The Gut Brain Axis: Overlooked and Undertreated

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Sean: Welcome to the Digestion Sessions.

Dr. Datis Kharrazian: Pleased to be here.

Sean: Pleasure to have you here. Now, my presenters, I feel like most of them have learned from you. Your name has come up many times. You're super-smart. You know all this stuff, inside and out. You know what I'm curious about – because I read a lot, right? – what's the process like for you, when you study this stuff?

Dr. Datis Kharrazian: The process, it starts with being in the clinical practice, so basically I work with patients and situations come up where I don't have answers for them. And I don't know, and that really bothers me. So what I try to do is I try to go through literature search – just spend at least three to four days on PubMed, and then I basically, at this point, can really speed-read abstracts very quickly.

And then I get the full paper, and once I get the full paper I re-draw it and put it all out. I'm really lucky because I can remember papers from years ago, and I store them really well and I can put them all together and I can kind of put the links together. I think my contribution from what I'm told, is try to link all the different concepts and principles together and make it then clinical.

So I take the information that is reviewed through the literature, and I apply concepts to my patients in my clinical practice, and then, once I feel comfortable enough, I'll then teach it to practitioners. That might take a year or two before I feel comfortable enough.

And then once they learn it, I get feedback from them, and I get whole new sets of eyes because they're all trying different things and making different observations. And then we create new clinical concepts in that whole process as well.

Sean: So you can take it, refine it?

Dr. Datis Kharrazian: It's constantly being refined, it's constantly evolving and it's changing. Sometimes, you know, you look back at old patient files – sometimes a patient, for medical reasons, needs an old file – so you go back and pull it out. Maybe it was two years ago. I always look at my notes and go, "Oh my God, I'm so embarrassed, I don't want to send this out." Or even look at old papers you've written or old books or whatever, you look back and go, "Wow, I wish I had never did that. This looks so outdated."

Sean: I first became aware of you with your thyroid book. Amazing book. I love that book! And then your next book was on the brain – it's *Why Isn't My Brain Working?* And I read that at least two or three times. Phenomenal book. Well-written. It's good stuff. I think everybody should read it. Why did you become fascinated with the brain?

Dr. Datis Kharrazian: I think, for me, I really don't have a personal preference. I don't really like the thyroid, I don't really like the brain, I don't really like any of this. It's just a matter of "What does my patient have?" I have a person who's suffering. What are they dealing with, and what do I need to know?

And the thyroid was one of these things where, when we were working with thyroids from an autoimmune perspective – 'cause up until my thyroid book in 2009 I was teaching that material way back in 1999. I have seminar material from 1999 that is the book of 2009 that is supposed to be revolutionary. We would teach – we were using that model for years and years and years.

And one of the things that happened is, we figured out a way to really help thyroid patients, and we realized that it's not just about tyrosine and iodine, axillary temperature and goitrogenic foods – this was all outdated, ridiculous information from constantly looking at lab work, trying different things and seeing patients change.

So for the first book I wrote, *Why Do I Still Have Thyroid Symptoms?*, it was really, "Hey, look at this from an autoimmune perspective. Look at all this research of all these things that trigger

autoimmunity. Now we know all these things like TH1 and TH2 and here's how we apply all of these concepts."

And at that time we were doing a lot of immunology cytokine testing, and it really helped us put it together. Now we look back and we're thinking about revising the thyroid book because we have TH1, TH2, TH3, TH9, TH21, TH22, TH17, and we're learning how to use all these things in a clinical setting so we want to share that. But, you know, everything takes time.

Sean: When can we expect that? 2016?

Dr. Datis Kharrazian: I don't know.

Sean: One day, it will be out.

Dr. Datis Kharrazian: Soon, I hope!

Sean: We're talking about the brain today. We've got Alzheimer's, we've got dementia, we've got anxiety, we've got depression, and you say this is linked to the gut. Break that down for us.

Dr. Datis Kharrazian: So one of the most neglected things that I think most practitioners don't understand, whether they're conventional or alternative, is that there's this brain-to-gut axis. And there's actual journals called *Brain to Gut*. There's multiple papers written on so-called brain-gut axis and gut-brain axis, and so in the scientific world it's a pretty prevalent area of research, but in a clinical setting we don't have that.

We have the average person who's into diet and nutrition, and they're really thinking of, "Here's my digestive enzymes, here's my bone broth, here's my glutamine, here's my Paleo diet," and they kind of live in that world and anything that's wrong with the gut has to be an infection or food or yeast overgrowth, right?

But when you work with a lot of chronic patients, what you realize is some of these chronic patients really have impairments in their brain-gut axis, and many neuro-degenerative diseases start in the gut. One of the first things I think people should know about if they have a digestive disorder, and how to clinically differentiate if the brain is involved, is, is there a motility issue or not? Because motility is brain-based.

Sean: Define motility.

Dr. Datis Kharrazian: Motility means how you move foods; when you eat something and when you have a bowel movement, right? Do you have constipation, do you have to drink coffee to have a bowel movement, do you have to take magnesium or some kind of laxative to have regular bowel movements, right? And if you do, that could very well be a brain-to-gut axis issue.

Because motility – the movement of food through your gut – is really a brain phenomenon that your brain has to fire your brainstem vagus nuclei and your vagus nuclei then fires into your gut to your enteric nervous system, and then you activate what are called migrating motor complexes and then you have motility and movement.

So, if you have a chronic digestive issue and part of the component to your digestive issue is you just don't have healthy amounts of bowel movements and your digestion's a little bit slow and you're constipated, then you gotta look at this as having a neurological or what we call a neurogenic component.

Sean: Always, or…?

