can linger for some time after the use of hallucinogens, which isn't that all too uncommon of a phenomena if you read on different psychedelic forums *(especially LSD ones)*, Dr. Abraham also mentions this phenomena at his homepage.

What are the underlying pathophysiological mechanisms of HPPD

Due to the lack of research into this disorder we don't yet know the exact underlying pathophysiological mechanisms. Several ones have been proposed, but the primary neurobiological hypothesis is the destruction and/or dysfunction of cortical serotonergic inhibitory interneurons with GABAergic outputs, which in turn causes a disruption of the normal neurological mechanisms that are responsible for filtration of unnecessary stimuli. This would also result in an imbalance between cortical excitation and inhibition, which has

long been suspected in HPPD and would explain why medications that decrease neural excitation (antiepileptics and benzos) have the potential to decrease the symptoms.

What causes HPPD?

HPPD is a disorder that can be caused by a wide variety of recreational drugs, but it also seems like some medical ones can, such as serotonergic antidepressants (1)(2). But when caused by the latter the researchers have for some reason classified it as Visual snow syndrome, which is a similar neurological disorder with many overlapping symptoms, it is however not caused by any drugs. But personally I've talked with quite a few people that have gotten it from a serotonergic antidepressant *(both when they started it, but some even after they've gone off it)* and several of them experienced symptoms that VSS is not yet known to cause, but HPPD is, like occasional pseudo-hallucinations. So if it's really VSS, and not HPPD, remains to be answered.

Traditionally HPPD has only been associated with classic hallucinogens, like LSD, DMT and psilocybin, however, entactogens, dissociatives, cannabinoids and atypical hallucinogens have all now been implicated in the development of this disorder, like cannabis, ketamine, MDMA etc. But from what's been observed so far, drugs that are strong 5HT2-A receptor agonists seem to be those that come with the greatest risk.

It's also worth mentioning that some people get HPPD after a single use of the drugs that are known to cause it, were others can use them regularly for many years before getting it. So it seems that some people have a really bad genetic predisposition/brain chemistry to get it. Another thing worth mentioning is a quote from Dr. Henry Abraham who dedicated the bigger part of his career to researching and helping patients with it, and that is:

"Once you have taken a psychedelic, you're never safe from HPPD."

For most people the onset happens the same day or within days after the use, and some get all the symptoms at once, were others have them gradually come on over days, weeks or months until finally hitting a baseline. But in rare cases the onset can manifest months, and even years after the last drug use. In these cases it usually happens during periods of high stress, anxiety, sleep deprivation, pregnancy, the use of other substances or meds (*e.g., alcohol, antidepressants)*.

An explanation for this might be that some researchers theorize that hallucinogens may leave dormant changes in neural circuits that remain silent until activated by certain physiological or psychological states. These changes are thought to involve alterations in brain connectivity and neuronal signaling, particularly through pathways such as the 5-HT2A receptor and the glutamatergic system. These mechanisms can result in prolonged effects, such as shifts in perception, mood and cognition, which as said above may resurface under certain conditions. Below are a couple of many articles/studies (2)(3) out there discussing the neural effects of hallucinogens and their potential for leaving dormant changes in neural circuits, most of these studies are however about their potential therapeutic effects for certain mental illnesses, were some actually have shown to be very helpful in treating for

example depression and PTSD, like ketamine and psilocybin, but if unlucky, they can do the direct opposite and end up ruining ones life.

As someone that got this from using cannabis a few times I'm going to go a bit off topic since i feel an obligation to mention some of the other risks that it comes with, such as psychosis, the extremely strong correlation that it has with schizophrenia, depersonalization and derealization disorder, how extremely bad it is for the adolescent brain and how chronic use can cause paranoia, depression and anxiety. But like psychedelics, it do possess some medical properties, but many of them are not very well researched and primarily linked to CBD, the non-psychoactive part of the plant. CBD has shown to be effective in reducing seizures, especially in conditions like Dravet Syndrome and Lennox-Gastaut Syndrome, but THC do possess some as well, like in helping cancer patients with pain, nausea, vomiting and increasing their appetite, also reducing muscle spasticity for people with Multiple Sclerosis.

