PYSCHEDLICS, PSYCHOLOGY, AND NERVOUS SYSTEM HEALING #therapy #rootcausehealing #addictionscience Transcript

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Introduction: Trauma, Addiction, and Psychedelic Medicine

Trauma is so often part of the story in addiction. Traum can fuel addiction, if you know me, you now I say that a lot. Untreated or undertreated trauma is frequently a huge part in the addiction and relapse cycle.

Earlier this year, an executive order brought psychedelic medicine, specifically ibogaine, into the national conversation around addiction or trauma, and also traumatic brain injury and treatment-resistant psychiatric illnesses.

Super exciting times for sure. Aside from ibogaine though, there's been focus on three other compounds that are generating some of the most significant psychiatric research we've seen in decades.

Psilocybin, LSD and MDMA. These are not fringe compounds anymore. They're now being evaluated in the same FDA framework used for traditional medicines like antidepressants, anti-psychotics, medications for addiction and so much more.

Today, We're going to review, it's going be a little complicated, but we're gonna review exactly where the science stands now. In 2026, what the clinical trial data actually shows, What phase two and phase three trials mean, and why these findings matter to anyone with or anyone treating depression, trauma, PTSD, anxiety, substance use disorders.

I'm Dr. Arwen Pedesta. For those new to this channel, I am a functional and integrative psychiatrist, triple board certified in psychiatry, addiction medicine, and forensic psychiaty.

My big focus is helping people understand and navigate the intersection of neuroscience, of addiction, trauma, mental health in general. You know, one of the biggest misconceptions that I hear is that psychedelic medicine is either a miracle cure or just a dangerous fad.

And the reality is it's neither.

Psilocybin Phase 3 Results for Treatment-Resistant Depression

The question is not whether these compounds produce effects. We know very well they do. we've known that for decades. the question, is whether they can repeatedly demonstrate safety and repeatable efficacy in rigorous randomized controlled trials.

That's the standard the FDA cares about, and that's what I care about as a prescriber. And in 2026, we're actually starting to get those answers. I keep saying it's a really exciting time to be in my field.

Exciting for me, exciting for patients in front of me. So let's start with the compound that is closest to potentially entering mainstream psychiatry.

That is psilocybin. It is the most advanced classic psychedelic and psychiatric development having completed two phase three clinical trials. A company called Compass Pathways recently announced positive results from its second phase 3 trial evaluating its compound This doesn't matter, but the compound is called COMP-360 for treatment-resistant depression.

Okay, treatment resistant depression, remember that and we're going to come back to that. So this announcement

about these two successful phase three trials is really important because The FDA generally expects at least two successful Phase 3 clinical trials before they consider approval.

Let's back up and start with Phase 1, the first step in pharmaceutical investigation showing whether a drug appears safe and identifying the side effects it might have.

All right, in phase two is next. In phase 2, we learn whether it works for a particular disease or condition and what dose might appear effective. And then we get to phase 3. They're longer and that asks whether efficacy and safety can be replicated in very large patient populations.

Phase 3 is the final major hurdle before FDA review. Well, psilocybin has now cleared that hurdle twice. In two trials, patients receiving the synthetic psillocyban through this one company showed a statistically significant improvement in depressive symptoms compared to placebo.

Now, the improvement in depression rating scores were three or four point differences. Critics kind of think that might sound small. But remember, these were real patients with real treatment resistant depression.

These are patients who have often failed multiple, multiple antidepressants, complicated medicine regimens, psychotherapeutic treatment failures, and sometimes neuromodulation interventions as well.

So any reproducible improvement, in that population is meaningful. And that's meaningful for data, sure, but really it's meaning for the individual. But what I find most remarkable about this whole thing is not the magnitude of change.

It's actually the speed. So check this out. Improvement was measurable the day after treatment one day. Think about that. Most antidepressants require four to eight weeks before we even begin assessing meaningful response.

Almost two months, and here we're talking about changes observed within 24 hours. And listen, by week six, a good number of patients achieved clinical meaningful improvement.

