

Hypervigilance and sleep issues

Guest: Dr David Brady

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[00:00:09] Alex Howard

Welcome everyone to this interview, where I'm super excited to be talking with Dr David Brady.

David is one of my favorite clinicians. I think he's a real master of bringing together many different pieces of the jigsaw, both from a functional integrative perspective, but also understanding the many great gifts of mainstream medicine as well.

In this interview, we're going to be exploring the relationship between complex fatigue related conditions and sleep. And we're going to go down some fascinating rabbit holes around this, particularly looking at the impact of hypervigilance in these conditions.

To give you a bit of David's background. David Brady has over 30 years of experience as an integrative medicine practitioner and 25 years in health sciences academia. He's a licensed Naturopathic medical physician in Connecticut and Vermont and is board certified in functional medicine and clinical nutrition and a fellow of the American College of Nutrition.

He is the chief medical officer of Diagnostic Solutions Labs and Designs for Health Incorporated. He's in private practice in the Integrative Medicine Group Whole Body Medicine in Fairfield, Connecticut. He is the former long term vice president of the Division of Health Sciences and director of the Human Nutrition Institute at the University of Bridgeport in Connecticut, where he continues to serve as director and professor emeritus of nutrition.

He has appeared on the Plenary speaking panel of some of the largest and most prestigious conferences in the field, including IFM, ACAM, A4M, ACN, IH, and many more.

Dr Brady has published a multitude of peer reviewed scientific papers and textbooks related to functional and naturopathic medicine, clinical nutrition, chronic pain, autoimmunity, and functional gastroenterology. He's also the author of the excellent book *The Fibro Fix*.

So David, great to have you. Welcome back. I always enjoy our conversations together.

Dr David Brady

Thanks, Alex. We've done this just a few times before and it's been a while since I've been over across the pond and saw you in person. We need to make that happen again. But it's a pleasure to be with you, at least remotely.

[00:02:34] Alex Howard

Fantastic. It's always a pleasure, David.

So there's a lot to get into here and I think probably a good starting point would be just to open up a little bit the relationship between these complex fatigue conditions, within that we could be meaning ME, CFS, fibromyalgia and obviously long covid has become a big part of that jigsaw in recent years. And how the relationship between those pieces and sleep as an issue, and often there's a lot of crossover and I know that these are all areas that you've dived a lot into. So maybe let's just start there and then we can go down some rabbit holes together.

Dr David Brady

Yeah, it's a great question and is something that really does need to be discussed in an event like this on sleep problems. Because sleep problems, to me, there are some exceptions to what I'm going to say, but for most of the patients I see with sleep dysfunction, which I'm sure my patient base is sort of biased and self selected toward disorders that have sleep problem as a component of them, but the majority of patients I see have at least some level of sleep dysfunction.

And I don't look at sleep disorders as an individual entity in and of itself. It's usually part of a bigger issue. A lot of the conditions that I've seen a lot through my career, done a lot of my research on, have done a lot of my publishing on, are some of the disorders you just talked about, whether it's global pain and fatigue issues like fibromyalgia, whether it's chronic fatigue syndrome, ME, and now long haul is just inundating us.

Those of us who do integrative and functional medicine, we're seeing just endless numbers of long haul patients, and me in particular, because I've been very involved in the long haul community and effort from the standpoint of running expert panels at conferences and things like that. So a lot of long haul patients seek me out, and my wife is a long haul sufferer. So I've been dealing with it on a personal and a professional basis.

And sleep is a big component of these disorders and, really, I think one of the fundamental issues or linchpins in what perpetuates the chronicity of these disorders. Because everyone needs good quality, and not only good quantity, but good quality of sleep for restoration of all their metabolism, of their central nervous system, of everything, all the cells of their body and all their functionality.

Even people in the best of health need really good sleep and restoration. But people who are dealing with a chronic, complex, multifactorial metabolic derangement going on, whatever that may be, whatever the initial insult or source is, they need quality sleep even more, and they're not getting it because the sleep dysfunction is integral to the problem.

And it's reflective of a lot of things that we can go into, which is this underpinning of hypervigilance and having your central nervous system in these disorders just locked in a sympathetic, dominant fight or flight scenario. And we know some of the reasons why that may happen.

We certainly know some of the mechanisms and altered biochemistry like underlying deep tissue inflammation, glial activation, cytokine aberrations. We don't exactly fully understand why and how it happens. But regardless, it's a big part of these disorders.

