Introduction to Medication Efficacy and Real-World Data

And the other thing I noticed coming back was the the efficacy of medications. This was so much less, we were so excited in the early 1890s. I think when accessorized came out and we were talking about, wow, the new wonder drug.

And now over the course of time, we're seeing that as a surprise or and all the hype is not whether it was meant to to be. And so we're talking about real world data now and we're not seeing that remission.

And I'd like a little bit for the audience to kind of understand some of the, the, the research behind this. The Star Detroit trial is, is something talked about in mental space, right.

That, you know, it's a long, multicenter, national study conducted over some several years looking at the likelihood of benefit of treatment when you're talking about first line treatment for, depression.

Two Curious MDs and the Power of Curiosity

Welcome to Doctor Talks, the podcast where every episode leads to a healthier you. Join us as we navigate the world of optimal health, uncovering groundbreaking strategies to conquer chronic disease.

In each episode, we'll bring you the latest insights from leading health experts, medical innovators, and wellness warriors. If you're seeking to transform your health journey, or if you're looking for answers to burning questions, you come to the right place.

Get ready to unlock the secrets of lifelong health and vitality. This is Doctor Talks real talk from real doctors only issues that matter to you most.

Good evening, good day, good morning. And this is Doctor Ahmad from two curious MDS where two curious doctors talk about medicine, science, psychedelics, ketamine, and of course, integrative medicine.

And finally narrative medicine. So I'm Doctor Ali and month and Doctor Soraya Rahman, and we are two curious MDS. And so I guess the question is why? One has to be curious.

Why is it important to be curious? Because, yeah. What do you think about curiosity? Well, I think we we're both very curious people. And and that probably goes back to, our links to childhood.

Where we were both very curious individuals and children, always asking the question why? And I think it leads to our perspectives as pediatricians, where we're curious about, childhood and well-being and what it takes to, you know, grow and develop, in a healthy way.

And so I think that curiosity has led us to all these different aspects of medicine and healing, has made it very personal, brought it down to storytelling, and now to this podcast where we get to have the room to explore all these different topics and, really share our expertise with our audience, hoping that there are other curious MDS as well.

When I think of the title two curious, it is a play on words, right? There's two of us, and we're two curious. We've been told in our lives, I'm sure each of us that.

Don't be too curious. But here we are going. No, actually, let's be curious. Let's be just just, Be to that edge of discovery. Because as you and I are both learning, there's a lot to see and and explore and a lot that we're finding out about, just all the how to be healthy in this world, that there's a lot to share.

Yeah. For me, curiosity feels fun. I feel like there's so much to learn and to be curious with it. And you can be. You can enjoy kind of that learning.

For me, curiosity was about why not? Why, but how like, how does it happen? And how does one, you know, get better at or become curious about why something doesn't work?

I think, you know, questioning the status quo, especially these days. I think we have to be able to question the status quo. Like, let's get curious with that.

Let's not ignore it or belittle it. Let's just get curious. Yeah. And it keeps that mind open. And, and again, even in medicine we talk about especially with ketamine treatment is this is the curious with with oneself as well.

I like that. I like that. And so as we're starting out, today's, exploration of just how all of this fits in. Let's start with just the fact that we're both, moms, and we're both pediatricians, and, maybe I've always been, asked the question.

People are curious about this going, oh, how do your kids, feel about this, new kind of, medicine that the, that you're, practicing called psychedelic medicine.

And so I'll, I'll start out by asking you that question. What's the reaction, within your, your kids. For me, it's I have three kids and three different types of questions.

One asks me, mom, that's neat. You never would have done that before. You know, that's my oldest. Because she knows me and she knows how I was.

Kids, Identity, and the Shift Into Psychedelic Medicine

Meaning I was a really straight arrow and didn't believe in any kind of substances or psychedelics or something. I would classify as a psycho. Psycho psychotic or psychotropic medicine that causes more harm. And, and so not understanding the science at that time.

My second one would be like, hey, that's pretty cool. You know, he would he would not attend and say, yeah, mom is pretty cool. You got this. He's my he's my intellectual.

He's the one who kind of agrees and follows and monitors. And he also is quite the a curious kid as well. But he never says a he is. He's always about me kind of discovering and under the into the, under the zone and then the radar zone.

My third child who is, you know, 12 years, you know, young, younger for my oldest. So he's young lives and he's this big age gap. He would be like, rock on, mom, you know, and and what I would see is each one has, understood that I.

