

## How a Probiotic Strain Calms Your Body & Brain Stress – Kiran Krishnan, Ph.D. – #927

Dave Asprey:

You're listening to The Human Upgrade with Dave Asprey, formerly Bulletproof Radio.

You're listening to The Human Upgrade with Dave Asprey. I promised that this year I'm going to tell you exactly what you're going to get in a podcast so that you know that it's worth your time to listen to it. Today, we're going to talk about psychobiotics, and as you know, I'm a fan of probiotics, and I'm an investor and advisor to companies who are quantifying the human biome in new ways.

What we've learned over the past 20 years is that it's not just having a healthy gut, it's that there are specific species in your gut that make specific compounds if they get the right foods. This has given us the ability to now say, "I'm going to choose the strains in my gut. I'm going to create an environment where they will survive, and then I can have onboard manufacturing that's different than what my mitochondria does, different than what I do in my endocrine system," and that you can get profound anti-aging benefits or what we're going to learn about today is the cognitive benefits, and the brain-modifying benefits of certain species of gut bacteria.

So if you want to cut your stress, have less anxiety and better moods, this is the episode for you, especially if you're interested in how the gut works with that. So welcome to the episode.

Our guest today is a research microbiologist named Kiran Krishnan. He's a PhD, and he's looking exactly at psychobiotics. Kiran studies something called gut commensal spore bacteria microbiology, and he is partnered with a company called Just Thrive, who's been on the show before, and he's been on the show before to talk about the latest stuff going on with gut bacteria, and the last time we talked about inflammation and immune function, this time it's about the gut-brain access and specific things you can do to hack it. So Kiran, welcome back.

Kiran:

Dave, thank you for having me. It's awesome to be back and exciting to have the Collective in the audience as well.

Dave:

It's really fun because they're getting some extra time to learn and they get to ask questions, and a lot of times they're giving me a little reminders like, "Hey, ask him about this." So I'm crowdsourcing some of the questions I'm asking you. It's one of the many benefits of being a member of the Upgrade Collective. You can go to [daveasprey.com](http://daveasprey.com) and there's more info on how you can join. I also teach all of my books and things like that as small classes. So you can really go deep on biohacking, but our episode today is going to be available for everyone because it is part of a podcast with, at this point, about somewhere around 275 million downloads. So it's going to reach a lot of people.

What I want to do is understand the new stuff that's happening with gut bacteria because everyone knows, "Yeah, you should have a healthy gut. You should probably take some prebiotics. You should probably take some probiotics." People don't really know which ones, but I want to laser in with you on what are the things that people don't know about that can change the brain. So what's new?

Kiran:

Yeah. A couple of things, and one really important message that I want people to really wrap their heads around and understand when we're talking about the gut-brain access-

Dave:

What are the things that people don't know about that can change the brain. So what's new?

Kiran:

Yeah. A couple of things, and one really important message that I want people to really wrap their heads around and understand when we're talking about the gut-brain axis is, of course, the gut, a healthy gut is incredibly supportive to the brain. It supports the brain in a number of really important critical functions like recovery, for example, or production of serotonin and dopamine and all these important neurotransmitters, but on the other end of the spectrum, an unhealthy gut is not only not supportive, but it's arguably one of the most toxic things for the brain, right? That's not talked about as much when you talk about gut-brain access.

So I want to make sure we cover both spectrums where we could talk about how the psychotics and new things and probiotics in the gut microbiome help the brain in a significant way, but then what happens if your gut is unhealthy? How is that actually toxic to the brain, and arguably, the most toxic thing to the brain?

So both of those things play in this same pod. So you're someone listening and you're thinking to yourself, "Oh, my God. I have some digestive issues. I've got some IBS-like symptoms. I've got loose bowels. I can't eat certain foods," and all that you've got gut dysfunctions, right? Not only may that be affecting your mood and your ability to sleep, but it's actually acting in a toxigenic manner to your brain overtime and driving all kinds of long-term neurodegenerative conditions.

So what you may be experiencing now as indigestion and bloating and discomfort, and then the corresponding anxiousness, mood disorders, inability sleep are actually early symptoms of much more serious issues that are coming down the road. So such an important topic to be talking about, and grateful to be here to do it.

Dave:

So if you get bloating after meals or you have room clearing gas, the way I did when my gut was really wrecked years ago, it means your brain's not working well or you're experience anxiety.

Kiran:

Exactly. Yeah, and then if you are experiencing those things acutely, you also know that the same pathologies are in place that drive long-term conditions like Alzheimer's, dementia, and so on.

Dave:

Even Parkinson's.

Kiran:

Even Parkinson's.

Dave:

Parkinson's and Alzheimer's are tied to bad gut bacteria from years before.

Kiran:

Exactly, 100%. So whatever we're talking about today, not only is it applicable for how you feel and function at the moment, but as you improve those things, as you improve your gut-brain connection and you get your gut to be supportive of your brain, you're actually protecting your brain from long-term damage that's occurring from a dysfunctional gut. That's where psychotics come in, right?

So psychotics are incredibly powerful organisms that seem to have a natural capability of modulating brain function, and very importantly, modulating stress response. That's a new, exciting field because what we know is that stress response, normal, innate stress response that everyone experiences, the flight or fight turn on, the sympathetic nervous system kick on, the cortisol increase when we experience a stressor, that's all normal, but whether or not we can come down adequately from that stressor is the key, and psychobiotics and certain microbes within the gut make that determination.

Dave:

Okay. So there's the baseline bacteria that we need to have for a healthy gut and that removes some of inflammation, but are there new species or is there new research about specific ones that will turn anxiety down or is it just, "Oh, I have less inflammation. Therefore, I have less anxiety"?

Kiran:

No. There are new species. For example, one of the ones that we're working with, I think we've published now four or five studies on it, it's a keystone species. It's a bifidobacterium longum, but what's unique about it is it has an exopolysaccharide covering, and this exopolysaccharide is made up of a compound called peptidoglycan. As it turns out, natural commensal bacteria that produce high levels of peptidoglycan are critically important not only for balancing mood, reducing inflammation, but negating the negative effects that cortisol has in the gut, and we could talk about what exactly happens when cortisol increases and ends up in the gut.