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And you have to come up with ways to improve sleep to get these patients well, and you have to deal with the other reasons why they're sick to help get their sleep better. So it's like a bi directional challenge for a clinician and ultimately for the patient or the person suffering from it.

And it's often, as you know and as many people listening will know, it's not as easy as that reflexive this for that recommendation. Take Melatonin. Take GABA. Take chamomile tea. Take Ambien. Take Trazodone. They all can do things, but none of them, just as these isolated interventions, get you home. They don't get you where you need to be.

Alex Howard

And I think almost by definition of a lot of the patients that you see and that we've seen over the years, they've often done those obvious interventions. And by definition of seeking someone like yourself out, they've not had the impact that they would have hoped that they would have had.

You said briefly about hypervigilance. Let's just open that piece up a little bit. So when you mention hypervigilance, what do you mean by that? And what's the relationship between that and these conditions?

Dr David Brady

Yeah, I wish I had all the answers there. It's been hotly researched and studied for quite a while now. But luckily that research and the money, the effort, the amount of people investigating these types of things is growing logarithmically because of long haul covid, because there's so many people now impacted.

It's affecting workforce, economy, and national health on a grand scale to the degree that we did not see with chronic fatigue, MEs, fibromyalgia, chronic lyme, other tick borne illnesses in a chronic state. Those were big impacts and there's a lot of people affected, don't get me wrong, but the number is pale in comparison to long haul covid.

So I'm hopeful that that will actually drive more understanding of it, fundamentally answering the question that you've asked me and get us to a place where we unlock some approaches, some understandings, and some therapeutic tools and interventions.

Whether they're drugs, whether they're lifestyle changes, whether they're nutraceuticals or whatever they may be, I don't care at this point. I don't care what form they take. I just want something effective that's going to be more universally effective for people to try to get them well, where before it was easy to just discount those problems and say, oh, are they real?

Are they not? It's all in someone's head and they're making it up. I'm too busy to deal with this chronic complex condition. I know I can't really get better quickly and easily. I'm just going to shuttle that off to another specialist or get that out of my office.

Well, those days are gone. You can't do it anymore. And the patient population is not going to go away and be silenced like that because this happened at a time where we have all of this social media. We have all these connectivity points that people are talking all across the world that have the same condition.

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And they're crowdsourcing information. They're getting together and they're putting pressure on regulators. On policy makers. And indirectly on researchers and everyone else. In fact, long haul covid, it wasn't named long haul covid by the medical community. It was named long haul covid by the people who have it by getting together and crowdsourcing. And that name got created.

And many people like yourself and many people, compatriots of yours like Gez Medinger and others have just put the word out and did great crowdsourcing. They did the original research on long haul to tell us who has it, what's their gender, what's their demographics, what's their age band, what symptoms do they have, how does it differ from acute covid, which symptoms are getting better, which ones are not?

All that came from the patients themselves by participating in surveys and crowdsourcing and things like that, long ahead of medical research finally getting it together to do some work there. And then, of course, they had to rename it pasc, post acute sequelae of covid. They couldn't go with long haul because they have to have their own fancy new name and acronym for it.

Alex Howard

Although of course, we all still call it long covid or long haul, but there you go.

Dr David Brady

Exactly. But sleep is a big part of it. And they all fundamentally, whether it's long haul covid, chronic fatigue, ME, true classic fibromyalgia, they have this underpinning of hypervigilance. And what is hypervigilance? Just like the name implies, it keeps you as a functioning organism and, even drilling down further, your central nervous system in a state of vigilance.

Meaning you're looking out for the next threat. You're in that posture, metabolically of waiting for the next shoe to drop. The next thing to come hurling at you, the tiger to jump out of the bush. And we know that that's part of our stress response and part of our sympathetic nervous system that largely is outside of our conscious control, that serves us well in short term acute events.

If we see a car coming, we get almost superhuman strength to jump out of the way or to lift it off granny who got run over by the car, or to climb the tree in the primordial forest because the tiger was coming at us. But today we have a lot of stressors that are not here and gone.

They're here and they stay, for whatever reason, whether it's trauma and we've talked many times and we've talked in the past about traumatic experiences growing up when your nervous system is very neuroplastic and learning how to cope with the world and what default stance to be in.

So if you have trauma, particularly abuse, physical abuse, sexual abuse, verbal abuse, those types of things, or even just neglect in early childhood, you can certainly develop a bias toward hypervigilance.