And they know me. You know, my daughter's kind of grown up with me in through my residency. And so they they see this and they know that I'm, I'm not one to kind of follow the rules sometimes.

And we kind of do have to question and they, they know that. So interest that some things change my relationship with my kids as well. Kind of being in the mental health field, knowing that, you know, it's as if you raise your raise your own children and as you raise other.

And I'm so involved in the families of children that you raise essentially in your practice, you're really having it goes one of them right now. So they, they, they see you, they've grown up with you as well in your training in professional space.

Yeah. That's so cool. It I love that. Even in the journey, of all three kids having different perspectives, it's a, kind of a, a little window into your own transformation as you have remained curious and open, and willing to change your mind.

And I think we both share that, that, in our own training, this is not a body of knowledge that was front and center as pediatricians, we knew a certain, few things about ketamine, for example.

And that's where it stood. And I think that's true for a lot of the medical profession now. And I think that's what's behind our, impulse to put out this podcast is to reach this audience that really is curious about it and is reading about it and seeing it on the media.

However, you know, it's different when, you can talk peer to peer, you know, to, to provide some of that, I think, evidence based perspectives that are also informed by our clinical practice and then just our understanding as pediatricians of like what we're dealing with.

So trying to solve the problem, talk about that which you just said clinical practice and, evidence based. And so what is the evidence. And I kind of feel when we coming back from being working overseas and after ten years of being away United States not directly practicing the what I call, you know, the, the trenches of medicine, coming back to those trenches, it was a very different trench.

It was a trench that was filled with patients waiting for beds. It was a trench filled with people who are disgruntled. And not trusting. And it was it was filled with patients, you know, of on some substance of some kind or another.

Complicated by all of the social disparities that surround surrounded any condition. And, and so, you know, methamphetamine. I came into the Central Valley of California and, after working overseas where drugs were, you know, there was no violence, there was no drugs.

And the practice of medicine was very different. The adolescent, practice was very, very different. But, to coming back into a new paradigm of mental health.

And the crisis really was a crisis. I kind of landed and I felt like I was in a foreign country.

Mental Health Crisis and the Wounded Healer

Yeah, it does feel like a war zone. I think both you and I have worked in the hospital, in the trenches, as you said, at the frontlines where, we see parents and, kids, just waiting for days, for placement, for a mental health emergency.

And that's just even gotten worse. So I think this leads us very nicely into the presentation. You have, then on on ketamine. So maybe we can go there and, start to unpack, the psychedelic medicine, realm of healing that we find ourselves at the intersection, take it away, and I can give that.

Yeah. Yeah. So this is about ketamine assisted psychotherapy. It doesn't just have to be about ketamine, but it can be about psychedelic assisted therapies, integrative medicine, your mental illness.

This is the two curious MDS. And we're opening up the realm of psychedelic medicine. Right. And what that realm of healing, is going to be like, in the practice of medicine as well, conventional and integrative.

So, I'm Doctor Alia Ahmad Chao Charmaine's Healing Center. A m Y and dds.com, and of course, Doctor Soraya Rahman and Southern Cal Paula medicine dot Paula Pamela and medicaid.com.

Look us up now plenty of resources on our websites about this kind of approach and treatment and philosophy. So let's talk it and what's your question number?

Oh my gosh. Why is mental health in such a crisis right now? You talked about this place. You found yourself, when you came back into the country. So you you recognized that.

Oh, this is not where we were before. And we are in a different place right now. So what to you is the components of that crisis? Well, in my opinion, I think it was it has to do multiple things.

One is, you know, the whole system conditions became much more recalcitrant. We talking about culpability attached to mental health conditions. We're talking about eating disorders attacked with generalized anxiety, with trauma.

You know, we had. And then that also again, you know, gut issues, you know, inflammation, recurrent admissions. We're talking about comorbidities like obesity and the again associated increase with, you know, and depression, anxiety and the like.

I think Covid was a big factor in really uplifting the the the, you know, the the surface of what was underneath the volcano. It just really erupted really through that.

And I think it was just became very apparent from household to household, right within the household itself. I think it's also important to talk about us as healers, in the health space, witnessing at the 26 some years, observing kind of the whole shifting of health care and how we were losing that touch, that human touch and the disconnection in practice, it's often felt because of, you know, we're really governed by the system and the insurance processes and the timing and, you know, 15 minute appointments in 20.