Then it also has the capability of sending signals through the enteric nervous system, the nervous system that covers the gut, all the way up to the vagus nerve to the brain to change brain chemistry and brain waves. So we've studied and published in all of that. So these psychobiotics are amazing modulators of brain response to the environment around you.

Dave:

Okay. That's making some sense. You've got five new studies that are showing the specific species, and it's a subspecies, right? How do you pick that out? I actually don't understand this. So there's all kinds of bifido longums that are out there. I don't know how many in total. How many different species of them are there or subspecies, whatever you want to call it?

Kiran:

I would mention, I guess, over 150-200.

Dave:

Got it. So how do you know which one to focus your research on?

Kiran:

Yeah. So we do a lot of screening, right? So the way this particular strain was actually discovered is we started taking in cohorts of individuals, looking at individual's stress response. So you initiate a stressor

to them. You look at their stress response. You look at cortisol levels, and then we are also doing something similar with sleep response.

So we were starting to group people into individuals that had really good stress response, good sleep efficiency compared to age match cohort that did not have good stress response and good sleep efficiency. Then we dive into the microbiomes, and we start comparing those microbiomes and looking for real clear differences between those two groups, and that's one of the ways in which we found this organism. We started seeing in individuals that had really good stress response, good cortisol cycling, good sleep cycles actually had higher levels of this particular bifido longum. The people that didn't have the bifido longum had much worse stress response.

So then as we started digging into what is this longum, we discovered that this bifidobacterium longum actually has this unique exopolysaccharide covering. So we said, "Okay. That's unique for bifido longum in itself. Most of them don't have this covering. So let's take this strain. Let's knock out the ability to produce the peptidoglycan, the covering, and then let's test it in animal models of anxiety, stress, and inflammation."

Sure enough, when we knock out the peptidoglycan, we come to find out that it doesn't do the same thing. Then compare it to the one that does have the peptidoglycan, it does reduce stress, it reduces anxiety, it reduces inflammation. So that's the long screening process of identifying normal commensal organisms that are really important and related to certain functions.

Dave:

I want to talk about glycans for just a minute. There's a bunch of polysaccharides and polysaccharides are basically sugars stuck together that cover a lot of our immune cells, and researchers like your predecessors probably used to call that junk sugar and are like, "We got to scrape that all off the cell to find out what's going on in there." I've just learned throughout my entire life, anytime science calls something junk, that's shorthand for, "We don't know what it does, so we're going to ignore it and pretend it doesn't matter," instead of maintaining curiosity.

Kiran:

Exactly.

Dave:

It's actually a really dangerous bias. So to me, junk means look here, look here. There's a company, well, probably 10 plus years ago, who was making a product, just a powder you could put in your coffee that contained a bunch of these polysaccharides for immune function, and they got shut down by one of the regulatory authorities because they're saying "That can't be," but it turns out there really is.

Another compound people may know about is AHCC, which comes from mushrooms and has beta-glucans, which are in the same family, right? So what you found is a unique species of gut bacteria that makes these polysaccharides on the outside of it that most of them don't, and those polysaccharides have direct effect on gut quality.

Kiran:

Yup. That's exactly right. In fact, this species, and what's so interesting about it is it's equally important in utero when your brain was originally developing, right? So now, there's a lot of research showing that bacterial glycans are picked up by mom's immune cells, as you mentioned, immune cells have a lot of glycan receptors on them. So they pick up mom's glycans that her bacteria are producing, take it

through the placenta into the baby's brain, and in the baby's brain, there are glycan receptors that bind these glycans, and then that is the stimulus of developing the brain itself.

We know that when mom's gut bacteria is compromised and they're less exposure to glycans through the gestation period, then the baby has the risk of underdeveloping the brain, and then you've got risk of things like spectrum disorders and so on.

So for immune function and neurological development and all that, these glycans are critically important, and this particular peptidoglycan from the 1714 strain seems to be able to completely negate the inflammatory response that stress causes in the gut and the leakiness in that stress causes in the gut.

Dave:

That's a huge claim. Completely eliminates?

Kiran:

We saw huge reductions in them in both the animal models and the human models because you need some inflammation, right? Inflammation is utilized as a way of creating perfusion during the flight or fight response. The body is trying to go, "Hey, I need to get blood to the brain, to the heart, to the muscles. No more blood in the digestive tract or reduce the blood in digestive tract so that you're ready to fight or flee." So you need some inflammation because that inflammation directs the blood to the right place, but you're supposed to be able to come down from it.

What tends to happen in the modern day is we experience those stressors and we keep getting that inflammatory increase and that cortisol increase, but we don't have the method of coming down from it because our guts are messed up, right? So our gut is a checkpoint for going, "Okay. Here's your flight to fight response. You're now safe. You can come down from it." The modern day it goes, "Here's your flight to fight response. Oh, and we're going to keep triggering the HPA access over and over again from a single stressor," right?

So the entire day after that single stressor, that one person that cut you off in traffic on the way to work, you're now experiencing continuous cortisol cycling and upregulation and the resulting inflammation. We can't come down from it so well.

Dave:

This reminds me of conversations that I've had for years trying to define what adaptogenic herbs do, and it's exactly what you talked about. When people are taking adaptogenic herbs, then it means that you can more quickly turn on your stress response, but as soon as you're done with it, you can turn it off all the way.

Kiran:

Exactly.

Dave:

This is why I've been recommending them for a very long time and taking them. They're pioneered by mostly China and Russia, pioneered as in thousands of years ago. They would use them before a fight in a war, before a battle because they're like, "Oh, our soldiers are actually much better able to return to baseline and then they can fight again." If you have multiple skirmishes, it actually makes a huge difference because you're not tweaked after the fight.

Kiran:  
Exactly.

Dave:

So when the rest of us take those, that's one way to do it, and it sounds like this new strain, for some reason, probably those polysaccharides on it, it actually has an adaptogenic effect because it allows you to return to baseline faster than you otherwise would.