But you can also have more of a fresh trauma. Some people can get into this after a bad traumatic event or a significant surgery. But what people don't realize is you can get into a hypervigilance sympathetic bias by a metabolic or an infectious insult.

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And a lot of what we see, a lot of it is post infectious derived hypervigilance, and the majority of it probably post viral. But I don't want to just keep it too viral, because we see evidence of that in bacterial conditions such as PANS and PANDAS and ticks and things that happen after, let's say, streptococcal infections.

But you see it in the case of lyme and other tick borne illnesses and Spirochetes and other types of infections. But it's probably most known in a post viral sense. And of course, the original models of chronic fatigue syndrome and ME were that they were post viral, that a lot of people developed these things after they've had in their history a significant flu like illness.

And that's why some of the original research was really trying to connect things like epstein-barr virus and things to chronic fatigue. And they never really made that direct connection that is just so proven undeniable, this is the only way people got into it, because there are other ways you can get there.

So it's not a clean, latch down, medical, direct, connect the dot thing, which is what conventional modern medicine loves. And if it violates those principles, they don't know what the heck to do.

So hypervigilance is this place that a lot of people can get to, but they can get to it by various routes. It could be long haul covid after SARS-CoV-2. It could be trauma, it could be bad childhood issues, it could be a lot of different things, which makes it puzzling.

But almost like innate immunity, inflammation is a general response to a whole bunch of potential different traumas or reasons or triggers. Hypervigilance is like that too. And if you get stuck in that hypervigilance locked loop, there's a lot of things that can happen over time.

And just one of them is you can't sleep because your brain is not in a place of rest and restoration. Your brain is in a place of defend yourself. So your body won't let itself go to sleep because it won't let itself be vulnerable enough to get into deep sleep because it's worried that something's coming at it, essentially.

Alex Howard

And in a sense, what you're describing in that hypervigilance state is, as you said a little bit earlier, it's a functional response or an appropriate response happening in a dysfunctional way...

Dr David Brady

Just like inflammation can be, and it's ironic that what's underpinning a lot of hypervigilance, we're finding out, is what we would call stealth inflammation. Not inflammation like we learned in medical school, it's swollen, it's red, it's throbbing. It's not inflammation you can see.

It's micro inflammation, deep tissue inflammation, that's affecting the glial cells in the brain, different brain centers, particularly very deep brain centers where you process things like pain. So people with fibromyalgia have fundamentally altered perceptions and responses to pain that are not just made up or psychological, they are because of dysfunctional pain processing deep in the brain in inflamed activated cells that are behaving aberrantly.

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So the old saying, oh it's all in your head, well, they were right. They just don't understand how they were right. They were implying it's all in your head because you made it up and you have a prozac deficiency, or you don't have enough antidepressant medications. Which is criminal. Just crazy.

Alex Howard

Or they were saying, it's all in your head, therefore it's not real. That it's like a phantom limb pain.

Dr David Brady

But in reality, it's all in their head, but it's real. It's physiological. There's irony across so much of this stuff. It's just unbelievable. But this isn't new. There were these post viral syndromes after, even when we had good understandings, not like we do now, but fundamentally pretty sound understandings of basic physiology and diagnoses and things like that in Western medicine.

So after the Spanish flu in the early 20th century, there was a significant post viral cluster of people with fatigue and myalgias and sleep dysfunction that's documented. And even then, later on, a band of people who were exposed to the virus that caused Spanish flu, when they were in that neuroplastic envelope, when their nervous system was still developing, they, in later life, went on to have much higher dementia.

And that's what we're worried about with the recent pandemic. And then, of course, even something much more recent would be SARS 1. In SARS 1, it was a much more contained situation. It didn't get out of the bag like covid 19 or SARS-CoV-2.

But particularly in healthcare workers who treated those SARS 1 patients, a large number of them went on to develop what we would now call long haul covid, but it was long haul, essentially. And they were just typified as having a post viral exposure, chronic fatigue syndrome.

Alex Howard

And I think one of the things that I know you and I have spoken about in the past that I think is important to bring here as well, is that one of the great frustrations is when people have these medically unexplained illnesses, that often the response of medics and establishment is, we can't find anything wrong with you, therefore there's nothing wrong with you.

Which then leads to, psycho emotionally, a sense of isolation, a sense of absence of support, which only goes to further drive this hypervigilance that you're speaking to.