And then the effect that that we when we experience even our training, the, you know, the, you know, that whole, development of the physician who comes in very wide eyed and bushy tailed and leaves very, beaten down and and mistrusting because things are not as clear and clean, we're all wounded leaders, yeah, yeah. Thank you for bringing that.

I think that's what we share for sure, in our journey towards this idea of how to understand that, and leading us to narrative medicine. Right, and how we did that healing for ourselves and even calling, you know, labeling it the wounded healer as something that's, not accepted or, is kind of, stigmatized still and recognizing that when our patients suffer, we suffer and we're both patients and, healers stuck in a system in which, you know, the suffering of, especially the mental health conditions, but the suffering of both parties is, occurring and, and ongoing and Covid, you're right.

Just, you know, drove that into the forefront for the both of us, I think. And that's when we think, just a year apart, decided that we were going to enter into this, into this practice, you know, unbeknownst to each other.

We only met a couple of years later. But, you want to explain a little bit about narrative medicine? Because I think for the odd, that term comes up. And often the question is, well, I've heard of that, but what is this really?

Narrative medicine? Yeah, it's it's an interest we both share. It's, you went to Columbia to do the Masters in, narrative medicine with Rita Sharon, who coined the term, and she was looking at, just this picture, right?

This picture that you have on the side of the healer and the patients sitting next to each other. And what occurs in that experience? And treating it as an experience and as in recognizing the metaphors.

Right. Recognizing, the languaging, recognizing the context that's occurring around the patient and the healer and how that is leading to well-being or not.

And negative medicine is a very interesting set of skills to, to recognize and then respond to what's going on. And so even in, in situations where there may not be a right answer medically that, you know, especially end of life situations or trauma situations where we're dealing with very difficult things, we're asked in narrative medicine to go towards this understanding of, okay, well, we can still make some meaning out of it.

We can still recognize it, we can still hold it and develop skills with which to hold difficult things that may not end with a prescription being written or procedure being done, and yet are still meaningful.

Right.

Narrative Medicine and the Context of Care

And so I think narrative medicine, and the Tldr that I talk about is like back in the day when doctors and patients got a lot of contact with each other and the system wasn't running the show, the relationship took front and center, and now we are kind of having to back door in the skills of relationship back into the medicine and narrative.

Medicine is one of the ways that we grow that aspect. Yeah, you're absolutely right. I had to, teach narrative medicine, to third and fourth years at UCSF when I was, training.

I mean, working there, it was profound to me that, you know, and it became apparent then the understanding of what what is, you know, the definition of compassion and empathy.

And how do you hold space with a patient or witness and, that condition as it manifests in the body and, and manifest in the system, the impact that that can have, not just on the person, but on the whole surrounding of that patient.

I call it the context of care. And how does how do you hold space for the how do you even understand the medical condition in the story of the illness has to kind of be basically understood as well.

And we tend to be very check listed in our, you know, our history and present illness we really become. Yeah. Is it this or is it that. But really in engaging with the condition in element of story and how that can be better understood and, and better, be treated because sometimes it's not about the headache, it's what, you know, what led up to the headache.

That's more important, right? Yeah. Yeah. I mean, like, you mentioned earlier also, in an earlier conversation, the idea of asthma. Right. I used to always teach that.

No to asthma asthmatic are the same because they both they live in completely different neighborhoods. And have completely different genetics and have completely different education about it or or even access to, you know, good food, clean air, you know, lack of pollution and all of that.

And there's not a lot of place in our discussions in, in medicine about, about how these factors can, can impact, and why it's important to recognize them and what impact that has on the healing process.

Yeah. And they don't have to be complicated. These are methodologies that are, you know, learnable, teachable and implementable because they're simple questions that you would just curious questions you can come up with in terms of, you know, for example, pain, what is that pain?

Where is that pain body which describes it, different types of pain. So draw me a picture of, of of pain in your body and, you know, color it and be creative with what that represents as you feel it.

And then I know about pain. I mean, I had this one patient and had to really have her draw out her feeling body, mapping her mind body to describe her reflux pain and which is very different.

Ulcerative colitis than her pain. Then, pain that she had from an injury or pain that she had from, you know, a headache or migraine that results from, you know, this whole course of action in.

But it, it, it it is, you know, because when we talk about pain scale, we say, well, what is her pain like today? And it's, you know, ten out of ten, really understand where that pain lives.