The neuroscientist, podcaster and associate professor of neurobiology and ophthalmology at Stanford University School of Medicine Andrew Huberman has a pretty good episode about cannabis on his podcast were he lifts some of the ups and downs that i mentioned above, but sadly he doesn't discuss DPDR disorder or HPPD in it. It and his sources can be found below (5).

1. https://rxisk.org/new-study-of-antidepressants-and-vision-problems/
2. https://pmc.ncbi.nlm.nih.gov/articles/PMC7803695/
3. https://www.pnas.org/doi/pdf/10.1073/pnas.1121358109
4. https://www.jneurosci.org/content/41/5/891
5.https://www.hubermanlab.com/episode/the-effects-of-cannabis-marijuana-on-the-brain-and-body

The DSM-5 criteria

As of today, the DSM-5 of HPPD is 'inaccurate', or rather not up to date, this because of:

1) The first point that says that one has to re-experience one or several visuals that one had during the intoxication. But today we know that it can be caused by drugs that don't, or very rarely cause any visuals, and extremely many people report that they didn't experience any visuals during the intoxication or got visuals that they had never seen while under it. So today's DSM-5 is based on the assumption that this only can be caused by hallucinogens, which is inaccurate. For example, I, as said above, got severe HPPD *(pretty much all visual and non-visual symptoms that it can cause)* from THC alone and I did not experience any visuals during the intoxication, nor had I touched any other drug than alcohol prior in my life *(4-6 times a year)*. I had however been on the SSRI Citalopram for 13 years prior, so the combination most likely increased the chances of me getting it.

2) It's lacking **MANY** of the symptoms that this disorder can and usually cause and is painted out as one that only causes visual disturbances, when in fact it also commonly causes psychiatric and physiological ones, as mentioned and listed under "symptoms". Quite a few of these symptoms that are not included in the DSM-5 are mentioned in more recent meta

analyses about it, also in studies about Visual snow syndrome were they bring HPPD up.

3) It doesn't make a distinction between type 1 and type 2 HPPD, but thankfully it's widely recognized in the clinical and research community that there are two types. This differentiation emerged in the early 2000s when researchers and clinicians noted that some individuals experience persistent symptoms, while others report episodic and transient ones.

I actually sent an email to Dr. Henry Abraham were i asked him about this, but since he's retired and probably gets bombarded by emails from other desperate HPPD sufferers the only answer I got was that he's aware of it and hope that it gets updated in the next version, also that someone continues the work he was doing. And a little backstory on Dr. Henry Abraham, he's widely regarded as one of the top leading experts on HPPD, i'd actually go as far as to call him 'the father of HPPD', because his contributions/research were crucial in legitimizing this disorder in clinical psychiatry. Sure, the DSM-5 is the product of collaborative efforts by multiple experts and committees, but his work was a cornerstone in the scientific understanding of it and what got it into the DSM-5.

Anyways, below is how it looks today. So, as you can see in recent meta-analyses and studies about Visual snow syndrome that also involve HPPD *(end of this pdf)*, it really is in need of an update, since it's current state prevents people from getting properly diagnosed, which contributes to this hell of a disorder lingering in the shadows.

"1. ***Re-experiencing Perceptual Symptoms After Hallucinogen Use***

• The person experiences one or more persistent visual disturbances following hallucinogen use. These disturbances may include: Geometric hallucinations (e.g., patterns, shapes, or forms not present in the environment).
• False perceptions of movement in the peripheral field (e.g., trailing lights or objects, also called "visual trails").
• Flashes of color or intensified colors.
• Afterimages or palinopsia (seeing an image after the stimulus is gone).
• Halos or auras around objects.
• Macropsia (objects appear larger than they are) or micropsia (objects appear smaller).