Kiran:

That's exactly right.

Dave:

For some reason, probably those polysaccharides on it, it actually has an adaptogenic effect because it allows you to return to baseline faster than you otherwise would.

Kiran:

That's exactly right. So in some of our studies, what we do is we take individuals, and these are healthy normal individuals to begin with, and then we dose them up on the strain for 30 days versus a placebo, and then we induce stress in them experimentally. As we induce stress in them, we're measuring the cortisol response and then their ability to recover from that cortisol response.

What we tend to find is that the cortisol peaks are lower in these individuals. So the perception of that stress is significantly lower. I'll talk about why the perception of the stress changes as well, but then also the inflammatory cascading that occurs in response to the stress comes down much more dramatically in these individuals once they have enough of this organism in them.

So it's absolutely correct where you can actually cycle up, but then come down and actually recover from it. That's the fundamental difference between humans today and our ancestors that use the flight to fight response to survive, right? It's such an important survival mechanism. The stress response is so critical for a survival of our species, but they were able to flee away from the danger and then come down from it versus a modern human, perceive danger, most of it is not life threatening, but they perceive danger and then they can't come down from it. So that's a critical difference.

Dave:

Okay. I love that. Now, I'm already asking myself. So I take Just Thrive probiotics. Is this species in the ones that are the standard thing or is this a new one?

Kiran:

This is new. So there's a new product called Just Calm. It's under a sub-brand of Just Thrive Health called Joot, and one of the reasons why they-

Dave:

Called what?

Kiran:

Called Joot, J-O-O-T.

Dave:

So Joot, J-O-O-T. So if I go to Just Thrive, can I find it?

Kiran:

Totally. Yeah. 100%.

Dave:

Okay. Good.

Kiran:

It's called Just Calm. That's the idea behind it. Really, it pairs amazingly well with the spores, with the standard spore formula, and the reason for that is the spores, as we've talked about, dramatically reduces LPS, lipopolysaccharides circulating in the body by slowing down the leakiness of the gut. LPS is one of those key triggers of inflammation in the brain and the central nervous system that drives anxiety, drives mood disorders.

Dave:

Let's talk about what LPS is because we're getting pretty nerdy here, but I know that listeners can handle this. So we talked about polysaccharides, sugars stuck together. Lipopolysaccharides are fats stuck to sugars, and this is the bad stuff that happens in your gut. Even if your gut isn't leaky, some of it makes it through your liver, ideally detoxes some of it, but the rest of it goes through, crosses the blood-brain barrier because of the lipo part of and wreaks havoc in your brain.

So a huge number of my antiaging and the whole Bulletproof diet thing is around managing LPS production and even things like activated charcoal binding to lipopolysaccharide, which we're going to call LPS. So basically, this is onboard, highly, highly bad for the brain toxin made in the gut, and that polysaccharide thing I think is key because it's immune-activating and the polysaccharide that's in the new Just Calm formula you talked about, that's a good one that's not stuck to a fat. So it works in the gut to protect the gut and stop the bad stuff, the LPS, from crossing the barrier, which is really cool.

Kiran:

Yeah, absolutely. It stops all the inflammatory cascading that the bad stuff, the LPS, causes not only in the brain but the rest of the body as well, right? We know we mentioned Alzheimer's and Parkinson's earlier. There's good amount of research now showing that some of the initial insult to the central nervous system that leads to those kind of conditions is the overt presence of LPS in circulation, right? So LPS, because it's made in the gut like you mentioned, it can continuously leak in. So it's continuous exposure to a pretty powerful toxin, and it's an endotoxin, meaning it's made within, so it's hard for us to get away from it, right? All we can do is really try to reduce the amount of it being made and dramatically reduce the amount translocating into circulation. So the two products, we know the Just Thrive. We've published on this. The original probiotic stops or slows down the LPS by about 60% in a 30-day period.

Dave:

Which is magic. That's a huge change.

Kiran:

Huge change, right? You feel that because we know that LPS creates all kinds of problems throughout the body. Then here comes this other psychobiotic that not only helps reduce further the impact that LPS has, but more importantly, it actually stops what cortisol ends up doing in the gut, right? Cortisol, when it cycles through the body in a stress response and dumps into the gut, and it's supposed to dump in the gut because there's a couple of things that happens to it in the gut that are important for the flight or fight response, in particular, cortisol gets metabolized by certain bacteria, into byproducts that are sent to the kidneys and those byproducts change the mineral transportation in the kidneys.

So you actually end up with more sodium in your circulation to increase blood pressure, right? In the fight or flight response, you want more blood pressure, you want more perfusion, but the other thing that cortisol does in the gut is it makes the gut leaky. When the gut becomes leaky, you've got more LPS flowing through, you've got more inflammation, and you've got this critical compound that you and I talked about before, and I know you talk a lot about is interleukin 6, right? So IL6.

Dave:

IL6, right.

Kiran:

Yeah, IL6. So IL6 scales up when cortisol levels go up and start dumping into the gut. The problem with IL6 in the stress response is IL6 has the ability to go into circulation and then retrigger the HPA axis, turning it back on, causing it to release even more cortisol. So a single external stressor that causes that cortisol release and that stress response can then become re-triggering over the next several hours, if not days, if the gut continues to stay leaky.

The other thing that IL6 does, it's especially egregious when it comes to stress response, is it reduces the expression of things called glucocorticoid receptors that are found all over the body, including the gut. These glucocorticoid receptors are supposed to bind cortisol as it increases in circulation and then start sending negative feedback signals to tone down the sympathetic nervous system, right? So that's the control mechanism for the stress response.

The body goes, "Okay. You're stressed. You need to fight or flee." Cortisol shooting up to help you do that, but as cortisol gets to a certain level, it starts providing a negative feedback from itself by binding these receptors, but IL6 when it's up, it lowers the expression of those receptors. So there's fewer of them to actually provide the negative feedback.

