

For informational purposes. Shared with OPAB Products and Research SC Members on 4.11.24 to support discussion that occurred during the 4.10.24 subcommittee meeting.

Wood Lover's Paralysis (WLP) review
Sarah Present, MD, MPH
3/3/24

I. OVERVIEW:

From:

Revell, Jack. What We Know (and Don't) About Magic Mushroom Paralysis. Vice (June 2020).
<https://www.vice.com/en/article/y3zp35/magic-mushroom-paralysis-heres-what-we-know>

"Anecdotally, the issue seems most widespread in Australia"

"Wood-lovers paralysis (WLP) is so-called because it appears to be caused exclusively by mushrooms that grow on wood. The effect has been most commonly linked with three species of the fungus: *Psilocybe azurescens*, *Psilocybe cyanescens*, and *Psilocybe subaeruginosa*."

"Researchers have come up with a number of elaborate hypotheses over the years, based on anecdotal evidence and scientific extrapolations, in an attempt to explain this strange and little-understood phenomenon. None of them have gotten very far."

"all of this is highly speculative as there are no studies that show the total chemical composition of psilocybe species. (Dr Andrew Chadeayne—CEO of American company CaaMTech)"

From my review of literature and internet sources, I agree, there is very little scientific literature on WLP. The vast majority of what is known about it is anecdotal, experiential and informally reported.

I found a survey of people who had experienced WLP was done by the Australian Psychedelic Society (APS) and reached out to them for more information. I heard back from Symon Beck, the secretary of the APS and also a medical doctor who helped run the survey with his colleague Caine Barlow. They are working on finalizing a write up of the result for publishing, but also have a video presenting their results (2021), which can be found here:

<https://m.youtube.com/watch?v=JQNzJvDEKIs>

He gave me permission to share, and offered to discuss further if desired. I have cut and paste some slides for others' convenience. They found, as I did, that there is really nothing in medical literature on WLP. They note this is "despite some people showing up to hospital with it, and [there are] no case reports or direct investigation of theories to date."

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II. THE EXPERIENCE OF WLP:

- a. I have summarized (and in much of this, directly transcribed) what I learned from this survey results presentation video:

WLP has been describe as far back as at least 2010. It is likely not a new phenomenon, but new interest in psilocybin including within legalized structures like ours, and increased discussion about it in the social media world, etc. has made it better known among mycologists and users of psychedelic mushrooms. Likely, WLP has previously been often dismissed as a psychosomatic phenomenon or being “too intoxicated.”

The Survey goals included helping to better define WLP, it’s consequences, potential contributing factors, and help define further research questions.

Several limitations to a survey study like this: sampling bias, limited statistical power (not designed for true statistical analysis)