2. ***Symptoms Cause Significant Distress or Impairment***

• These perceptual disturbances lead to significant distress or impairment in important areas of functioning, such as social, occupational, or other daily activities.

3. ***Not Due to Another Medical Condition or Mental Disorder***

• The symptoms cannot be better explained by a medical condition, another mental disorder (e.g., schizophrenia, epilepsy, or migraines), or substance intoxication or withdrawal.

4. ***No Current Intoxication***

• *The person is not actively under the influence of a hallucinogen at the time the symptoms occur."*

How common is it?

This is a question that we most likely won't get a real accurate answer to in many years because of how many factors that seem to play a role in the development of this disorder. Like if there's a genetic predisposition, pre-existing psychiatric disorders *(this has been seen to increase the chances of getting it)*, that people combine drugs that can cause it, which without a doubt increases the chances because of the drug > drug interaction, some drugs comes with a higher chance than others etc. Add to this that the war on drugs makes research more difficult to get done, the stigma keeping people from seeking care and the lack of awareness of it in the healthcare system, which leads to most people never getting a diagnosis or misdiagnosed as psychotic and put on an antipsychotic medication, which are well known to worsen the symptoms for many.

That psychedelic companies now also act like tobacco companies used to do by shoving the risks under the carpet/not talking about them (especially Rick Doblin at MAPS) because of how much money it is and will be in it in the future will also prolong any proper research being done about it. But from the surveys that have been done and Dr. Abrahams estimation, about 4-5% of psychedelic users will get it to a degree were they seek clinical help, but much more gets it milder or type 1, as can be seen below.

In one of the latest studies (1) 2,455 users of psychedelics via Erowid, found that up to three-fifths of psychedelic users reported lingering perceptual changes, 25% in ways that were seemingly-permanent, and 4.2% in ways so distressing that they seeked clinical help. Dr. Matthew Baggott, MDMA researcher and the primary author of the survey said, and i quote:

"HPPD may be much more common than we ever believed"

In another survey (2) from 2010 with 626 participants via Imperial College London 34% experienced moderate visual changes after their use of psychedelics and 6% more extreme ones.

And in the latest one with 415 participants (3) over 40% reported some HPPD symptoms *(these were primarily having type 1)* and 4.3% had type 2. And a worthy quote from it:

"Interestingly, only four participants reported having received a formal diagnosis of HPPD, highlighting a potential gap in clinical recognition of the disorder."

The reason I found this worthy quoting is because of what I said previously, most never get a diagnosis. Abraham has also provided insightful observations about the challenges faced by HPPD patients in seeking treatment and the underreporting of it. He actually noted that HPPD patients sometimes have to visit as many as 10 to 15 doctors before finding one who knows about it. He has also said that the actual prevalence of HPPD is likely much higher

than what is documented and that many individuals experiencing symptoms might not seek help, may be misdiagnosed, or might not associate their symptoms with previous drug use, which means that the majority of HPPD cases remain unrecognized or undocumented, making it a significantly underreported condition in clinical settings (4).

When it comes to people not seeking help I've actually made a few polls about this on some of the more active HPPD forums/groups, and in every single one the majority had not done it. From the comment section there were several reasons for this, but the leading ones were that they had gotten it at a mild level were it didn't cause them much distress. Others were the stigma and laws surrounding these drugs and that they had read about how hard it is finding a doctor that knows about it, also how hard it may be to treat. Most of those that had seeked help had gotten misdiagnosed and put on meds that worsened it.