Dave:

It's really interesting. IL6 is one of those inflammatory signaling molecules that goes up when you have an infection. In fact, I got censored for a piece that I wrote about IL6 and how it goes up after a very popular viral infection, and all of the many things you can do to lower your IL6 levels because I've dealt with chronic inflammation for most of my life. Partly 15 years of antibiotics will do that to your gut bacteria, but mold exposure, lots of other things. So I know IL6 well because it's been stalking me for years, and this is fascinating that a probiotic can do this. I'm a little bit worried. though, because cortisol is not a bad thing.

Kiran:

Right.

Dave:



In fact, many people don't know it, but they have low cortisol, whether it's because of adrenal dysfunction, genetic things or other reasons, and I'd rather have high cortisol than low cortisol because you can do stuff about high cortisol, but low cortisol, you supplement with cortisol, and a lot of people with autoimmune conditions, that's exactly what's wrong is they need more cortisol, not less. I take cortisol as a bioidentical form. Is this going to eat my cortisol? Is it going to make me not have enough or is it going to work systemically but it just takes it out of the gut where it's not helping?

Kiran:

Yeah. So that's a really important distinction. I'm glad you brought that up because this has no impact on your body's ability to make cortisol at all, which is, of course, coming out of the adrenals. So you'll make all the cortisol you make. What it's doing is negating the negative effect that cortisol has on your gut microbiome, and cortisol in an unhealthy gut creates that intestinal permeability. In a healthy gut, it's perfectly fine, right? It's exactly what we need. It does what it's supposed to do for the fight or flight response, to get you ready awoken in the morning and so on. So it's not going to impact the ability to make cortisol. What it's doing is counteracting the negative effect of cortisol in an unhealthy gut.

Dave:

Got it. It's going to be game-changing because people who have cortisol issues, whether it's high or low, their guts aren't going to be working right, and it sounds like this is going to modulate it, whichever one you have, it's going to happen because low cortisol equals higher IL6 as well because cortisol is responsible for dampening that inflammatory signal.

Now, if you're listening to this going, "Dave, I wanted to be into biohacking and living forever," here's the thing. If your IL6, which is a primary inflammatory signaling molecule in the body, if it's high, your brain will be inflamed. You're more likely to get Alzheimer's. You're more likely to get every bad thing that happens, including probably cancer. So having a gut bacteria onboard that breaks this cycle, the one you described of lipopolysaccharides crossing the gut, creating inflammation, which creates cortisol and then which creates more inflammation, breaking that cycle means that your cortisol is probably going to be just better regulated regardless of whether you're high or low.

Kiran:

That's exactly right because remember, a key part of cortisol regulation is the presence of those glucocorticoid receptors because those are the guys that bind up cortisol and go, "Okay. We've got enough. Let's now shut down the negative effects that cortisol can have on your sympathetic nervous system," and then that also gets your body and your adrenals reset to be able to produce cortisol again because most people end up going into this adrenal fatigue area with continuous and overproduction of cortisol over time, right? Then their adrenals that aren't designed to be producing it constantly every minute of every day, it's supposed to cycle appropriately those adrenals going into a fatigue and can't function anymore. So now, we're giving the body a chance to allow cortisol to function the way it's supposed to without all the negative effects that increases IL6 and screws up the whole loop, the whole feedback system.

Dave:

All right. So I'm really interested in this stuff, and full disclosure, I haven't tried the new Just Calm product. So I'm actually now sending a text message to my team going, "Guys, how come I don't have any of this stuff?" So it's probably on its way. Living in Canada right now. It has to go through the Berlin Wall between Canada and the US.

Kiran:

Oh, my God! Yes.

Dave:

So I'll tell you guys how it's working for me, but the science behind this is it's pretty clear, to be honest, and the results are not what I would expect. I looked at the studies before deciding to do this interview, and one of the studies that just came out last year, improvements in sleep during exam stress from the specific strain that's in Just Calm, the bifidobacterium longum 1714. So tell me about that study. What happened with exam stress?

Kiran:

Yeah. So what we're finding out, obviously, is that during exam stress or any periods of stress, the gut tends to become leaky and it actually drives dysbiosis, right? So there are certain organisms that thrive under that condition of leakiness, inflammation, and so on, and in fact increase their virulence factor. So during those periods of stress, you can get an increase in opportunistic organism growth, which means that we start negating the microbes that produce serotonin and dopamine, in particular, another precursor, which tryptophan.

So tryptophan can be metabolized in two different pathways in the body. You take tryptophan, if you're healthy, your gut is healthy, your immune system's healthy, it's going to get metabolized to serotonin and then dopamine, both of which that are important for resting, relaxing, sleeping, feeling happy, and so on.

Now, if you have this continuous HPA activation due to stress and the inflammation that goes along with it, there's a shift to metabolizing tryptophan to something called kynurenine and quinolinic acid, which are actually neurotoxic, and those neurotoxic compounds prevent the release of things like melatonin and so on to be able to sleep and rest.

Dave:

Wow.

Kiran:

So we know that it's all timed, right? So we know exam stress is going to impact your ability to fall asleep, so the time to sleep and then the quality of sleep as well, which means, of course, your brain's not absorbing that information. It's inflamed, it's not really helping you when you're studying.

So what we did is we said, "Okay. That's a great challenge scenario to see that if we can take people who are under certain amount of stress already, and then see if we can improve their sleep patterns, then we're really breaking up that negative cycle of inflammation, leaky gut, LPS increase, serotonin, melatonin production, compromise, and so on." So yeah, and we saw very significant improvements in duration of sleep, so how long it took them to fall asleep and then the quality of sleep throughout the period that they're sleeping.

Dave:

That's profound. You also brought up something that maybe the explanation for tryptophan restrictions. Tryptophan is an amino acid, and long-time listeners have heard me talk about amino acids are the building blocks of proteins. You string different ones together to make peptides, and pretty much every protein in the body is made of a relatively small number of aminos.

Studies show that restricting tryptophan in the diet equals longevity. So eating a lot of tryptophan is bad for you, and then people say, "But, but serotonin," and what you're saying is here's the microbial pathway that's going to force the tryptophan to go down the "it's good for you" path versus the it's bad for you and increases all-cause mortality path.