I think, our audience may, recognize and, some people in the audience, maybe in the health care field and recognize how one dimensional that pain scale is, right?

It erases the meaning of the pain. It erases the origin, the story around it, the resiliency, factor, and really boils it down to, a numerical scale just for the purposes of, giving medication or not.

And that's just so reductive. Right. So we're we're here kind of being anti reductive in some ways and expansive,

and the other thing I noticed coming back was the, the efficacy of medications.

This was so much less and we were so excited in the early 1890s, I think, when as this race came out and we were talking about, well, the new wonder drug, and now over the course of time, we're seeing that as a surprise or, and all the hype is not whether it was meant to to be in.

So we're talking about real world data now and we're not seeing that remission. And I'd like a little bit for the audience to kind of understand some of the, the research behind this.

The Star Detroit trial is, is something talked about in mental health space. Right. That, you know, it's a long, multicenter, national study conducted over some several years looking at the likelihood of benefit of treatment when you're talking about first line treatment for, depression, in the efficacy is only about 27%, meaning 27% of patients are going to go into remission in a first line treatment.

Okay, maybe that's a good number. But, you know, when you move on from first line to second line to fourth line, your efficacy diminishes, down to about 7% by the time you hit fourth line treatment.

So that means 93% of people are not in any form of remission, not even close. And that the likelihood of them discontinuing their treatment over the first line, second line increases in general.

Over. Well, right. But, about 41% of patients by the time they hit the fourth line treatment have will will stop the medication either due to a side effect or this story that, you know, I'm treatment resistant and nothing is working on me.

Yeah. What an what a stark, kind of, story here that as the as we get further and further away from, you know, further and further into the diagnosis of depression, the longer that depression lasts, then it doesn't get treated.

Not only are we developing, quote unquote treatment resistant, but what does treatment resistant mean when you're talking to the patient? It may mean despair.

It may mean they've given up hope. It may mean that they this is who they are and they can't recognize who they are outside of this condition because it's become so difficult to treat.

And there might be side effects. And there's the the labeling and all of that. And, you know, I think, there's this interesting idea that you have to be, thick enough to get the treatment.

Yeah. And you have to continue to be sick enough to get the treatment. However, what we know what was once a condition, depression that used to, traditionally be treated.

And the expectation was that this was episodic has now become a chronic condition. And I think, we recognize that the, the function of the pharmaceutical industry in promoting, the chronicity of this condition and throwing more and more of the same, but different medications, you know, at the problem, has left a big gap in, in the possibilities of treatment.

And I think that's the part that we are really, serving here as we step into this, new world of, rapid anti depression treatments through psychedelics and other medications.

And I'd like to pause here to it and reflect on the story of illness. Right. The context of care.

Limits of SSRIs and Treatment Resistance

We talk about, you know, this treatment resistant and even question and be curious about what is treatment resistant really mean and what is this and how is this represented in the story of that illness?

What do you think? Oh my gosh. So we know that the longer we wait to treat, depression or the longer it takes to

bring it under remission, the depression becomes more and more treatment resistant, to the extent that trials have now, you know, before treatment resistance used to be, defined with much more strict rules of, oh, you've got to have failed three, medications to be, to qualify as treatment resistant, so you can qualify for a treatment for treatments for treatment resistance.

Right. And the recognition that, the, one of the main factors of why something becomes treatment resistant is when depression has just hung around for long enough and has kind of become more and more, stabilized and isn't responding.

Is this right? Who is the resistant? Right. Who is resistant, you know, to the word patient who's resistant to the medication or is a medication resistant to the patient?

Right. And we're talking about, you know, so this is where we this is where you have to think outside the box. Yeah. And this is also a point of narrative justice.

Right. This is where we can really point out that who is resistant and how are we languaging around resistance and who are we blaming. Yeah. You know, who is being blamed for this quote unquote failure?

Has been now nicely packaged into this label of treatment resistance. But we're not going to say, oh, we have ineffective treatments, okay. But even the person in your treatment resistant, like, I can't do anything for you, right?

It becomes it becomes a patient's problem. Not only the pain feels like they're broken, but they're, we're actually even establishing that and highlighting that you're just treatment resistant and there's nothing else for you.

So it's, and that's that really is in the context of care. And I think the care paradigm, right, between the doctor and the provider or the patient in the, in the, and yeah, it leads to a lot of futility, a lot of, you know, broken relationship, a lot of, as we see health care, trauma, a lot of loss of hope.