1.https://pubmed.ncbi.nlm.nih.gov/21035275/
2.https://www.researchgate.net/publication/232053401_User_perceptions_of_the_benefits_and_harms_of_hallucinogenic_drug_use_A_web-based_questionnaire_study
3.https://www.psypost.org/hallucinogen-persisting-perception-disorder-might-be-more-common-than-thought/
4.https://www.bps.org.uk/psychologist/when-trip-doesnt-end

What are the symptoms of type 2 HPPP

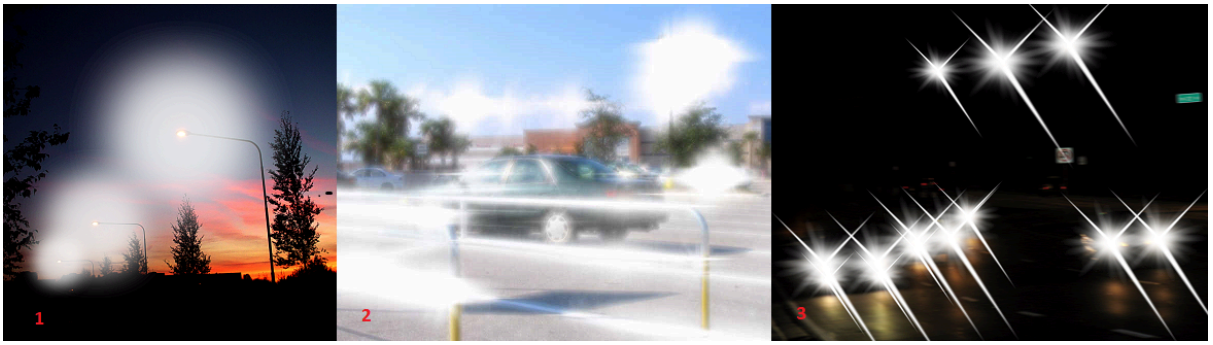
As said, type 2 HPPD can cause a long list of visual disturbances other than those in the DSM-5, and it's not uncommon that people also get several non-visual symptoms as well. And as I also mentioned in the beginning, the spectrum of severity is HUGE, which can be seen under "how common is it" and on forums/groups. But below is a list of the most common reported and documented visual and non-visual symptoms that you can get. I embedded some gifs and pictures in some of the visual ones to give an example of what it can look like.

Visual

• Visual snow, which best can be described as a constant flickering static/pixelated overlay over one's entire field of vision, Here is an example in a GIF format of what it can look like and below is an example of a still picture. This is a symptom that the vast majority seem to get, the severity of the static also varies and even how it looks like, were some get a colored static, black and white and others more transparent. The latter seems to be more common with HPPD and is how I have it, so more like in the GIF picture.

• Palinopsia, which is afterimages and so called trailing. This is the persistent recurrence of a visual image after the stimulus has been removed, like when you look into a camera flash it will linger in your vision for a while. The difference for people with HPPD or the similar neurological disorder Visual snow syndrome that gets this symptom is that it's both stronger, lasts longer and we get it from things that a healthy brain doesn't. When it comes to trailing it's afterimages that follow behind moving objects *(fast and slow)*, like a smear/tail. Here is an example.

• Halos (1) around objects, most often light sources, also day time glares (2) and so called starbursts (3). The glares are in my opinion a real pain in the a** on a sunny day, since you get them from so much! Which results in annoying afterimages, and night time driving isn't very fun either since the headlights of meeting cars cause real nasty starbursts and afterimages, plus they blend you like you were looking into the sun.