Dr David Brady

Yeah, it's the height of hubris and ego and a lot of different dysfunctions that just thread through medicine, which drive me crazy. One of the reasons I never wore a white coat after I was done with my training. The whole separate yourself from the patient, elevate yourself, write in some crazy script that no one can read and use Latin and all these things. It was all in the early culture of medicine of separating yourself as this higher level entity or something, which is just the furthest thing from what you should do.

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Another irony is you talk about how in the medical system they would be just cast off, told this isn't real, you're making it up, just left abandoned. And it leads to isolation, which is not a good thing. We know that can really drive chronicity of illness and be a real barrier to recovery.

And on the flip side now, I talked about a bit of the benefit of this connectivity we have with the modern internet and social media. That people can get together, we can very quickly try to figure out what's going on, crowdsource some people and get even ahead of the medical research.

But there's a downside. There's a dark side. There's a yin and yang, right? You can get people with chronic illnesses that get involved in groups which they feel supported in because they have other people like them. But they can also become pits. They can become places where people with a chronic illness begin to form their new identity around the chronic illness.

Even conventional medicine is not innocent in this. Like even the phrases we use. Oh, you're a diabetic, you're a diabetic. Not, you're a person that happens to have diabetes and let's see what we can do to try to change it. But you are a diabetic.

It's a way of thinking. And in chronic disease it can get really severe and lock in and it's almost another barrier to recovery. As if they don't have enough barriers because they have a complex metabolic multifactorial problem that they really need a skilled clinician that's trained outside of the box to try to even help them tackle, not that they can necessarily have magic answers for them, but help navigate them in the right direction.

But if they're also identifying as that condition and they don't want to be kicked out of it, they don't want to get better, they won't be in the club anymore. And I don't mean that to mock or diminish. It's a natural human phenomena and instinct that all of us would probably be extremely susceptible to going there, put in that scenario.

But I don't hesitate to talk about that phenomenon because I've seen it. I've been doing this 30 years and dealing with chronic illnesses for 30 years and I've seen this play out thousands of times. And I'm not going to not talk about that phenomena because it's uncomfortable, because I feel it's my duty to talk about it because it's part of overcoming another one of those barriers to getting better.

Alex Howard

One of the other ways that I see it play out is people's instagram handle, their name on instagram becomes something to do with the condition. And as you say, that often it's initially forged by the isolation and people looking for their tribe and looking for their community.

But then it's almost like the breakthrough at one stage becomes the limitation at the next stage. The thing that helps someone feel supported then becomes a prison or becomes a trap.

In terms of this hypervigilance and as I think you very articulately laid out, how it lays across these different conditions, of course, which are all related to sleep. What are some of the practical ways that you've observed for working with it?

Because one of the things I very much appreciate about you and your work is that I think you're a real master of integration, of how understanding how these different pieces play a role. So maybe walk us through some of the almost greatest hits, as it were, of things that you notice have an impact here.

[00:24:09] Dr David Brady

Well, with sleep in particular, I know that's our concentration here and as I said, it's just an element of most of the conditions I deal with. But it is an important thing. If someone asked me, I've been asked in interviews in the media before, okay, you're this wellness doctor. You're a functional medicine doctor or whatever. What are the biggest things someone could do to be healthier or have a healthy life and more longevity?

And the three biggies are you gotta eat real good, clean food. Not a bunch of junk and prepackaged science food. You got to move. You got to keep active. You gotta keep moving to the best of your ability. And I understand people have limitations, whether they're physical or metabolic or what have you, and how they can engage in that, but at least engage in it to the level that they can.

And the third one is quality sleep. I mean, it's one of the three pillars. It's like a three legged stool of being healthy. And one of those legs is quality, restorative sleep. And if you're not getting it, it's a big problem.

So one of the first places we go, in addition to trying to fix the sleep or improve it, which we'll get to in a minute, but you gotta look at the other two legs of the stool, too.

They got to start eating. You can't eat junk. You can't eat inflammatory stuff. You can't eat fake food. You gotta eat real, whole, good, quality food that is in the same form that you can identify as if it was 100 years ago. So you have to lower the inflammatory burden and the metabolic and toxin burden on the body to just be fundamentally more metabolically sound.

You have to be active during the day and keep moving to the best of your ability. And then when it comes to sleep, there are a lot of things we can do to try to improve sleep around the margins. I've mentioned some of those. And these are not things that I don't use by any stretch of the imagination.