For those that did respond, benefits frequently persisted 26 weeks after only one or two doses. The quickness, the durability, that's almost unheard of in psychopharmacology.

Let's reconnect this to addiction. A common pattern clinically in addiction is a patient whose substance use is just intertwined with chronic depression, with hopelessness, emotional pain, and trauma.

The substance becomes an attempt at self-regulation and self medication. And if depression were to improve rapidly and meaningfully, then relapse risk would improve as well.

Also, there is research exploring psilocybin and alcohol use disorders and other addictions, not yet as far along as the treatment-resistant depression studies.

But even before we have addiction-specific indications available, reducing severe depression will indirectly reduce one of the major drivers of substance use and substance relapse.

Well, effect is great, but at what cost? Safety is also key, right? That's part of that assessment. Good news about this too, across more than 1,000 participants, the most common adverse effects resolved within 24 hours.

Safety, efficacy, onset, adherability, durability.

LSD Research for Anxiety and Neuroplasticity

This is why so many psychiatrists and people in the field are excited about psilocybin, likely to be the first classic psychedelic approved through modern FDA pathways.

And if, well, when approved, it will represent one of the most significant paradigm shifts in psychiatric treatments in decades, in my career for sure.

We're going to move over and talk about another exciting compound. Actually, it's LSD. MindMed, which is now under the name Definium, is a company studying a compound called MM120.

That name doesn't matter, but it is the pharmaceutical formulation of LST. And they recently reported positive phase three results in generalized anxiety, Which obviously is frequent driver of substance relapse too.

This is a major milestone. Phase 3 success means the FDA now has a large-scale efficacy and safety data to evaluate. The most amazing finding in this one, guess what?

A single administration produced clinically meaningful reductions in anxiety symptoms. Not daily treatment, not weekly treatment. One. Uno. Administration.

And improvements remained measurable for approximately 12 weeks. Blowing my mind, right? Hopefully it's blowing your mind. So let's think about how different that is from what we use with our conventional treatment.

I use SSRIs all the time. They can be extraordinarily helpful, but they require daily taking, daily adherence, often taking weeks to even start working and frequently with side effects or even losing effect over time, and here we have evidence suggesting a single administration of LSD can produce months of benefit for anxiety.

Wow, researchers find that least part of this effect involves modulation of what's called the default mode network. This is a huge topic and another video will do for sure, but in broad strokes, the Default Mode Network is associated with kind of self-referential thinking.

with rumination, with repetitive negative thoughts and that rigid cognitive pattern we commonly see so frequently in depression, in PTSD and in addiction.

And when patients describe feeling trapped in that same emotional loop, that's exactly the circuitry these researchers are targeting. Not only that, but LSD also appears to promote neuroplasticity.

What's that? Well, simply it may temporarily increase the brain's capacity to form new connections and new patterns. I call brain stuff, all of the brain staff, the neuroplasticity, new connections, and new patterns.

It definitely matters for addiction because addiction is often the result of deeply ingrained neural pathways. All right, think about it. A treatment that increases psychological flexibility may help patients develop alternatives to those entrenched reward pathways and behaviors that they know through their substance use disorder, through depression, et cetera.

So historically, LSD has shown intriguing findings in alcohol use disorder, actually. Several studies dating back way long ago, decades and decades ago suggest reductions in problematic drinking following psychedelic assisted interventions.

Modern research is revisiting those observations with contemporary methodologies. Although PTSD-specific data remain earlier in the development than the anxiety studies, researchers are increasingly interested in LSD's potential role in trauma-related disorders because of its effects on emotional processing, on fear extinction, cognitive flexibility.

Doesn't that sound very hopeful? Again, these hypotheses are still being tested, but the rationale is very compelling, because if trauma locks patients into survival mode, treatments that help loosen those rigid patterns may have profound implications, which brings us to the psychedelic most directly linked to trauma itself, and that's MDMA.

Right, current psilocybin studies are looking at depression, LSD studies looking anxiety.