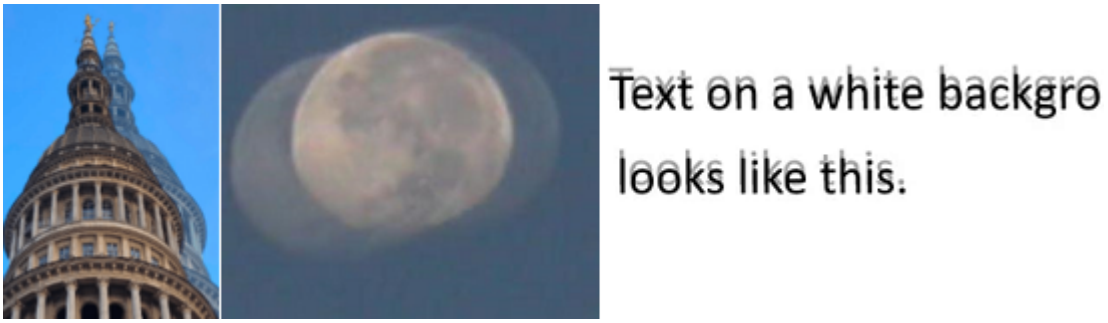
• Seeing an excessive amount of floaters and blue field entoptic phenomenon. An example of floaters and BFEP can be seen here and here in a GIF format. Personally I had never seen a single floater or BFEP before I got HPPD, but now I have around 20 wormlike and circular floaters floating around in my field of vision. It was the same thing with BFEP, I had never seen it, but now a blue sky, a bright colored wall if the sun shines on it or snow looks like it's covered with a swarm of fireflies/hundreds of tiny bright dots moving in all kinds of directions.

• Photophobia, also known as sensitivity to light.

• Macropsia and Micropsia, which makes things look either bigger or smaller than what they are.

• Color enhancement.

• Diplopia, also known as ghosting. This makes the person see one or several more transparent images next to the original one, below is a few examples of how it can look like, but personally, and from most I've read about getting this, white text on a dark background is way worse, especially on phones, tv *(subtitles)* etc.



• Visual pseudo-hallucinations, like walls 'breathing', letters and light sources moving around, seeing patterns form, ground zooming out or looking like it's moving, the perception of movement in one's peripheral sight, curving of texts, straight lines *(like the edge of a door frame)* etc.

Non-visual

• Tinnitus.

• Impaired cognition, which for example causes trouble processing information, memory loss etc, or as it says in the literature about this: *"Acquired dyslexia and a notwithstanding normal intelligence"*.

• A head pressure, or a balloon-like feeling, making it feel like the head is about to pop. Personally I'd describe mine like my brain was being squeezed together, but sometimes it's on the top of the head and other times at the temples. So it's not always at the same place for those that get this symptom.

• An increased frequency of migraines for those that had it prior, and there's also quite a few reports on forums and in FB groups were people that did not have it prior to their HPPD started getting it afterwards.

• More intense/lucid dreams.

• Depersonalization and derealization disorder, for some episodic, others constant. According to a smaller survey that can be seen below 92% got it along with the onset of their HPPD (1), and if you read on HPPD forums it's anything but uncommon. As someone that got this constant *(primarily derealization)* and pretty bad *(spectrum of severity is big here as well)*, i must say that it's amongst the top of the worst symptoms that i got along with my HPPD. Most people, or actually everyone that I've talked to that got chronic DPDR with their HPPD say the same thing. Below is a quote from Mayo Clinic that lists some of the symptoms that it can cause (2), but I'll provide a link to Wikipedia as well, since it describes it pretty good and way more in depth (3).

*"**Symptoms of depersonalization include**:*

• Feelings that you're seeing your thoughts, feelings, or body parts of your body from the outside. For example, you may feel like you're floating in the air above yourself.
• Feeling like a robot or that you're not in control of what you say or how you move.
• The sense that your body, legs or arms appear twisted or like they're not the right shape. Or they may seem larger or smaller than usual. You also could feel that your head is wrapped in cotton.
• Emotional or physical numbness of your senses or responses to the world around you. A sense that your memories lack emotion, and they may or may not be your own memories.

***Symptoms of derealization include**:*

• Feeling that people and your surroundings are not real, like you're living in a movie or a dream.
• Feeling emotionally disconnected from people you care about, as if you were separated by a glass wall.
• Surroundings that appear out of their usual shape, or are blurry or colorless. Or they may seem like they only have two dimensions, so they're flat with no depth. Or you could be more aware of your surroundings, and they may appear clearer than usual.
• Thoughts about time that are not real, such as recent events feeling like the distant past.

Unrealistic thoughts about distance and the size and shape of objects."