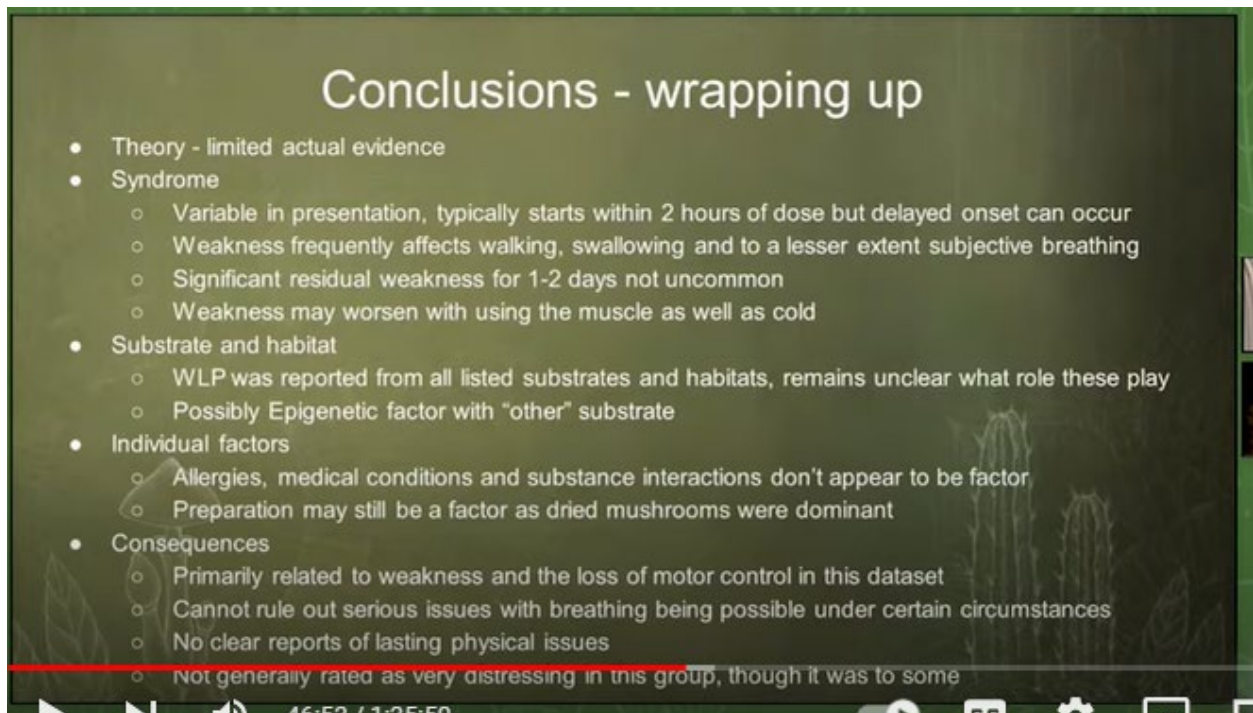
Here is an overview of some results presented:

- Time to onset: w/in 1st 2 hours after ingestion, some noticed it the next day.
- Body part: legs and hands primarily.
- Most often affected functions: Walking (80%, about 53% completely unable to walk at some point), swallowing (26%) and breathing (17%) not infrequently. Muscle groups effected migrate during the experience, as well as come in waves. 50% with sensory loss symptoms.
- What made it better: rest, ?antihistamines, staying warm
- Geography – Australia only—put out a global call for experiences on social media, but primarily respondents were from Australia, so they focused here, found location of people experiencing WLP correlated with population centers and area wood-loving mushrooms grow.
- Substrate on which mushrooms eaten during WLP episode grew: Eucalyptus, pine/conifer, other, uncertain—no one substrate seems obviously over-represented among those who had WLP vs not. Most when harvested from woodchip beds, but this was also the most common habitat reported.
- Multiple episodes:
 - 61% had multiple episodes of WLP,
 - 68% of those had multiple episodes from the same patch,
 - 62% from different patches.
- Wood loving species of mushroom ingested?
 - Vast majority “yes,” of n=166,
 - 1 was cultivated *P. cubensis*—they looked at this more closely, seemed a plausible case of WLP that could spur further research in the future.
- Individual factors:
 - No association: Allergies, any specific medical conditions, for those who reported medical conditions, psychiatric conditions were common.
 - Preparation: most consume dry mushrooms, but no one prep (dry, tea, fresh, lemon tek, others)seems overrepresented among prep in most recent episode of WLP

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- 31% report other substances during most recent experience of WLP: cannabis, antidepressants, alcohol most common.
- Response:
 - Did you have a dedicated trip sitter (23% said yes)
 - Did you seek help: 19% said yes, 3 people (out of n=165) had ambulance called for them
 - Why didn't you seek help? Multiple reasons: Most felt prepared, knew it would go away, felt safe. Didn't think it was necessary. Only 4 reported being physically unable to seek help.
 - Impact on ability to self care: variable
 - Falls and accidents as a consequence of WLP: 22% reported yes, primarily fall with inability to get back up.
 - One reported hospitalization in which SSRI, plus St John's wort and other unknowns were also being used—diagnosed ultimately as serotonin syndrome by medical providers.
- Lasting effects: vast majority had none. N=164, 10 said yes.
 - Fatigue, painful legs lasting weeks.
- Level of distress: variable
- Traumatic memories during the event? 6% said yes
- Anxiety about future episodes: 27% worried about taking psilocybin mushrooms again, 5% wouldn't take same species again, 7% unsure.
- More people had anxiety about it who hadn't experienced WLP before than those who had. Most of those who had experienced it before felt equipped to deal with it (77%).

