THE TOX LAB

Podcast Transcript

Episode 3: Psychedelics

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TRANSCRIPT

Hi everyone, welcome back to The Tox Lab. I'm Rebecca.

I'm Rob. Today we've got an episode on psychedelics, which should be quite interesting.

But before we get into that, why did the mass spectrometrist podcaster buy new microphones?

I don't know.

He wanted to improve his signal-to-noise ratio.

That is appalling.

Yeah, I worked on that joke all week and still couldn't make it good.

But it does let me mention that we have got new microphones, which is exciting. And thank you to everyone who has given us feedback so far, we really appreciate it.

Please do keep sending more. You can find us on Instagram at @the_tox_lab.

So before we get into the papers, let's talk a bit about psychedelics.

Rebecca, when we say psychedelics, what are we talking about?

Psychedelics are hallucinogenic drugs that primarily alter consciousness and can cause psychological, visual, and auditory changes.

Broadly, you can group the classical psychedelics into three families: tryptamines, phenethylamines, and lysergamides.

The key thing that links the classical psychedelics is that they primarily act through serotonin 5-HT2A receptor agonism.

So when we're talking about psychedelics here, we're not talking about every drug that can cause hallucinations by any mechanism. We're not really talking about things like ketamine or MDMA. We're talking about the more classic serotonergic psychedelics.

Exactly.

So let's jump into the first paper. This was a new paper at the time we recorded the episode and it looked at psychedelic-related deaths in England, Wales, and Northern Ireland between 1997 and 2022.

Why don't you take us through it, Rebecca?

This paper used data from NPSUM, which is the National Programme on Substance Use Mortality.

For anyone who doesn't know, NPSUM is a database that collates information on deaths involving psychoactive drugs from coronial jurisdictions in England, Wales, and Northern Ireland. Not every coroner contributes, but coverage is quite broad.

The study period ran from 1 July 1997 to 1 November 2022.

The authors looked specifically for deaths involving serotonergic psychedelics, meaning drugs with agonist activity at the serotonin receptor. That included compounds such as LSD, psilocybin, mescaline, various NBOMe compounds, some of the DOx compounds, and DMT.

They identified the cases in the database and then categorised them according to whether the psychedelic was directly implicated in the death, plausibly implicated, or merely detected but not thought relevant.

In total there were 103 cases where one of these psychedelic compounds appeared somewhere in the record.

But 75 of those were excluded because the psychedelic was not thought to be relevant to the death.

That left 28 cases to analyse in more detail: 21 where the psychedelic was considered implicated, and 7 where it was considered plausibly implicated.

And even before we get into the detail, one thing that jumps out is that 28 cases over roughly 25 years is actually a very small number compared to what we see with things like heroin, cocaine, benzodiazepines, or alcohol.

Yes, definitely.

Looking at the 28 cases, 19 involved tryptamine-related psychedelics and 9 involved phenethylamine-type psychedelics.

And just to pause on that for a second, the way the paper groups the compounds is slightly broad. In practical terms, when we're talking tryptamine-like psychedelics here, we're really talking about things like LSD, psilocybin, and DMT, while the phenethylamine group includes compounds like NBOMes and some of the hallucinogenic amphetamine derivatives.

Exactly.

Around 86 percent of the deaths were classified as accidental.

A really important point is that 68 percent involved multiple drugs. MDMA, ketamine, and alcohol were among the most commonly implicated co-drugs, while MDMA, alcohol, and cannabis were among the most commonly detected more broadly.

So already we are looking at a heavily polydrug context rather than a neat "one person took one psychedelic and died" picture.

Yes.

One of the themes that emerged very clearly was physical environment.

Several of the deaths involved falls from height, and a number involved water. So in many of these cases, what seems to have happened is that the psychedelic may have contributed to a dangerous behavioural or

perceptual state, which then led to fatal misadventure.

That is one of the most interesting parts of this paper to me.

The acute direct biological toxicity of classic psychedelics appears to be fairly low overall, but that does not mean they are harmless, because altered perception, impulsivity, panic, disorientation, and poor judgement can still kill people.

Exactly.

Another clear theme was parties and social settings. Several of the deaths occurred in party environments, which probably makes sense given where people often use these sorts of drugs.

There was also an interesting subgroup involving NBOMe compounds.

NBOMes are worth highlighting because they are a bit different from something like LSD or psilocybin. They are potent phenethylamine psychedelics, and for a period of time they were sometimes sold or misrepresented as LSD.

In the paper, several of the NBOMe-related deaths involved people who apparently thought they had taken something else, often LSD.

And NBOMes are generally thought to have a higher acute toxicity than classic LSD, which makes that especially concerning.

So this is another reminder that people often do not know what they have actually taken.

The paper also touched on mental health and other background factors. A couple of the cases involved individuals with diagnosed mental health conditions.

One had ADHD and another had bipolar disorder and was reportedly on fluoxetine and lithium. In that latter case, there were seizures after LSD use.

That is interesting because lithium and classical psychedelics are known to be a potentially dangerous combination, with an increased risk of seizures.

We don't fully understand the mechanism, but it is a recognised concern.

So what do you think the overall conclusion of this first paper is?