I rarely use them in isolation. I usually use them in combinations, and we'll work with different combinations in an individual to try to find one that works for them. And it may be a combination of things like melatonin, like theanine, like fermented GABA, the neurotransmitter GABA.

It may be some botanicals, like German chamomile, you can even use GABAergic botanicals, valerian, passiflora, scutellaria, things like that. And you can find different mixtures of these things and different dosages, particularly with melatonin. Different dosages do very different things in different people.

To try to help them, number one, get to sleep, there's three components to try to improve sleep in my book. Helping them get to sleep, helping them stay asleep, and then helping them while they're asleep to go through all of the phases of sleep and get into deep stage three and four sleep, because that's where restoration happens.

And there are three different things. Getting someone to get to sleep easier doesn't necessarily make them stay asleep or get deeper sleep. So you have to look at the whole thing. And we use wearables or we'll use sleep studies when we need to. But a lot of times patients can just tell you, hey, I wake up every night at 03:00 A.M. and I'm up for an hour, I can't get back to sleep.

Or some people, particularly chronic fatiguers, fibro patients, they'll be like, I really can't get to sleep at night because they're hypervigilant, but when I do get sleep, I can sleep for 10 hours, but I wake up

and I feel like I never slept, right? So clearly they're not getting restoration. They're not going into stage three and four sleep when you monitor them in some way with their brainwaves.

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So we'll use other things. Sometimes we'll use a couple of grams of glycine before bed. That can help get them into more delta wave sleep. We'll use things like, if we're using natural agents, we'll use sustained release or time release melatonin that comes apart slowly in the gut rather than just this off the shelf melatonin.

Melatonin is very fast acting. It can help people get to sleep. It doesn't do good at keeping them asleep 3 hours later unless it's time released. And then again, some people don't do good on melatonin. I've had people have paradoxical reactions to melatonin. It wires them or it'll help them sleep, but then they have a sleep hangover. They're groggy in the morning. Or they get terrible dreams or whatever it may be.

Most people tolerate it well, but not everybody. But we'll also sometimes use pharmaceutical agents if we need to, short term, to try to just get them some restoration sleep, but get them off of this stuff. Because none of the drug agents, I don't think, give people the quality restorative sleep that we want.

A lot of the modern sleep medicines, they definitely knock you out and they help people sleep. They used to just be in two to four hour blocks. Now they have more sustained release versions of them. I have patients who use those things and they say if I don't use them, I just can't get to sleep. But I never feel like I sleep well, like I don't have restoration. I wake up groggy.

And there's a lot of side effects with those medications. Some people that really have that hypervigilant racing mind, they just can't go to sleep because they're wired at night, they tend to be going through their checklist that they need to do the next day, and they'll be given anxiolytic medications, even Benzos, things like that.

And it can help them get to sleep, it can help them sleep, but they're addictive and they have other side effects. So those chemical agents are things we play around with, but we really first start at making sure the sleep hygiene is correct. And I know everyone who has sleep problems has heard all of this.

It's nothing new, but a lot of them have heard it, but they don't do it. They kind of halfheartedly try to do it, but they don't want to give up the things that are dysfunctional, like being on electronics and devices, which includes their iPhone in the evening. So after 08:00 at night, shut the devices off.

Even at any time when it's getting dark, they should be in night mode. They should be in a mode that pulls the blue light out of the screen, whether it's your computer, whether it's your iPhone. And it's hard to do that with televisions. So I don't like people being on television late at night. It's just super stimulatory.

Use those last couple of hours before you go to sleep to do things that are common. Yoga, stretching, deep breathing, reading a book, those types of things. Make sure you're using your bedroom mainly for sleep. Don't hang out in your bed and do other things that are stimulatory, like watch TV.

Don't sleep with a St. Bernard that's rolling over all night and waking you up or a cat or whatever else it is. It's cute and sweet and all that, but if you're not getting sleep, man, you got sleep. And a lot of

people don't want to make the hard changes that are involved in sleep hygiene that really make a difference in them.

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Or I've had people come in, they're metabolically a wreck. They really fundamentally are ill, particularly as they're getting into middle age and older and they're on shift work. They're changing their shifts. They're nurses or they work in some situation where they have to do swing shifts. Maybe they're law enforcement or firemen or whatever.

It's really hard. You're really bucking up against a hard wall with that stuff. And I've had patients finally make career changes because they just couldn't metabolically cope with the scheduled demands. In many professions, for instance, nursing, I've had a lot of that. And as they get more seniority and they're getting a little older and these things are nipping at them because they don't have the resilience of youth, they can transition more.