This is a screenshot of their conclusion slide:



The screenshot shows a presentation slide with a dark green background and white text. The title is 'Conclusions - wrapping up'. The content is a bulleted list of findings, with each main point followed by several sub-points. The slide is part of a video recording, as evidenced by the video player controls at the bottom.

Conclusions - wrapping up

- Theory - limited actual evidence
- Syndrome
 - Variable in presentation, typically starts within 2 hours of dose but delayed onset can occur
 - Weakness frequently affects walking, swallowing and to a lesser extent subjective breathing
 - Significant residual weakness for 1-2 days not uncommon
 - Weakness may worsen with using the muscle as well as cold
- Substrate and habitat
 - WLP was reported from all listed substrates and habitats, remains unclear what role these play
 - Possibly Epigenetic factor with "other" substrate
- Individual factors
 - Allergies, medical conditions and substance interactions don't appear to be factor
 - Preparation may still be a factor as dried mushrooms were dominant
- Consequences
 - Primarily related to weakness and the loss of motor control in this dataset
 - Cannot rule out serious issues with breathing being possible under certain circumstances
 - No clear reports of lasting physical issues
 - Not generally rated as very distressing in this group, though it was to some

46:52 / 1:25:50

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- b. There is another author who has written about both the experience and theories as to etiology of WLP, Barbara E. Bauer, MS, who has published a couple articles on WLP in the Psychedelic Science Review.

This list of symptoms are copied and pasted from her article:

Psychedelic review – Bauer, B.M. (2018). Wood lover paralysis: an unsolved mystery.

<https://psychedelicreview.com/wood-lover-paralysis-unsolved-mystery/>

Symptoms of Wood Lover Paralysis

Below are some first-hand reports that are taken from popular magic mushroom discussion forums like those on [Shroomery](#), [Erowid](#), and [Bluelight](#). Bold text shows the symptoms that appear to be consistent across all accounts. In summary, they are:

1. Loss of motor control, ranging from incoordination to complete paralysis
 2. Loss of motor function in face/eyes
 3. Delayed onset of about 4-6 hours
 4. Resolution of symptoms within 24 hours
- “the ‘paralysis’ manifested as waves of **losing most of the motor control of my limbs**. If I was standing one minute, I was crumpled on the floor flailing about the next.”
 - About 4 hours into a trip, “I got half way to the kitchen and suddenly my legs felt like they were going to collapse. I sat down for 5 minutes, got up again, walked for a bit- and then my legs DID **collapse**. It was a little scary because I felt clear headed, there was no pain or numbness... just **non-functional legs**.”
 - “I **collapsed** in the middle of a field. I **couldn’t walk** 5 blocks. My co-tripper **couldn’t smile** the next day. I have experienced many muscular problems on these two species [psilocybe cyanescens and psilocybe azurescens]. They effect these muscle parts/groups: eye, facial, esophageal, hand and leg.... I have never had similar effects on [cubensis].”
 - “First noticeable symptoms are blurred vision, hand cramping/numbness, then **loss of facial/mouth movement** followed by having a **hard time walking** then **full loss of the ability to walk properly or even stand period**.” [Link](#).
 - “during the comedown, well passed the peak, I experienced first a **weird “jumping effect” in my vision** where the center of focus in my vision would seem to spontaneously jump away from where I was commanding it to be, disorienting and blurring my vision. Then I experienced “clipping” of the energy in my legs – it was like the signal to walk or stand would flicker out, causing **a lot of difficulty with walking** (this effect went away when I would just sit down). And finally, there were weird twitchy contractions around the muscles that controlled the mouth that made **regular speech difficult**.”
 - “My friend ... would try to stand up and **his legs would collapse** like jelly....he was also getting **weird facial contractions where his mouth would distort similar to a mentally disabled person**.”
 - Onset of “about **6 hours or so after eating them**”
 - “One time **walking to the bathroom was a massive struggle**, I probably **looked like I had cerebral palsy**... and once I did make it to the bathroom, I **couldn’t even raise my arms** more than a few inches, and my **legs were trembling, barely holding my weight**. My **vision was blurred**, and when I looked in the mirror, I was literally **slightly cross-eyed with one pupil still heavily dilated and the other in a normal state** (lol).”