MDMA Studies for PTSD and Social Anxiety

Well, MDMA studies that are in the works right now are look at PTSD. That makes it so relevant to addiction medicine because trauma is often the hidden engine driving substance use.

For years, Mdma assisted therapy has demonstrated some of the largest effect sizes ever observed in psychiatric research for PTSD, Many clinicians expected FDA approval after a certain number of studies done around 2024. Well, guess what?

That didn't happen. Nope. The FDA declined approval and requested additional evidence. Some interpreted that as a failure. Not me. You know, science is almost never a straight line because what happened next is actually more important.

Researchers continued to study the molecule. New formulations entered development. new study styles were approached. New indications were explored. One recent phase two study evaluated a propriety formulation of MDMA for social anxiety disorder, and the results were so encouraging.

So patients receiving active treatment experienced a greater reduction on a particular social-anxiety scale versus the placebo arm. Clinically, nearly 50% of the treatment arm responded, those taking the MDMA, versus 15% percent of those that got placebo.

And the number needed to treat was approximately three, which is quite impressive for clinicians and for patients. Even more notable, these results occurred only after two administrations.

Two, not chronic daily medicines, no years of treatment, two sessions. All right, so let's get back to talking about PTSD. MDMA remains one of the most extensively studied trauma-focused interventions in psychiatric history.

The reason is understandable. Unlike classic psychedelics like LSD and psilocybin, MDM appears to decrease fear response while preserving emotional engagement.

Patients often describe being able to revisit traumatic memories without becoming overwhelmed by them. And that might help explain why MDMA has consistently demonstrated strong effects in trauma-focused psychotherapy settings.

For addiction specialists like myself, this matters enormously. Many patients don't relapse because they forgot their recovery skills. They relapsed because of unresolved trauma, which continues to generate distress.

I see it time and time again. If trauma remains untreated, recovery often remains fragile at best. While MDMA's future depends on additional confirmatory studies, of course, but the molecule is far from dead.

In many ways, we're watching the next chapter of its development rather than the end. All right, let's go back to the big picture of psychedelics at the moment.

psilocybin. It's shown to positive phase three trials for treatment resistant depression. LSD has generated positive Phase three data and anxiety disorders and holds FDA breakthrough therapy designation.

That's cool. MDMA continues advancing through new clinical studies focused on trauma and on anxiety-related conditions. And what we're watching, what were witnessing is the transition from an anecdote to scientific evidence, randomized controlled trials, from counterculture and fringe to clinical science.

I do want to emphasize something crucial. These compounds are not replacements for current evidence-based care. If someone has opioid use disorder today, medications like buprenorphine and methadone and naltrexone saves lives.

Naloxone, saves, lives if someone, has an alcohol use, disorder safe stopping and then medical stabilization.

Big Picture: Psychedelics in Modern Psychiatry

and then maintenance medications such as naltrexone and acamprosate and more remain essential tools. If someone has PTSD, trauma-informed therapy and other types of therapy, medication management, communication remains foundational and it will continue to be so.

Psychedelics really eventually become powerful additions to our current toolbox. and soon it seems, but they're certainly not a replacement or a reason to delay treatment today.

And they are not reason stop using interventions that already work. The most exciting part of the story isn't the compounds themselves, it's what they represent.

For decades, many patients with severe depression, with PTSD, anxiety, and substance use disorder, they just cycle through treatment after treatment without meaningful relief.

And for the first time in a long time, we're seeing entirely new therapeutic mechanisms emerge, and some will succeed. You know, some are bound to fail and that's how science works.

That's what we're doing here. But the overall direction is very encouraging, very positive for me and for my patients. We're entering the new era of psychiatry, one that focuses not only on symptom suppression, but on facilitating meaningful psychological and neurological change.

Neuroadaptation, neuroplasticity, wellness, that is what I want. And for patients whose trauma, whose anxiety, who's depression continue to complicate addiction, that possibility is definitely worth paying attention to.

If you enjoyed this update, be sure to watch my previous video explaining why trauma feels addiction and why treating trauma is often the key to sustainable recovery.

Thank you for staying curious. Let's keep building better outcomes together.