Absolutely. And in this aspect that these medications are FDA approved and, you know, and the efficacy, you know, I think the this book called The Emperor's New Drug, talks a lot about, the clinical trials, one step in the Freedom of Information Act, and able to really open up the non published data on SSRI businesses in our eyes with placebo, randomized, placebo controlled studies.

And this is this opening up not just looking at what is published but not published. And now looking at your data on efficacy. No better no better than placebo.

And you know, and no better than another crazy, crazy cycle as well. So which goes to this idea that SSRI eyes have really flooded the market like the, the so much, energy has been placed in marketing the SSRI and cherry picking the data.

Now, only now, 10 to 15 years later where we see the real world, kind of, impacts of how these medications work and also have grown our model of what depression really is.

This now seems like, you know, it took up a lot of the room, a lot of the investment, in the pharmaceuticals, when it came to mental health treatments and and that that may soon need to shift.

And we're in the midst of that shift, right. And I invite our audience to really Google these things. You know, these these are things that we don't necessarily talk about in conventional medicine.

Yeah. The book that you're mentioning is called The Emperor's New Drugs by Irving Kirsch. So highly recommend that, you read that if you're interested in this topic.

I want to talk a little bit about that. You know, a lot of times our focus is medicine, and we tend to get, like, drawn into just a medicine. But I'd really like to talk a little bit more about the certain setting and that relationship that one has in behavioral health with the doctor, with the with a therapist or a behavioral health specialist.

And again, going back to the context of care, right to depression. What is the what is that set in setting like for that patient in the in the context of that condition that they live in and the certain setting of that context of care where a patient seeks, you know, support or even, you know, treatment.

Yeah. And I think a lot of the randomized controlled trials miss this information. Right. They're not looking at this. There's not a lot of awareness of the relationship between the therapist and the client, for example, and how, that can lead to effective effectiveness in addition to medication and how by just focusing on the medication, we've kind of left those behind.

And so I think what you have here is, the psychotherapeutic model for psychedelics. That and not an ordinary state of consciousness that really helps us to realign that relationship.

Of, okay, what is really happening here? Yes, there's medicine, but there's also the relationship. There's also that context of care that you talked about.

And the story that's being and that story of that condition and really allowing for, an expression of that story, right, of depression for the patient who, and then that therapeutic alliance, that is the first step to any kind of treatment approach.

We tend to, as doctors, jump to treatment. But without really fully understanding first that set setting and then second, that alliance that you often need with the with the patient, it isn't about what you, you know, subscribe to or prescribe to.

It's really about having them invite into that conversation of treatment for themselves. What they seek would be, you know, something that would be work for them.

And in any type of treatment, you know, there has to be some preparation, even in, even in conventional medicine, when we talk about, you know, really building in, you know, as we do in pediatrics, you know, really see the family in the child grow and anticipate, you know, and so you're really prepping them for their treatment for that visit, but also for their next upcoming type of care.

I think that might be a reason why more and more pediatricians go into this, because we actually think systemically and, in, in this kind of mindset of relationship and trust, and that container of safety that needs to be held.

So, yeah. Well all right. What do you think about ketamine. Oh my gosh I mean as a treatment. So here I was you know in the trauma center doing moderate sedation with ketamine and other medications for painful procedures.

And I had no idea that ketamine is a at a lower dose as a psychedelic only. More recently did I become aware of the, research that's been around since the 90s.

Only recently did I kind of understand that it's even, you know, safe to use in the office setting and all of that information.

Ketamine: Safety, Uses, and Mechanism of Action

So, I'm really excited to share this part of the, conversation because I think this is something that, a perspective that isn't, widely known in, the medical system.

However, it's becoming more and more known. And so I think, there's a lot of curiosity about this part. So, you know, getting being a dissociative anesthetic, right?

You think about it being dissociative anesthetic. That also causes hallucinations. So, yes, even in my practice, little did I know that while you're suturing somebody and they're having, you know, talking to you in the ER, that they're actually having a very therapeutic discussion with you and you're often sitting there going, well, you know, you're right.

And then you have this conversation. It's a very relaxed, semi relaxed setting because you have this certain bond that you have. And when you're taking care of them and they being, you're in, they're dissociated and they're talking about sometimes seeing balloons and, you know, flying elephants is what I remember one patient told me.

So yeah, it is a dissociative anesthetic. It's used commonly in emergency rooms and especially in children for short procedures. And yes, if there's some anesthetic dosing, it is in a psychedelic, schedule three, of course, controlled substance.