Kiran:

That's exactly right. Yeah.

Dave:

Okay. I have to just underline that because I've written about tryptophan and methionine restriction and because of biohacking, because of all of the things we're learning about microbiology, all of a sudden we're saying, "Oh, here's a little tiny thing we can do to hack our system so that when we eat tryptophan, which comes from animal meats and things like that, there's probably some vegetarian sources too, but not that many, and when that happens, now it may not be causing aging." Do you know anything about this bacteria and mTOR by any chance?

Kiran:

I don't. We have not studied mTOR. We do want to look next at epigenetic changes. My guess is that it could have an impact on it, but that's a super exciting area to look at as well.

Dave:

Okay. For listeners, mTOR is something that is a really big thing in the anti-aging field right now. You need mTOR to grow tissues and stay young and build muscles, but if you have mTOR that's elevated all the time, it makes you age quickly and increases your cancer risk. So we have this weird thing, you want it, you don't want it, and part of the reason I recommend cycling in and out of ketosis and things like that is because cycling back and forth seems to make a lot of sense. So going some time without protein called intermittent fasting, it's to lower mTOR, and then mTOR can go back up when you exercise or when you eat some protein or very particularly carbs, but we don't know if this is going to affect that, but we do know that it's going to have a beneficial effect on specifically tryptophans. So maybe you won't get that aging effect from eating it.

That is something that I don't think you've talked about much in research there, but from an aging perspective, if you do eat meat, which is correlated with living longer, to be really clear, so I think you should eat meat, this is probably going to make it even better. So I'm pretty excited not from a psychobiotic perspective, but just from an aging perspective about the Just Calm, the bifido longum 1714.

Kiran:

Yeah, absolutely. No, and when you think about all of the neuro inflammation that comes about from stress and having a dysbiotic gut that can't help you deal with stress adequately, that has a huge antiaging effect as well, right? The neurodegenerative conditions when the mitochondria and the neurons start to die off, and we start to see reduced ATP production over time, that is a hallmark of aging.

So as we can improve the inflammatory cascading, we can reduce the inflammatory response that stress has, we can improve what tryptophan does instead of going towards the neurotoxic side, becoming more neuroprotective, turning into serotonin and melatonin. Those are all going to be things

that really improve not only your existing mood, your sleep, but it has long-term implications for your overall health.

Dave:

Wow. That's a pretty serious stack of things for just a single species. Second study that came up was modulating brain activity during social stress. So these are things, okay, exam stress is a really common thing, even if it's not because you're taking an exam, but it can be I have a big presentation at work or whatever, but brief stressful periods where you have to perform well cognitively. So talk to me about social stress. What did you find it does there?

Kiran:

Yeah. What we're looking at is a couple of different things. So we're looking specifically at brain wave activity. We wanted to see what areas of the brain were being triggered when you were on the probiotic or not on the probiotic when you induce social stress in individuals. The way we did that is actually a really cool thing. It's a professor in Germany that specializes in this, in psychiatric medicine, and there's a machine system that you put people in and they play a virtual game and it's a ball throwing game. What's super interesting about it is it's a virtual game, but the other virtual components are AI components and they avoid throwing the ball to you, right? Just that little bit-

Dave:

Like kickball in third grade or something, which you get really stressed.

Kiran:

Exactly. Yeah. I guess every adult has had that experience where they tap into it because, man, do their anxiety go way up in playing that virtual game. It's like being picked last at gym class, right?

Dave:

Right.

Kiran:

So that same old memory. So you can really induce an amazing amount of social stress in these individuals. What we found was that when people took the probiotic for 30 days before doing this experiment, what we found was a dramatic increase in theta wave function, right? That's the flow state. So we're changing that brain wave function and a lighting up of the coping centers of the brain. The coping centers of the brain is the rational thinking that helps you talk yourself out of being bothered by the situation too much, right? It negates the negative emotions that come along with that stressor, and it's those negative emotions that keep eating away at you and you keep thinking about it and thinking about, and then it has this prolonged effect. So we saw real and true brainwave changes from taking this strain, which is really fascinating.

Dave:

Okay. I'm intrigued because social stress for most people, they're not passing the ball to me, but they go into a crowded place, they don't know anyone. It's really a much more common thing than people realize. There are people who'd say, "Oh, I know I have social anxiety," but that's probably 10% of the people who actually have social anxiety. So all of a sudden now, for some reason, I don't know if you can

describe the mechanism, but it makes it easier for you to think about it instead of just feel about it and be tweaked.

Kiran:

Yup. Exactly, yeah, because think about social stress, and this is, like you mentioned, different than the people with severe social anxiety that really can't do with the panic and all that. Social stress is really a mix of confidence issues with a bunch of negative emotions that swell up, and because these negative emotions, as you're entering into a social situation, really eat at you in your brain. You really talk yourself out of being able to function in that environment because all those negative emotions keep going, and then the brainwaves that drive that anxious, negative thoughts are firing.

So what we've been able to see in the study is turning on the flow state wave, the theta wave. So now, you're much more functioning cognitively, much more in a relaxed manner, and the coping centers of the brain help you negate some of that cycling of negative emotions, right? So you get there, you might feel a little bit awkward still, but then you are able to go, "Nah, I'm fine. I can deal with this," go in there, pick and hone in on something and start working on it, whether it's a conversation with somebody or some other task and really overcome it much more easy.

Dave:

Have you ever had someone with stage fright, or some extreme anxiety try it? Have there been differences?

Kiran:

Yeah. Yeah, we have. So we had worked with a number of even people within the company itself that had a hard time getting up and speaking, which I think maybe the second most common phobia, right?

Dave:

It's actually the number one fear, at least in the US, the top fear, more than snakes and planes. Yeah.

Kiran:

Crazy or snakes on planes, which is even worse. So yes, we've been working with that empirically with our employees, and it seems to make a world of difference. So we dose them up 25, 30 days before we know they're going to have to get up and do a presentation and it completely changes how relaxed they are, how they feel before it, and how well they can prep for it because people who have that fear are prepping with the fear mindset, similar to that stress during studying for exams, which means your brain's not absorbing all that information, right? You're not in that flow state. You're not picking up the information and feeling confident about it.