Even if they're making a little less. Or maybe it's not the exact specialty they want to be in. They can get into something where they're working just a consistent day shift. And it works for them.

And then finally we're really trying to treat the greater picture of whatever condition they have if they have something that sleep is just a component of. So we can get into a whole nother discussion on our therapeutic approach to fibromyalgia, chronic fatigue or ME or long haul, but fundamentally doing everything we know to do at this point to get those disorders better and make the person metabolically more sound is definitely a part of what we do to try to fix their sleep. Like I said, it's bi directional.

Alex Howard

Yeah, I was just going to say that, exactly that, there's in a sense this cybernetic loop where you improve one, the other improves and then it goes back.

In terms of specifically the hypervigilance piece, when you're working with someone where you recognize that that overactivation is happening in the system, of course part of what you're doing is addressing these other elements which in and of itself will help calm the system down. But what else specifically to target that piece do you find to be effective?

Dr David Brady

Well, as I mentioned before, hypervigilance, at least from a physiological metabolic standpoint, is fundamentally driven by microinflammation in the tissues. So we do use agents that are known to tackle that problem and they include natural agents, anything from specific response modifiers, from fish oil, SPMs.

We'll use various anti-inflammatory botanicals, whether it's things like curcumin, ginger and so forth in different formulas. Lowering the inflammation in someone's diet is important.

But we use drug agents too. Low dose Naltrexone in long haul now for that reason and others, they're using even things like, dare I say, low dose statin medications, not because of their cholesterol lowering effect, but because of their effect on deep tissue inflammation.

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Vitamin D is very effective with dealing with this deep tissue inflammatory cytokine aberration. And that's just part of why it was the biggest hero to come out of covid in the natural realm and maybe of all, was vitamin D status. So we really work hard to get someone's vitamin D status up.

And then in hypervigilance you have to deal with the functional aspect of it, as you know. I mean, your program goes right at the heart of that and it's a tremendous program that I have referred a lot of patients to. My wife has done it herself. And that's just trying to retrain and reprogram your brain to be less biased towards that sympathetic hypervigilance and more to calming.

And that can take many different forms. I mentioned some of them, deep breathing, meditation, yoga, prayer. You have to find something that works for that person. Processing, if there's trauma, past events, things that need to be dealt with on that level, that has to happen. We use a lot of functional EEG in our office, sort of brain mapping, neurofeedback things to do that.

And we have more intensive therapy in the office. But then we have home units that people can take advantage of, or even now with wearables and all of these different things, you can really inexpensively use heart rate variability training. We also do Vagus nerve stimulation, and that can be low tech, it's like gargling, vocalization, things like that.

But the intermediate technical way to do it is to just use a Tens unit on the tragus and then on the deltoid and sometimes along the chest wall and stimulate the vagus nerve. And then there's more specific, very well studied vagus nerve stimulator devices that you place up to the triangles of the neck.

And they have software algorithms that really calm the Vagus nerve down. And a lot of the hypervigilance is mediated through the Vagus nerve. So doing that Vagus nerve therapy has definitely proved useful and beneficial.

Alex Howard

Yeah, and I want to back up to something you said a few minutes ago around vitamin D status because that may be something that not everyone is aware of. And you made the point around, effectively, people's vitamin D levels was a good predictor in terms of their prognosis, in terms of experience with covid.

Do you want to say a bit more about that? And perhaps also, I don't know if there's a known correlation between vitamin D status and sleep?

Dr David Brady

Well, if you dig enough in the literature, you can find a correlation between vitamin D status and almost anything at this point. And I don't say that in a derogatory sense. It's just truly one of these molecules that, I mean, we know it interacts directly with over 400 genes. Gene loci. And that's growing all the time.

And as we all know, it was miscategorized as a vitamin because it can be carried in food and you can get it through food, but you can get it through other ways. As we know, sunlight and conversion and so forth. It's really a hormone. So it's a hormone and a metabolic switch substance that does a lot of different things.

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It really fundamentally can change how the immune system behaves, how it reacts to things, which then in turn affects various cytokine balances, lymphocyte subsets, and many other things that determine what our immune system does and does not do.