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- “The next day after a high dose trip I **couldn’t hold a spoon properly, brush my teeth etc.**”
- “I was fine that night. The next morning I woke up and was having a **hard time focusing my eyes** and felt very uncoordinated....All of a sudden I **completely lost control of both legs**, and my **hands got seized up** weird and stuff. I was in the middle of the road in the campground **paralyzed**. My mind was clear but I **couldn’t get up** no matter how many times I tried....My **hands were seized up** and my **face was numb** and the **muscles unresponsive** for up to a couple of hours and it went away.”
- “...my **knees almost buckled** under me. **Major muscle weakness**, I wouldn’t necessarily call it paralysis though.”
- “Not full on paralysis, but I did realize how **wobbly and weak** my muscles were feeling under me.”
- “I’ve experienced the [paralysis] situation after [consuming] fresh, dried and boiled (steeped) [mushrooms]. “
- “I have had **severe paralysis** on ps cyanescens to the point I had to hit the floor because **my muscles just gave out.**”

III. BIOCHEMICAL THEORIES

a. Histamine Reaction:

Source: same article by Barbara Bauer:

Psychedelic review – Bauer, B.M. (2018). Wood lover paralysis: an unsolved mystery.

<https://psychedelicreview.com/wood-lover-paralys-unsolved-mystery/>

Discussed early theories focused on WLP being a histamine reaction of some sort, given that anti-histamines seem to help symptoms for some. The theories including correlations to movement disorders such as Parkinson’s disease and the extrapyramidal symptoms caused by antipsychotics being relieved by the acetylcholine antagonism at muscarinic receptors by diphenhydramine (Benadryl)