Dave:

It sounds like it's magic if it can lower that stress even a little bit for most people. I have a couple friends who actually take beta blockers, and beta blockers, they're not blocking cortisol, but they're blocking adrenaline receptors in the brain, and it's the only way they can go on stage. So this is something that's well-known in nootropic circles is that you can do that. These are prescription drugs that lower blood pressure. Problem is lower blood pressure is also less blood flow to the brain when you might need it when you're speaking, and also, if someone asks a hard question, you need a squirt of adrenaline, it won't do anything. So you can be caught flat-footed. It's not a great hack unless it's the only way you can

and speak. So this might actually mean some of those people don't need to use a beta blocker when they go on stage just because they've now changed this gut bacteria. It's really profound, actually.

Kiran:

Yeah. It'll bring out their natural personality, their natural capabilities because it allows them to actually be themselves and have that level of confidence to be themselves without all of that negative brain wave function that occurs in them. So we've seen the most profound effects when you pair the two, when you pair the spores with the longum 1714. They work on slightly different mechanisms. The spore is ceiling up the leaky gut, reducing that LPS. This particular microbe, reducing the negative impact that cortisol can have, reducing the inflammatory response, modulating brain wave activity. Between the two when you add them together, we think of this as really great total brain support when it comes to the gut-brain access.

Dave:

That's so cool. There's more, though, from these studies. It's why I want to have you back on to talk about this because this is a brand new probiotic. It was a study. This is actually going back in the early days. It's 2016, but it talked about electrophysiology and neurocognition. In addition to modulation of stress, what did they find about cognitive function and neurocognition and the electrical brainwave stuff?

Kiran:

Yeah. So that was part of one of the early studies on looking at whether or not we can trigger the theta wave, which is that flow state that people want to be in, and then having them do recall exercises and so on. What we found was that we can actually improve brain function especially under a stress state and even under a non-stress state, right? So we know under a stress state, we've all been there when you're stressed, your brain is rambling in 100 different ways. You're not really functioning properly.

So we know that we can improve cognitive function in a stress state, but we also know that if you're not dealing with daily stress, it's still going to improve brain wave function and put you more in that flow state. The flow state is that where the artists and athletes and all feel like they're running, and they're moving at their highest peak, and it's really about shifting that brain wave.

Dave:

Wow. It's interesting, though. Theta, during the day, theta's the daydream state, right? When people have a trauma response to stress, quite often they'll disassociate and they'll go into a theta state. So I typically don't want too much theta during the day, unless I'm meditating in which case you want alpha, and these are broad. You need it at the right frequency within theta, at the right part of the brain, at the right time. It's a symphony. You can't say, "Oh, it's a tuba. Tubas are good." It has to play at the right time, right?

Kiran:

Totally. Yeah.

Dave:

So do you have data showing this is a healthy theta response during the day?

Kiran:

It is, yeah, because then we measure it against cognitive ability, right? So what we're seeing is that what you're doing is rescuing people from the disruptive brain waves, and then putting them in a better theta function, which means that they're calming down from that disruptive brain wave and getting to this more coping high functioning state, where then when we test their cognitive capability, they're actually responding better, and they're actually performing better.

So it's different than like what you mentioned with trauma, where you actually go into this full theta wave state and that's because you're trying to escape the trauma, like you said, going into a trance or green wave state. What we're really looking at is bringing back some of the theta wave that's not present and then allowing them to be calm so that they can actually function a little bit better.

Dave:

Okay. I like that. This is the first time that this has been available commercially, even though the study has been going on for a while.

Kiran:

It is. Yeah. So we're doing one more study, which is super interesting, which is at the Concordia station, which is in the Antarctic, and the researchers that live there live what would be a very exaggerated and accelerated version of how a lot of people in the modern world live, which is in isolation, and they live in a lot of darkness because there's good part of the year where there's no sunshine at all, in a very sterile environment because that station is especially sterilized because they're so far remote they can't afford to get sick. They can't afford to pick up a virus so it's so sterilized.

What they find, which is similar to what happens in the space station is their health declined so rapidly, and one of the first things they noticed is brain function, stress response, sleep, cognitive ability, and so on. So we're doing a one yearlong study where we're dosing up some of those researchers on the 1714 strain to see if we can negate some of that negative effect, and that's exciting because the conditions that they're in are much more accelerated form of what a lot of people do here. More people live more and more in isolation and don't interact with others and stay indoors a lot and so on. So that's another super exciting study that's going on.

Dave:

It's weird. This has very broad effects. I was really impressed when you guys reached out and said, "Hey, we should talk about this." I'm like, "Oh, we already talked about probiotics, and God, I talk about this lot on the show. I don't want to recover too much territory." It's helpful for listeners if we repeat some important things like corn oil is bad for you. You might've heard me say that before, and that's because not everyone hears every show and all, but this is really big new stuff, and really, the studies are mostly from 2014 and on, and it's taken about, that means about six, no, eight years for it to come to market.

One of the other things that stood out, though, and this is one earlier studies as well was looking at not just anxiety and depression and all the neurocognition stuff, but looking at visceral pain. Talk to me about that study.

Kiran:

Yeah. One of the things that we find is that the type of inflammation that is triggered by leakiness in the gut and that the increase in IL6, and especially with an increase in LPS because when the gut becomes leaky in response to stress, you're going to get LPS flowing through into circulation. One of the things

that LPS can do that is pretty egregious is bind into these parts of the neurons called nociceptors, and when it binds into these nociceptors, it triggers pain signaling.

So your body thinks you're injured, right? It's the same pain signaling that will occur if you have a physical injury, but you don't have a physical injury. You just have LPS in that part of the neuron triggering an inflammatory response, which is causing that nerve to send a pain signal to the brain.