1.https://journals.lww.com/addictiondisorders/Abstract/2020/03000/Faces_of_HPPD__Hallucinogen_Persisting_Perception.6.aspx
2.https://www.mayoclinic.org/diseases-conditions/depersonalization-derealization-disorder/symptoms-causes/syc-20352911
3.https://en.wikipedia.org/wiki/Depersonalization-derealization_disorder

Treatments

Treating type 2 HPPD can be hard, but there are three meds that has quite a lot of anecdotes behind them, also some case reports and studies in the literature, and they are:

1. Clonazepam *(and other potent benzos)*
This is by far the most effective treatment and the one that has the most support in the literature *(and anecdotal)*, which can be seen in the meta analyses below, but also on HPPD forums and groups *(even for visual snow syndrome)*. This is believed to be because of it's strong anticonvulsant properties, rapid rate of absorption, long lasting action and activity at cortical serotonergic inhibitory interneurons with GABAergic outputs *(Abraham and Aldridge, 1993; Abraham et al., 1996)*.

But since it's a benzodiazepine, tolerance is generally developed fast, especially towards it's anticonvulsant properties *(generally within a few months)*, add to this that some become physically dependant in a matter of weeks and are by many considered to be one of the hardest class of drugs there is to come of, much ofcourse depending on genetics, dosage, how long one has been on it and how fast one weans off them.

In the study below (1) a dosage of 2 mg/day for 2 months actually pretty much cured 16 patients with LSD induced type 1 HPPD, since the improvements remained after they had weaned off it. Sadly for type 2 it's no cure, but as said, for most it drastically decreases the symptoms. But due to the unavoidable tolerance because of the GABA-a receptor downregulation that occurs with daily or regular use and physical dependence, it's sadly not a sustainable long term treatment.

My own experience with Clonazepam *(started at 1.5 mg)* before tolerance gradually came knocking at my door around week six was amazing! It took away pretty much all non-visual symptoms and I hadn't felt that close to my old self since getting HPPD. Add to this that it improved pretty much all visuals by 60-70%. But then I had to increase the dosage for a maintained effect, or the effect actually lessened, even though the dosage got higher, which is because of the desensitization of the GABA-a receptors that occur with chronic use *(damn the human body for it's ability to build a tolerance towards meds!)*. So treating HPPD with Clonazepam is a real slippery slope.

Lamotrigine
This is as far as i know the most commonly prescribed drug for this disorder *(also visual snow syndrome),* but sadly there's no data on how many that experience symptom relief

from it, so all we have to go on is anecdotes and a few case reports, were (2) is one of them. But there is actually one smaller study were people with Visual snow syndrome were given it, and in that one 20% experienced symptom relief (3). However, after all the reading I've done, which is ALOT, it seems that people with HPPD more often respond to Lamotrigine than those with VSS.

And just as with Clonazepam, I'm going to give my personal experience with it. Lamotrigine was the first medication that I got on, and at only 25 mg on day six *(one increases 25 mg every fortnight)* I felt how some of my worst symptoms started to fade, like the derealization, impaired cognition, tunnel vision *(from the derealization),* occasional pseudo-hallucinations etc.

Anyways, our goal dose was 100 mg and the higher I got, the more the non-visual symptoms decreased, and if I remember right, it was around 75 mg that around 70% of the non-visual symptoms had subsided and the rest decreased ALOT *(except the tinnitus).* It also improved some of my visuals and took away the occasional pseudo-hallucinations and tunnel vision completely.

I estimate that it decreased my photophobia by around 40%, tracers by 20-25% and the rest by 10-15% *(it did nothing for the ghosting/diplopia though),* so not that much, but once it kicked the shit out of the non-visual symptoms *(especially the derealization)* I became functional again and went from being isolated and in a couch/bed around 90% of my waking hours to get like 80% of my old life back. I could resume my studies, go back to work, train etc.