And of course, it was first known as for health and bone density because it facilitates calcium uptake in the gut and does a whole bunch of other things in that regard. But it's involved certainly in clock genes, what we call them, which have a lot to do with our circadian rhythms and why a lot of people wake up at 7:30 every day. No alarm, no nothing. It's every day, 7:30. It doesn't matter when they went to sleep.

That's a clock gene in action. It's really an amazing thing. A lot of people's clock genes are really messed up. Whether the genes are messed up or whether they're just expressing themselves in an aberrant way is another thing.

But yeah, vitamin D is a really important agent and it's also something that in a lot of people, even though they're supplementing it, it just doesn't want to go up. So there's been a lot of studies into that. A lot of people are bleeding it off and converting into another metabolic form of vitamin D rather than 25, more bleeding into 125.

And some of that has been somewhat latched to happening more in autoimmunity when there's an underlying inflammatory bias in the body. Some of that work is controversial, but I think there's enough there that there's something there. We don't fully understand it, but it is interesting.

And even people's body composition, the more overweight or obese someone is, the more they have this tendency of not allowing vitamin D to rise to the level we want and throwing it over in the other metabolic direction. It's not fully understood why that occurs, but we certainly pretty predictively observe it in clinical practice.

But vitamin D is important. I'm not putting it off as the panacea and just take 10,000 IUs of vitamin D every day and your sleep problems will go away. But again, it's part of the soup.

Alex Howard

To take that point a bit further, David, you're one of the people that I consider one of the real detectives of medicine. We were talking before we started filming a bit about some of the journey with your wife.

That personalized approach is so important, isn't it? And I think there are a lot of people that may be watching this, that sleep has been a struggle for many years and it may well be they are watching this interview because it's also sitting part of that wider jigsaw in terms of these complex fatigue conditions.

But I think so many people are still so habituated to trying to find the one thing that's going to work for everyone, as opposed to the recognition that although there are many patterns, that individualized approach is so important.

[00:41:48] Dr David Brady

Yeah, that's an interesting point because I think it's a combination. There are some generalities that are true, like some of the things you've asked me like what are the big ticket items to help you with those things, that are more generalized advice, sort of to the masses, if you will. They have validity. I mean, they make sense.

They work to a degree, they work to different degrees in different people, of course, but they make sense. They're not things you should ignore, but they don't always get you all the way there. If you're one of those people that it doesn't get you there, you really need to look under the hood much more in a much more precise and personalized way.

And we do that by looking at metabolomics and we'll look at, how are you metabolizing and spinning off downstream products in your serotonin pathways, your GABA pathways, your catecholamines? How are your mitochondria working and what's going on?

And we have the tools to do that now in a very cost effective way, using organic acids, metabolomics, microbiomics. Sometimes we'll use sniper genomic testing, whatever it may be, to get the job done, not only to tackle the sleep, but the bigger problem that people may have.

And some people just have a sleep problem, but most people have sleep problems as a component of bigger metabolic problems. So yeah, I think that personalized approach is where you need to go. It can get a little wonky.

So the average family physician has no idea how to do any of this stuff. And they're just going to throw single agents at you, usually pharma agents, to see if you feel better and they're trying to do something to help you. But it's a very simplistic myopic way to look at the larger issue for sure.

And sometimes, I have to tell you, I don't bet 1000 at this. I have a lot of patients that I've gotten their sleep a lot better. I have a lot of patients who I've gotten their sleep perfectly fine from being dysfunctional. I also have patients I haven't done a very good job with, apparently, because they still have sleep problems. And they're just really difficult cases.

They have really treatment resistance on really tough sleep problems. And they tend to be these super, uber, hyper vigilant, wired up at night, that's when they're up, that's when they feel good, that's when their creativity is, they're night owls and all of this stuff. It's very difficult.

And in patients that, listen, if someone's just like that and they're okay being like that, well, then okay. But I have patients who are like that, but they're riddled with fibro or chronic fatigue or long haul and anxiety and depression and in some cases, even suicidal thoughts. And in those cases we'll pull out heavier guns.

We'll do things like I think we mentioned in a personal conversation, even using a Ketamine reboot. Ketamine infusion. It's one of the few tools that we have to reboot the central nervous system and its bias and where it stands. It's almost like when your computer is doing weird things, finally you just forget it, I gotta hard reboot it.

I got to power it down and power it up and hopefully everything magically goes back to what it should be. That can happen in Ketamine reboots. Sometimes in one treatment. Often it's a series of them. And of course, Ketamine at a higher dose than is used in what I'm talking about, is an anesthetic agent.