So you've got all of these peripheral pains that you have no physical explanation for, and it can be not only, of course, really impactful in your quality of life just because pain sucks, but pain also leads to anxiety and depression, right? We know chronic pain, people who suffer from pain all the time tend to be in a very depressed state. So we took a look at that to see, "Wait. Is that something that can also be modulated because it works in very similar mechanisms?" Sure enough, we saw some benefits in that area as well.

Dave:

It's interesting. This week, we accidentally bought the wrong gluten-free baked thing. One of the local places where I live loves to use Garfava flour, which is garbanzo and fava beans.

Kiran:

Oh, wow.

Dave:

These are just nasty substances. It's one thing, if you're going to pressure cook your garbanzos or whatever, maybe they're going to be tolerable. They're probably still not going to be great, but fava beans are just, as a flour, they're not something you should eat. So one of the kids, "Oh, my neck is hurting," and my son, he's like, "My foot hurts. It never hurt like this," and it lasted for three or four days, and it's probably what's going on here. This stuff causes leaky gut. It's got lectins that cause localized inflammation, et cetera, et cetera, and if we measured his cytokines, his IL6 would've almost certainly been high.

Kiran:

100%.

Dave:

If he had this stuff onboard, maybe that response would've been different.

Kiran:

Totally.

Dave:

So I'm pretty darn excited to give this stuff a try. So like I said, it's probably on its way to me, but the studies here really blew me away when you shared these with me.

Kiran:

One of the exciting things we notice, which a lot of people report to us within I'd say the first four or five days, is the vivid dreams that they're having because it does.



Dave:

Oh, interesting.

Kiran:

Yeah. It puts you into really high quality sleep, right? So that is an exciting part, and I'd be super curious to know what kind of dreams you end up having, Dave, when you take it because they're going to be pretty vivid and fun.

Dave:

What if they're just embarrassing? Is that going to be a problem?

Kiran:

I think you should disclose it, anyway. I think everyone will want to know.

Dave:

Full transparency, all right. I don't know what the giraffe was doing in there. That's all I can say.

Kiran:

There's so much domestic animals there.

Dave:

Giraffes are weird. You ever seen two giraffes fight?

Kiran:

Yes. It's the weirdest thing, the way they use their neck.

Dave:

I love watching those videos. Their necks are wrapping around like that. It's like, "How could Mother Nature invent that?" The answer is the same way that Mother Nature invented a bacteria covered in polysaccharides that turn off stress and pain and cortisol. I'm like, "All right." There's a lot of freaky stuff out there, which is also why maybe we should stop spraying glyphosate on our soil because we're killing all of these species of bacteria that actually run the world. So I'm pissed off about that, too, but that's a question for you. What kills 1714, this new strain in Just Calm? Is glyphosate going to take it out? I'm guessing antibiotics take it out. What are the things that it hates?

Kiran:

Yeah. So absolutely, glyphosate will take it out. Antibiotics, most antibiotics will take it out. It's a more resistant strain than your typical bifidobacterium because of that peptidoglycan layer. So it will survive the digestive tract, the stomach acid, and so on, but most antibacterial chemicals will kill it. Unlike the spores that can survive through most of those things, it is sensitive in that way. So with the spores, we always tell people, "Hey, you can pull it out of the capsule, mix it in almost anything and take it and it's still good." With this, it's probably better to keep taking it in the capsule.

Then by the same token, those things going into your body, glyphosate, antibiotics, and all that will kill these kind of species, and that's probably one of the reasons why when you look at

fluoroquinolones, that whole class of antibiotics, one of the key side effects of that type of antibiotic is panic disorders and anxiety, right? So you take that kind of broad spectrum antibiotic, it kills off these kind of bacteria, and then now you're much more susceptible to anxiety and panic disorders.

Dave:

What is it like in terms of prebiotics? From my antiaging book, there's so much evidence for soluble fiber. If you're on a carnivore diet, I hate to tell, you're not getting that stuff and it's fine to go carnivore for a week, but you need to feed the stuff you want to have surviving. Does this strain eat meat? Does it eat collagen? Does it eat acacia gum? What are the types of prebiotics that you should take with it to make sure it sticks around?

Kiran:

It's exactly what you mentioned, soluble fiber, and that peptidoglycan is made from a lot of the same carbohydrates that come from soluble fiber. Bifidobacteria-

Dave:

So the standard prebiotic stuff that ... I know Just Thrive makes a really good prebiotic that tastes fruity. I don't know. I wouldn't put it in my coffee. I like it in just a glass of water and they also make capsules. So when I travel, I usually take the Just Thrive prebiotic capsules so that I know I've got some of that onboard. So that's at least enough to feed things even if I'm not getting 30 or 40 grams of prebiotic fiber a day like I normally do.

Kiran:

100%. Yeah. Those are oligosaccharides. Bifidobacteria, in general, love oligosaccharides, oligosaccharides being these unique prebiotic compounds. You don't need a whole lot of it to really increase the growth of bifidobacteria in general, including this longum strain like the exopolysaccharide that we work with, the XOS or the one from Kiwi, the Actazin. Those will actually dramatically increase bifidobacteria growth. So they love polysaccharides. Sorry. They love oligosaccharides, and they love soluble fibers as well.

Dave:

So if you're just tuning in or your head is spinning of what kind of saccharides, the basic deal is that you have prebiotics, which are a type of carbohydrate that your body can't eat but that bacteria love, and there's different kinds of prebiotics that different kinds of good bacteria love. If you get enough of those from food or probably these days from supplements, you're going to have abundant good bacteria, which fight off the bad bacteria, and then there's probiotics, which is what we're talking about here, the Just Calm, which is made by Just Thrive, and the probiotics are the specific species that eat the prebiotics, and then you have postbiotics, which is basically what the good bacteria poop out when they're done metabolizing something, and the most famous one of those is butyrate or butyric acid, which is made in the gut.

Funny enough, butter is named that way for butyric acid or maybe butyric acid is named because it's found in butter more likely, but the idea here is it there's a whole bunch of different postbiotics that we're just discovering. I've done several shows on, "Oh, wow. Look, you can't get this postbiotics because you don't have the right probiotic because you don't have the right prebiotic."