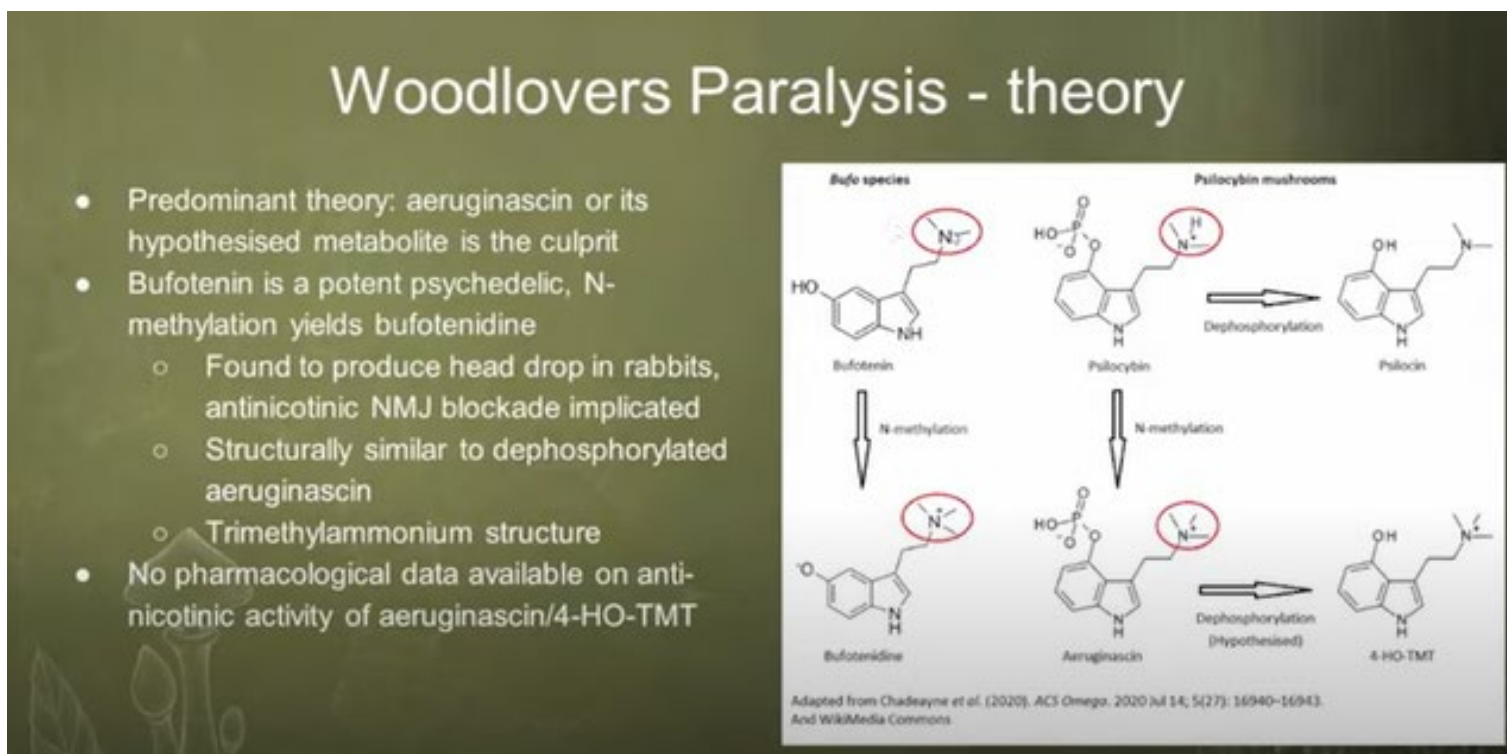
Sarah’s Takeaway: There is no biochemical research or hypothesis to support a histamine reaction theory.

b. Aeruginascin or it’s hypothesized metabolite:

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Psilocybin gets dephosphorylated to psilocin in the body. If it were to undergo n-methylation it turns into aeruginascin, which, if dephosphorylated turn into (4-Hydroxy-*N,N,N*-trimethyltryptamine, which is very much like a chemical called **bufotenidine** (only difference is location of hydroxygroup-one carbon away- Bufotenin and bufotenidine have a hydroxyl group on the 5th carbon while aeruginascin and psilocybin have a phosphate group on the 4th carbon)

The biochemical theory slide from Symon Beck's video is helpful here:



Source:

Vigerelli et al. Biological Effects and Biodistribution of Bufotenine on Mice

Biomed Res Int. 2018; Published online 2018 May 31.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6000854/#:~:text=Bufotenine%2C%20a%20tryptamine%20alkaloid%20resulting,family%20%5B2%2C%203%5D>.

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“Bufotenine, a tryptamine alkaloid resulting from the methylation of serotonin, is a common metabolite spread throughout different living organisms, that can be found, for instance, in the skin secretion of many Brazilian toads of *Rhinella* genus [1] as well as in plants of Leguminosae family [2, 3].”