[00:45:42]

But it's used at a lower dose and it was first used in treatment resistant depression and particularly with people with strong suicidal ideations where the drug therapies weren't working. And it worked. And slowly and surely it's been studied for other situations, from depression it went to anxiety.

And when it was successful treating anxiety in many people, then anxiety is a major component of hypervigilance, which is a major component of CFS and long haul and fibro. So more clinicians started trying Ketamine reboots in people with these chronic disorders and there's definitely a success story there, although not a universally successful story, but what has a 100% universal success story? Very little in medicine.

Alex Howard

I guess, this is not a fully formed thought, I'm somewhat thinking out loud, but it reminds me of some of the work that's been done over the years of electroconvulsive therapy, which of course is potentially more damaging and controversial because of the impacts they can have...

Dr David Brady

Ketamine has largely replaced it and it's much safer. When it's done right under proper medical supervision, there's very little side effects at all. It's very safe at the doses they do it at. The most common side effects someone might have is a little bit of nausea proximate to treatment, just where they put the IV in a little local irritation.

Some people just feel a little foggy for a day or two afterwards, almost like a bit of a hangover. Most people don't. A lot of people describe the experience while they're under the Ketamine, especially when they have these chronic disorders, as the first time in years they felt normal, like their body, they didn't have pain.

They didn't have anxiety, they didn't have this going on like they're trying to crawl out of their skin. They were at peace, they just wanted to stay there, which is good and bad. Some people can develop almost, I don't want to say an overt addiction, but a proclivity to want ketamine treatments because it's so amazing to some people.

I had a very good colleague, Doctor Todd LePine, a really good functional medicine doctor here in Massachusetts, in the States. And he had a patient that had arachnoiditis really bad, terrible, wouldn't wish it on my worst enemy pain situation where it's very resistant to treatment. It's one of those disorders that literally makes people jump off buildings. They just cannot live with it.

And it was very early in ketamine therapy and he had talked to me about the case and we both almost at the same time said, what about just trying a Ketamine reboot? And the guy did it and, gone. Gone. And not every case goes like that, but that made me go, whoa, something is here.

And I don't do ketamine drips, I'm not an expert in them or anything like that. I have people who do and are so I don't want someone to think I'm overselling it because I have some interest in it or something. I don't. I'm just looking for something that works.

[00:49:30] Alex Howard

Well, I think David, because it's a new one for me, but what I think is really interesting is it's, beyond the fact that I think it sounds like for some people a really important potential area to explore, also making a wider point around, and I appreciate your humility that none of us have all of the answers, but what we hope we have is an openness and a curiosity and an inquisitiveness to go and find these new pathways forward for those patients that have tried many, many things and find themselves still stuck.

Dr David Brady

In these types of disorders, Alex, I fundamentally think that the thing that we arrive at that's the key that goes in the lock and really, fundamentally changes these disorders, it's going to be something that's very central in functionality and physiology and all of that.

And something like Ketamine, for instance, is central. It's acting in the deepest centers of the central nervous system. That's why it's an anesthetic and rebooting it, or trying to do that. Most of the things we use in these disorders are nipping around the edges.

They're treating around the periphery, they're bandaids on deeper wounds. You have to get something that goes deep. Whether that eventually is some sort of pharmaceutical agent that's hitting some metabolic target, I don't know, but hopefully whatever it is, is coming.

Alex Howard

Fascinating. There's so many rabbit holes left but we're running out of time for today. David, I want to highly recommend your book, *The Fibro Fix*, but also if you can mention your website where people can go to find out more and some of what they can find.

Dr David Brady

Yeah, if someone has fibromyalgia or knows someone and wants to know more about that, you can pick up my book *The Fibro Fix* or just go to fibrofix.com. There's a lot of resources, a lot of interviews, a lot of papers of mine, a lot of articles, information, and you can order the book from there.

If you want to know just more about me and other things that I do in my approach and my practice, just drdavidbrady.com. So dr for doctor, drdavidbrady, B-R-A-D-Y, .com.

And then for some of the innovative things we're doing on the diagnostic side with Metabolomics and things like that I mentioned, you can see some of the testing options that you can talk to your providers about just by going to diagnosticsolutionslab.com. So, diagnosticsolutionslab.com.

Alex Howard

Fantastic. Dr David Brady, it's always a pleasure. I really appreciate your time and yeah, thank you so much.

Dr David Brady

Thanks, Alex. Appreciate it.