So what I'm hearing you say is that if you want the Just Calm strain, the bifidobacteria 1714 with all these special powers, you would take the probiotic. You could hope that you're getting enough probiotic or you could take some probiotic along with it. Guys, you need to be taking a prebiotic if you want to live a long time. The evidence is very clear, and you probably want to take a lot of it unless you have SIBO, which is we're not going to go into, but small intestinal bacterial overgrowth. So if you take a prebiotic and then you fart death for a week, well then you clean that up. That's a different episode. Then we get into postbiotics. What are the compounds that are being made by this strain of bifido that's causing all this? Do we know?

Kiran:

Yeah. So the main one is that peptidoglycan, that it's making and releasing into the system. We know that it also impacts serotonin and melatonin production. It also impacts dopamine production. That may not be a direct synthesis of those compounds by this strain, but it's certainly helping the system create that.

One of the things we talked about earlier is tryptophan metabolism, right? So if it's bringing down that inflammatory process that occurs during a stress response, it's allowing tryptophan to actually be metabolized or synthesizes down into serotonin and melatonin. So we'll see all of those protective neurotransmitters going up as you start taking this strain. So at the end of the day, I think it's that peptidoglycan that's really important.

We also know, and we don't know exactly what this is just yet, but we do know that this strain has a way of binding to receptors on the intestinal lining and creating a neurotransmitter release that impacts the brain. That may be part of how the brain wave changes occur. We don't know exactly what those neurotransmitters are, which we're working on right now, but we do know that it does some positive neurotransmitter effect that goes directly up the vagus nerve and impacts the brain.

Dave:

Wow. That's incredible. Do you think that we'll have a time when we can just take the glycans directly or it seems more efficient to just have onboard production here?

Kiran:

That's exactly right. Yeah. I mean, I think you could probably take the glycan to a certain degree, but having that peptidoglycan factory in the gut is going to be, I mean, that's where you really get the long-term benefit because the goal is, let's say you take this for some time and you take the right prebiotic with it and you grow enough of this bacteria within your system, then maybe you can go to not having to take it every single day, and knowing that if you miss it for a little bit, you're still going to have that onboard effect.

Dave:

So that was my next question. So I take the Just Thrive, their standard probiotic that reduces lipopolysaccharides, just stupid amounts, and I think it's been beneficial for me, and I take that almost every day. Some days I miss it for whatever reason. Do I take the new Just Calm every day as well? Can I take it every other day? I mean, people are always trying to economize. What's the regular dosing schedule. Do you take it in the morning, take it at night? Just how do you use it?

Kiran:

Yeah. So this one is just one a day and you can take it at any time during the day. You can take it with a meal or without a meal. We haven't found there to be a big difference between whether taking it in between or with a meal. My recommendation to people is always for the first almost two months to try to take it every single day because more than likely, you tend to be low in peptidoglycan-producing microbes in our gut. That's just the fact of living in a sterilized, antimicrobial modern world.

So getting a lot of this organism back in and starting that peptidoglycan metabolism in the body is going to become really important. Typically, after month two, you'll find that you could start forgetting some doses and be okay. You might even be able to go two or three times a week on a regular basis of taking it and not seven days a week. People can play around with it a little bit once they feel the mood changes, they feel the stress response changes, they feel the sleep changes. They can dose it back and scale it back. For me, for example, right now, and I've been taking it now since I think September, and by December, I was able to forget to take it two, three days and be totally fine and still feel the ongoing effects.

Dave:

So what we're doing here is a farmer, right? First, you till the soil. That's your prebiotic. Then you plant the seeds and you got to plant enough of them because some aren't going to make it, and eventually, it can become self-reproducing, but you probably still need to tend the system by adding more. It makes sense. I think most probiotics are like that. You take them religiously for a while and then you take them often enough to get the benefits, and it will colonize the gut and reproduce by itself if you're taking prebiotics, but you still want to keep the strain coming in. Okay. I get it.

I'm really excited about this, the research. I mean, it's eight years of research, just coming onto the market, and I tend to cover stuff like that on the show where we didn't know we could do this before, and for every one of these that I find, people always bring me 10 other things and I'm like, "There hasn't been any research to that," or copying something that's already out there, but this is new and really, really interesting. So I appreciate all the work you've done on it, and we've got, what, five studies we just talked about and there's probably some other ones, too.

Guys, go to [justthrivehealth.com](https://justthrivehealth.com), use code ASPREY, and they'll give you 15% off if you want to give it a try. I am, as soon as it arrives to my house, I'm going to be doing this for several months, and if I see the changes in that first month and I'm having crazy dreams about giraffes, I have no idea why I mentioned giraffes, but I'm just picturing them fighting again and it makes me laugh, but whatever crazy dreams I may have, if you see a change in dreaming, that's a sign something very substantial is happening, and that could be from the theta state because theta is where dreams happen.

Also, also all the stress reduction and things like that, and cortisol regulation, this is apparently a really strong mega, mega multiple channel probiotic that didn't exist before. So I hope you enjoy giving it a try. It's called Just Calm and it's made by [justthrivehealth.com](https://justthrivehealth.com), code ASPREY.

Thank you, Kiran, for just doing cool and interesting research and knowing what you're talking about, and also for being able to talk coherently about it. We got pretty geeky here, but-

Kiran:

We did.

Dave:

... not so geeky that I think someone who's paying attention would be unable to follow it. Except I was watching the Upgrade Collective here, our live studio audience, and I was noticing in particular, Larry. He

looked just completely like he just didn't understand a single thing here and I was feeling embarrassed on his behalf. I'm just kidding, Larry, but if you guys are interested in joining the Upgrade Collective, go to [daveasprey.com](http://daveasprey.com). There's information. This is my mentorship and membership group, where you get to be a part of a small studio audience during the podcast and part of all the classes I teach on my work. I'd love to see you there, and it's a lot of fun to do it. Again, just [thrivehealth.com](http://thrivehealth.com), use code ASPREY for 15% off. This one is worth a try.