It's regulated heavily by the DEA for good reason. And a commonly used anesthetic in, in in battlefield. This is really where kind of it came up, as a rapid and acting safe anesthetic that didn't require airway support.

Right. In Vietnam, when you go ahead. Exactly, exactly. We're hearing so much about ketamine in the news, but we don't really hear about how safe it is.

In in trained hands. And the safety profile of it is what made it safe to use in children. And also, yeah, to administer it as a quote unquote buddy drug.

Right. That's what it was called. You break a leg out on the battlefield, you get a shot of ketamine, and you'll be able to still breathe on your own and still be transported to the next level of care.

And that was very useful. Oh yeah. So the evidence on it's treatment for multiple conditions right. In mental health. Seen in severe and chronic postpartum depression suicidal ideation, bipolar depression, post-traumatic stress OCD and some substance use conditions as well.

I bet you're wondering now how this how it works. What we did was work in the brain. What is it actually doing? What do you think? What do I think? Oh, my gosh, it's crossing the blood brain barrier.

You know, I think, when we, think about what's the perfect medication to use on somebody who is in a mental health state, right? Right. Now, what we have are the antipsychotics.

If they're having a crisis, we give them a medication that just sedate them. And and that's it. It just kind of puts a blanket on the fire and calms everything down.

And, and then the person goes to sleep, and then they emerge, and they still have the condition here. We're actually causing an excitatory glutamate surge.

Your blood pressure is increasing, your heart rate's increasing. There's, this upregulation of these receptors and more synaptic proteins. There's actually brain derived naturopathy like factor Bdnf being released, which is the factor we know that leads to greater neuronal plasticity, neuroplasticity, meaning more new connections being formed.

And then we know that the metabolite hydroxy nor ketamine actually has an antidepressant effect, a rapid antidepressant effect. And so this is a whole different paradigm.

You can give a medication to somebody and within one dose they might cease having the suicidal ideations that they might have been having just before you gave them medication.

They might, you know, have, remission of their depression symptoms. They might just have relief, of their, pain, that they're carrying. Right. And all of this is happening, and they might have an increased ability to grow new, pathways in their brain.

So what we're seeing in depression, for example, is this idea that the pathways in the brain kind of get overdeveloped in one direction. The negative thought patterns just really become very, that.

Right. And here we're seeing that, oh, no, you can actually build different thought patterns. You can actually learn.

And so I think this is the fascinating part for me, and I think for you, is that it's bringing together learning is bringing together the idea that the brain has the ability to shift on a systems level.

If we can harness the power of this medication and also combine it with psychotherapy and relational healing, and that we get the boost of the antidepressant effect, which is really cool because then they're able to help themselves more, you know, and it's immediate, it's rapid.

It's happening on, hours to days basis. So this is this amazing activation. Say this ketamine is an NMDA antagonist, right? Blocks glutamate. This and this glutamate release, causes this gap with this inhibition.

So whatever is causing holding the brakes, the frontal cortex, you know, the executive functioning, whatever's holding that activity is quiet and right.

And not only does it work at that receptor, the upregulation of the Ampa receptors, which is now we're working at production level, where we're able to increase synaptic neurotransmitter production for other neurotransmitters.

And of course, I have to talk. Oh, look at this balloon. I have to talk about the activation. That was mind blown, right? Was one of right. So. If the first time I have heard of BD and if I was in bed, I was at Baylor.

I was doing research on, the, actually was the cabinet system, but in the, in the hippocampus, and I was my job was to kind of help dissect out the hippocampus in rats and, and take the hippocampus and create those cells, those neurons on a plate and grow them, and basically incubate them so that we could test those, those neurons with acetylcholine.

Nicotinic was that receptor or neurotransmitter system. And I when I used to play them, there was a little bottle of BNF and we had we actually actually sprinkle it onto the, the.

So here you are doing that now in the clinical using Bdnf, you know, and the activation mTOR. And of course as you talked about this, the secondary metabolites of ketamine which, which is a hydroxy ketamine which has extended 7 to 14 days of antidepressant effect depending on how it's metabolized in that body.

Right. Yeah. So, plasticity, I, I love this, because I think what we were often told in is that the number of neurons you get is the number of neurons you get, and then the rest, you know, we're only losing.

But this aspect of regeneration, chronic stress is also very, very, inflammatory and has and can be seen on EEG reading. So you can actually see me, you know, the, the inflammatory waveforms that are also there.