After a couple of months on 100 mg I wanted to see if a higher dose could improve my visuals even more, so I upped it to 150 mg, but sadly it didn't. After a couple of months on that I wanted to make one last try and upped it to 200 mg, and it did improve them a tiny bit more, but after two years on Lamotrigine, were nine were spent on 200 mg, my body started building a tolerance to it and all my worst symptoms gradually came back and once again my life fell into ruins, and increasing the dosage did absolutely nothing. So this is where I in desperation started Clonazepam. I did however want to try Keppra first, since I was aware of the risks with benzos, but since my doc isn't a neurologist and that it's a pure antiepileptic drug which she had no experience with, it ended up with me going on Clonazepam first. But to put it short, Lamotrigine gave me a big part of my life back for two years. So once again, screw the human body and it's ability to build tolerance.

PS, I also want to add that it completely took away my regular aura migraine attacks, which it sometimes is prescribed for off label in more severe cases, so that was a big plus.

3. Keppra *(aka Levetiracetam)*
As mentioned above Keppra is a pure antiepileptic medication that has quite alot of anecdotes, it especially did at HPPDonline.com, but as said at the top, the site recently went down. And as with Clonazepam one study actually showed that it could cure type 1 HPPD, which can be seen in (4) along with some testimonials from members that have been helped by it, also some more in (5). It's also one of the meds mentioned in the last meta analysis

shared below *(it dives more into treatments than the others).* When it comes to my experience with Keppra we did eventually try it since the Clonazepam tolerance just got worse and worse, but sadly it didn't have any effect on my symptoms, and it gave me some less fun side effects.

Other medications that have shown some improvements are dopamine agonists. Henry Abraham found that drugs like Tolcapone and Levocarb, which are typically used for Parkinson's disease, decreased the visual disturbances in a third of the participants in a smaller study (6). The biggest thread in the medical section at HPPDonline was also about dopamine agonists (7). Besides these meds that have some anecdotal reports here and there are other antiepileptics, like Perampanel, but also the ALS medication Riluzole, which possess some major antiepileptic mechanisms of action.

It is also worth mentioning neuromodulation treatments, like rTMS, which as I write this is being researched in treating VSS and have a couple of studies going on. But there are actually two case studies were it has helped two patients with type 2 HPPD. In one it decreased the patients pseudo-hallucinations (8) and in the other it actually led to complete remission (9), it is however worth mentioning that the six other HPPD patients that they treated *(i contacted them)* did not experience any major improvements. So just like medications, some seem to respond to it and others not. It's also worth mentioning that rTMS has some evidence behind it in treating DPDR when used on the right temporal junction (10).

When it comes to medications that are pretty well known to worsen the symptoms for many with HPPD is serotonergic antidepressants, antipsychotics *(especially Risperidone)* and stimulants like Methylphenidate. Many also experience a worsening of their symptoms from caffeine, nicotine and alcohol, or rather when the alcohol leaves the body. This isn't very surprising though, since both caffeine and nicotine in short do the opposite of what the meds that have the potential to treat this do *(they increase neural excitation)*. When it comes to alcohol some report that it actually decreases their symptoms during the intoxication, which i quess is because it enhances the GABA-A receptors and lowers glutamate, but when it leaves the body the opposite happens.

1.https://journals.lww.com/intclinpsychopharm/Abstract/2003/03000/Clonazepam_treatment_of_lysergic_acid.7.aspx
2.https://pmc.ncbi.nlm.nih.gov/articles/PMC3736944/
3.https://www.aao.org/education/editors-choice/lamotrigine-can-lead-to-remission-of-visual-snow-s
4.https://www.hppdonline.com/topic/618-hbbs-compilation-of-user-testimony-on-effectiveness-of-keppra-to-persuade-doctors/
5.https://www.dpselfhelp.com/threads/keppra-findings-has-cured-hppd-and-dp.64290/
6. https://www.henryabrahammd.com/the
7.https://www.hppdonline.com/topic/495-the-thread-about-dopamine-agonists-and-supportive-agents-eg-levodopa-and-reuptake-inhibitors/
8.https://pmc.ncbi.nlm.nih.gov/articles/PMC8987195/
9.https://www.brainstimjrnl.com/article/S1935-861X(23)01980-0/fulltext