I think the big conclusion is that deaths directly involving classical psychedelics are rare relative to many other drugs, but when deaths do occur they are often complex.

It is not just about the drug itself. It is about the environment, polydrug use, existing vulnerability, mental health, and physical risk.

Yes. Compared with the thousands upon thousands of deaths involving drugs like heroin, opioids more broadly, alcohol, and cocaine, 28 relevant cases over 25 years is a tiny number.

So this paper does support the idea that the classic psychedelics tend to have relatively low direct acute toxicity.

But the paper also makes very clear that "low toxicity" is not the same as "no risk."

Exactly.

Any major limitations?

The main limitation is that this is all dependent on the quality of the coroner reports and on whether psychedelic use was identified, recorded, and considered important enough to note.

So some cases may well have been missed, especially in earlier years when testing for compounds like LSD was less routine.

That said, many of the included cases also had clear circumstantial evidence such as falls from height or water-related deaths in the setting of known psychedelic use, so I do not think the whole signal is just an artefact.

No, I agree.

So let's move on to the next paper, which looked at national and regional trends in seizures of psilocybin mushrooms in the United States between 2017 and 2022.

This is a much shorter paper, but I thought it was quite interesting.

The basic take-home message is that seizures of mushrooms increased over that period.

And that could reflect a few different things: greater availability, growing interest in microdosing, increased general interest in psychedelics because of the therapeutic research, or simply changes in law enforcement practice.

Microdosing, for anyone unfamiliar, is the idea of taking a dose below the threshold that would cause a full psychedelic experience, with the hope of achieving subtle psychological or cognitive benefits.

It is quite a popular idea, but the evidence base is still very mixed.

Yes. There is a lot of enthusiasm and a lot of anecdote, but much less certainty than people often assume.

This paper is also very US-specific. Some states and local jurisdictions in the US have moved toward decriminalisation of psilocybin possession, which makes the legal landscape very different from the UK.

So seizure data there are not directly comparable to our setting.

And, importantly, seizure data tell you something about law enforcement activity and supply, but not necessarily actual prevalence of use.

Exactly. More seizures could mean more use, or more supply, or better policing, or simply more focus on that type of drug.

One other paper we ended up reading from a reference in the first paper was on psychedelic use in people with spinal cord injuries.

This one was really interesting because there was a little signal in the mortality paper suggesting that spinal cord injury patients might be over-represented, and that sent us down a rabbit hole.

So what was the basic issue?

People with spinal cord injuries have a higher burden of mental health disorders, which is not surprising.

At the same time, there is growing discussion about psychedelics as possible treatments for conditions like treatment-resistant depression and PTSD.

So there is a world in which people with spinal cord injuries may be interested in psychedelics for symptom relief, mood improvement, or even because of speculative ideas about neuroplasticity.

But some self-reports, including online reports, suggest that people with spinal cord injuries can experience unusually intense and uncomfortable muscle spasms after taking serotonergic psychedelics such as psilocybin mushrooms.

The paper discusses several possible mechanisms.

After a spinal cord injury, especially a complete injury, descending serotonin input below the lesion is lost. That means the serotonin receptors and downstream networks may adapt over time, potentially becoming more sensitive or dysregulated.

So if you then take a direct 5-HT2A agonist, you may get exaggerated responses in the altered spinal networks.

Exactly.

The paper also discusses the risk of autonomic dysreflexia in patients with injuries at T6 or above. That is a potentially life-threatening state where a stimulus below the lesion can trigger massive sympathetic activation, causing dangerous rises in blood pressure and other autonomic instability.

If psychedelics alter sensation, autonomic tone, muscle spasm, or reflex activity, then there is a plausible reason why they could create particular risks in this population.

What I found really striking about this is that it is the sort of risk that probably would not occur to most people.

No, not at all. Until I read this, it had never crossed my mind that spinal cord injury might specifically interact with psychedelic effects in that way.

And I think it highlights a wider point. There is a lot of excitement at the moment about therapeutic uses of psychedelics, and some of that excitement is justified.

But there is still a huge amount we do not know about drug-drug interactions, special populations, long-term effects, and how these compounds behave in people with underlying medical conditions.

Completely. And years of prohibition almost certainly delayed our ability to study these compounds properly.

So now we are trying to catch up very quickly, and people are also using them in the real world while the evidence base is still developing.

Which is always slightly concerning.

So in summary, what have we learned?

The first paper suggests that deaths directly involving serotonergic psychedelics are relatively rare over a long time period, especially compared with many other drugs.

But when deaths do happen, they are often linked to environment, behaviour, co-drug use, and pre-existing vulnerabilities rather than just straightforward one-drug toxicity.

The US seizure paper suggests that psilocybin mushrooms may be becoming more prominent in the US, although seizure data cannot tell us exactly why.

And the spinal cord injury discussion is a good reminder that even where psychedelics may have promising therapeutic potential, we still need to think very carefully about special populations and unintended risks.

I do not think I have anything else to add.

No, I think that is a good place to stop.

Thank you all for listening. We hope you have enjoyed it.

Do drop us a follow, a like, and some comments. We really do appreciate the feedback.

And if you have seen any papers recently, or you have recommendations for things you want us to talk about on the podcast, please send us a message over on Instagram.

Have a great week, everyone.