And on a, on a stress brain, and the, the atrophy effect, you know, the loss of synaptic, you know, response, the retraction of neurons and ketamine and having this and other psychedelics also having this ability to really treat and support this chronic stress brain, and re again, regenerate dendritic budding.

This is a picture electron micrograph of a the rat brain before and after ketamine. And this is within hours after, of course, where you have a faster rate of regeneration, where you can actually see, you know, before the ketamine, and after ketamine, seeing, what the, you know, the that no amount of dendritic budding that's seen post infusion.

Of course we don't have any human studies here for obvious reasons. Yeah, but here we are. You know, that's the mind blowing slide right there is we can actually see evidence.

Now in electron micrograph of exactly what we're talking about. Which is that I always describe this aspect to my patients as well. You know, you imagine a plant, right?

The, the brain's, kind of, branches and root system and everything. It follows the kind of, ways that a plant grows. And imagine a plant that you have in your home that just doesn't have enough branches.

Right? And sometimes what do we do? We we cut it. We we prune, we trim to increase the number of branches.

And so, and we do that because we know that when there is a plant point of growth that some sort of growth factor, right, when we cut it, some sort of growth factor arrives at that place in the plant and allows it to grow new branches.

And so that's a phenomenon that we can see happening in our real world, everyday world. And that's a similar phenomenon that's happening in the inner world, you know, in our brains, which we can't yet see, but we can see in the rat model, which is just really, fascinating and changes the whole idea of the fact that the, you know, adult brain cannot learn.

Right. Yeah. So I want to pause here because I know there's more questions, and I want our audience to really, you know, take this in. You know, this is a lot of information.

We provided you the references. Look it up, do your research. You know, I've been in this practice for now, over three years. And you two a symposium.

You've been at this for some years now and seeing kind of this transformation. But my question to the audience is. Who is treatment resistant? What is treatment resistant really mean?

And why would this ketamine or psychedelics be an option for a treatment resistant condition? Or should it be an option in general? Right. As a as possibly first line treatment if if we can see the efficacy of this right, you're jumping ahead two moves.

I have Christo right. And I think I want the audience to really, you know, ask themselves. Yeah. So the question is why are we saving this mode of treatment for only treatment resistant, when really if we're looking at the model of depression as a chronic stress on the brain, and not just a certain allergic model, right.

There's treatment resistance in the surge allergic model. But if we think about it in the systems model of depression, where we're talking about the context, the nutrition, the inflammation, the environment, the relationships, and then we're talking about the brain and what's happening in the brain.

And oh, we have a medicine that can actually help with increasing the connections in the brain. And what we see with those increased connections can be self-efficacy, improvement in thought patterns, improvement in relationships, improvement in the energy and motivation to engage in, some of the, habits and behaviors that you want to grow, you know, and so we're seeing that this is a practical tool that becomes very useful whether you're in the first three months of being diagnosed with depression or, you know, 30 years down the line and you've tried everything and you're kind of reaching for ketamine as a last ditch effort.

So I think we're kind of recalibrating. What's the story here of ketamine and depression events? Because we're being told one story, but that we know from, from narrative medicine that the single story is a dangerous story.

Right? You should always go into a single story, right? That is not the whole story. Quoting Amanda A and ago and in her talk, saying that we do a disservice.

Absolutely. Yeah. So again, for the audience, what makes a treatment treatment resistant? You know, what are the top things that make something resistant?

Who is resistant patient or the medication or the options and what else is what else can we do? What else can we do outside of this to really love that if we get out of the yeah, sorry.

If we get out of the mold of thinking of treatment resistant, we are breaking in a in a way the thought patterns that get stopped. Right. When we say some of these treatment resistance, we we stop thinking about it.

We we start thinking of the possibilities of how to blast through. But if we can retool that and understand that it's a

language problem to, as you're describing, who is treatment resistant, right?

Yeah. And recognize that as a language problem and not really a patient problem, then the possibilities could maybe open up again. Yeah. I love that. Thank you. Yeah.

Thanks for joining us on the Two Cures and podcast. We hope today's episode inspired you to ask new questions and explore fresh perspectives. We challenge you to ask us those and ask questions that you're curious about in your medical practice condition, health, and wellness.

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Lister. Comment with a question or curious inquiry that you have and seek to explore or learn with us. Stay curious and we'll see you next time.