(it was also evaluated in this article as a rabies treatment)

1. Pharmacologic theory- Serotonergic receptors

Source: Psychedelic review – Bauer, B.M. (2019). Wood lover paralysis from magic mushrooms: The aeruginascin hypothesis. <https://psychedelicreview.com/wood-lover-paralysis-from-magic-mushrooms-the-aeruginascin-hypothesis/>

- Psychedelic effects of compounds like psilocin and LSD are mediated by the serotonin receptor subtype 5-HT_{2A}.⁴ The 5-HT_{2A} receptor is concentrated in regions of the forebrain, primarily the cortical areas, caudate nucleus, nucleus accumbens, olfactory tubercle, and the hippocampus.⁵ A different serotonin receptor subtype is the 5-HT₃ receptor. It is located throughout the body including the brain but also widely distributed throughout the PNS.
- Due to its large trimethylammonium group, it is unlikely that aeruginascin can penetrate the blood-brain barrier.³ Because of this segregation, the effects of aeruginascin are confined to the peripheral nervous system (PNS) outside of the brain and spinal cord, making it a candidate for the cause of Wood Lover Paralysis
- Studies have found that the frog venom bufotenidine (the one that causes paralysis) binds to the 5-HT₃ receptor with ten times the affinity of serotonin.

Source: Chadeayne et al. Active Metabolite of Aeruginascin (4-Hydroxy-*N,N,N*-trimethyltryptamine): Synthesis, Structure, and Serotonergic Binding Affinity. [ACS Omega](https://doi.org/10.1021/acsomega.0c02208). 2020 Jul 14; 5(27): 16940–16943. [10.1021/acsomega.0c02208](https://doi.org/10.1021/acsomega.0c02208)

- Aeruginascin’s binding affinity at serotonergic receptors was been assayed, demonstrating that it is not active at the 5-HT₃ receptor, as previously predicted, but shows strong binding at the 5-HT₂ receptors which was unexpected

Sarah’s Takeaway: the serotonergic theory is less likely.

2. Pharmacologic theory- Antinicotinic blockade at the neuromuscular junction

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This is the theory laid out by Symon Beck in the referenced video. I have summarized (and transcribed) some of what he explained. This seems to be the most recent plausible pharmacologic theory for the etiology of WLP. Future research could focus on this.

Methylation of bufotenine can yield bufotenidine, which has evidence of antinicotinic neuromuscular junction (NMJ) blockade in rabbits (head drop). This theory makes WLP similar in etiology to myasthenia gravis (MG). WLP also has symptoms similar to those of MG, supporting this theory.

Myasthenia gravis is an autoimmune neuromuscular disorder characterized by fluctuating motor weakness due to an antibody-mediated, immunologic attack directed at proteins in the postsynaptic membrane of the neuromuscular junction (acetylcholine receptors or receptor-associated proteins).

Weakness worsened with using muscles—this is similar to myasthenia gravis, a disease c/w nicotinic receptor blocker theory.

Tubocurarine which comes from a vine used on poison arrows, and was used as a muscle relaxant/anesthetic used in 50s has similar chemical structure.

Cold impairs cholinergic transmission at NMJ also. Subjective results suggest cold makes WLP symptoms more likely to come on or to worsen. Warming up and not using the muscles seems to improve symptoms. These supports this theory as well.

Concerns: If aeruginascin or it's metabolite is actually a nicotinic NMJ blocker, it should under some circumstance or level impair breathing substantially.

Also increases concern with other substance interactions, such as other drugs that repress respiratory drive-opioids, benzos, high doses GHB or etoh. This was not experienced in any of these 165 reports.

References:

Beck, Symon and Barlow, Caine. Woodlover Paralysis: 2020 APS/PMANZ Survey results. EGA Microdose Webcast 6: Woodlover Paralysis with Symon Beck and Caine Barlow
<https://m.youtube.com/watch?v=JQNzJvDEKIs>

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<https://psychedelicreview.com/wood-lover-paralysis-unsolved-mystery/>

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Chadeayne et al. Active Metabolite of Aeruginascin (4-Hydroxy-*N,N,N*-trimethyltryptamine): Synthesis, Structure, and Serotonergic Binding Affinity. *ACS Omega*. 2020 Jul 14; 5(27): 16940–16943.

[10.1021/acsomega.0c02208](https://doi.org/10.1021/acsomega.0c02208)

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