10.https://pubmed.ncbi.nlm.nih.gov/20837362/

Some meta analyses/systematic reviews
https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2022.878609/full
https://www.frontiersin.org/journals/psychiatry/articles/10.3389/fpsyt.2017.00240/full
https://pmc.ncbi.nlm.nih.gov/articles/PMC5870365/
https://www.frontiersin.org/journals/neuroscience/articles/10.3389/fnins.2021.675768/full
https://pmc.ncbi.nlm.nih.gov/articles/PMC5870365/

Visual snow syndrome studies that also mention and/or involve HPPD patients.

Visual snow syndrome is as said a neurological disorder that usually has alot of overlapping symptoms with HPPD, the main differences though is that it is not caused by any drugs, many are born with it, it can't cause psychedelic like pseudo-hallucinations, and from what I've gathered isn't near as common to cause the non-visual symptoms that type 2 HPPD can. And just like with HPPD, the spectrum of severity is big with this disorder as well. Anyways, I'm not going to deep dive into VSS, but I wanted to include VSS studies and surveys that also touch on HPPD, especially since some of them show how much of a need the DSM-5 is for an update.

A pretty recent study about VSS (1) showed that people with it *(and aura migraine)* has shown to have an abnormal connectivity in glutamatergic and 5HT2-a serotonin receptor enriched networks, which might be an underlying pathophysiological mechanism that HPPD and VSS shares. Below is a quote from the study:

"Aberrant serotoninergic metabolism has also been implicated in visual perceptual syndromes, particularly hallucinogen persisting perception disorder (HPPD). HPPD typically arises following consumption of lysergic acid diethylamide, a potent partial 5HT2A receptor agonist. It has strong pathophysiological links to VSS, often presenting with overlapping symptomatology. The 5-HT2A receptor is abundantly expressed in layers III and V of the brain's visual cortex, particularly in inhibitory interneurons within V1 and V272, and an imbalance between cortical excitation and inhibition mechanisms has long been suspected in HPPD. It is thus not surprising that the activity of serotonin and the 5-HT2A receptor may be associated with a disruption of visual and salience networks in VSS, particularly given the high density of serotoninergic projections from the thalamus and LGN to the visual cortex. Interestingly, a recent case reported VSS symptoms arising after exposure to citalopram, a selective serotonin reuptake inhibitor. Further, lamotrigine, which has an inhibitory function on 5HT2A receptors and is widely used in patients with typical migraine aura and HPPD, has also shown anecdotal efficacy in VSS. However, a larger case series has shown that both citalopram and lamotrigine are mostly inert in patients with VSS, thus suggesting that serotoninergic transmission has a more complex role in the biology of this condition.

An interpretation of our current findings is that serotonin might be modulating the altered connectivity within areas of the visual motion network in VSS, via dysfunction in the salience network, and could thus be causing wrongful allocation of attention to the noise-like percept of snow and increased neural gain within the visual system. Our findings further provide

evidence for a serotonin-5HT2A involvement in the pathophysiological association among VSS, migraine with aura, and HPPD."

And here is a big web-based survey including people with VSS, VS *(not the syndrome)* and HPPD, which showed some of the overlapping symptoms that HPPD has with VSS (2). Here's also an interesting quote from it:

"Studies with confirmed HPPD would be necessary to shed more light on the interesting overlap between VSS and drug intake, which may indeed represent different aspects of a same disorder or 2 distinct conditions with shared pathophysiologic mechanism. Our data do suggest that VSS itself is not part of HPPD but rather that HPPD can manifest in the VSS clinical spectrum."

1.https://onlinelibrary.wiley.com/doi/10.1002/ana.26745
2.https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7136068/