Dr. Datis Kharrazian: Well it's something you have to clinically rule out. It's not always, but then that's like, "Hey, this is something I gotta rule out, 'cause if I don't, I can totally fail at this case." Right? And unfortunately, many practitioners fail on those types of cases, and they become chronic and they go from one practitioner to the next and to the next. So the red flag is, "Hey, I have a gut issue no one's been able to figure it out, and I've done every kind of diet and I've done every kind of supplement and no one can figure out my gut."

One of those, when they have motility issues, are really brain-gut-related issues, and here's the thing: when you lose motility, you don't move your food. When you don't move your food, it ferments, so you get bacterial overgrowths, you get yeast overgrowths. When you don't have gut activation from your brain you don't release enzymes. You get enzyme deficiencies.

You create the environment for parasites 'cause you don't have enough hydrochloric acid released, digestive enzyme release is actually brain-based. So over a period of time, if someone has a brain-gut issue, and if someone does a digestive workup where they do like a lab test, they're gonna see abnormal bacteria counts, they're gonna see abnormal bacteria species, they're gonna see yeast overgrowths, they're gonna see bacteria overgrowths—maybe even see yeast infections.

And obviously you would go, "Well let's go and treat all those things." The only problem with some of these patients, they've had all those things treated *forever*. And it's not helping.

Sean: So you're saying that the brain is where the signal comes from to get stuff moving in the intestines, help things move along properly. Now how does one rule that out?

Dr. Datis Kharrazian: So, the first thing is from the history: is there a motility issue? And the motility issues you would look at: Do you have to take laxatives? Do you have to drink coffee to have bowel movements? Is your bowel movement slow? How many bowel movement do you have a day, right? And that's your first clue. In a clinical setting, what we do is we listen to the abdomen. If you have a stethoscope you can do it yourself, but you may not have the ear to know what you're looking for.

So from a clinical setting, well, I should take a stethoscope and listen to the abdomen, and then you should hear bowel sounds. Bowel sounds should have an intensity, like, "RURR!" Like "Rur-ur-ur!" It's gonna sound like that. And it sound have a frequency. So, here's a normal bowel sound, for example: "Rubburt, rubburt, rubbut—"

Sean: Oh, I've heard it before! Yeah, yeah.

Dr. Datis Kharrazian: And here's what you hear when you see brain-gut axis and motility issues, you hear like: "Grt……ert…" It's telling you that there's no activation going on; that those muscles are not contracting, right? The other thing that we do is we look at vagal function.

Vagal function, clinically, as you see it through a cranial nerve exam – so, one of the things we look as we look at the back of the throat and the pallet, the punching bag, and you have these arches, and those arches are innervated by the vagus. And if the vagus is failing, which is the area of the brain that fires into the gut, when people say "aaaaah," their arches should move with the punching bag in the middle.

Sean: Right.

Dr. Datis Kharrazian: It doesn't do that. It just—

Sean: The uvula, right?

Dr. Datis Kharrazian: The uvula, right. But we're not really concerned with the uvula. We're looking for the arch. Sometimes if it's really bad you'll just see the arch totally falling when they say "ahhh," nothing moves. Sometimes when they say "ah" nothing moves, and other times, when their brain is starting to degenerate, neurons, when they start to degenerate, come closer to threshold, so they spontaneously fire on their own.

Sometimes when people just say "ah" and stick out their tongue, they starting going into a gag reflex, or sometimes you can't even get a gag reflex with people, and sometimes you just touch the tip of their tongue and they already start having a gag reflex. People call those exaggerated gag reflexes at times, but they're not always exaggerated.

Those are sometimes developed over a period of time in that area of the brain stem where the vagus is degenerated. So we look at the history for motility. We would expect if the motility is wrong to have all the digestive enzymes, leaky gut, bacterial and yeast overgrowth history that comes with it.

Then we listen to their bowel sounds, clinically see if those are okay, look at the uvula, see in their pallet and see if they're having activity there, look at their gag reflex. And if those are impaired, we know that there's a brain to gut axis issue. And it's probably a handful of people who would know to do that, and people that do, fix chronic gut patients.

Sean: Hm. I remember from your book, gargling and singing are good for getting that vagal tone and getting that going again, right?

Dr. Datis Kharrazian: Right. So my brain book that I wrote, I have a whole chapter on the brain-gut axis and I'm trying to get this information out to as many people as "this, without question, works." We've really been able to help a lot of chronic gut people that have this. So here's the first thing: if a person has a brain to gut axis disorder, they're not gonna fix it with digestive supplements for their gut.

They may still need it to function properly, 'cause their brain isn't making them produce enzymes. They may need to take enzymes. Their brain vagus isn't firing so they can't get blood flow to the gut. They'll have leaky gut. So they'll probably feel better taking digestive support and changing their diet and having a clean diet so they don't have as much inflammation and bloating and swelling, but that's not gonna fix it. They have to start from the brain down.

And when you look at supporting from the brain down, you really can't just do it with a supplement; you have to develop plasticity. You have to develop connections, right? So neurons have to fire into each other for you to have your brain firing to your vagus, you vagus to fire into your gut nervous system, and then for those migrating motor complexes to work.

And that neurological firing pathway not only helps motility, but it's the pathway that helps you neurologically release enzymes, and neurologically fire your parasympathetics to get blood flow to your gut.

Sean: I want to back up a little bit. Migrating motor complex. Dr. Siebecker covered that, but just in case somebody didn't watch that, what does that mean?

Dr. Datis Kharrazian: So the migrating motor complex is just a group of what they call motor neurons, or muscle neurons, and your intestinal cells have what they call smooth muscles, and those are the neurons that cause you to have your intestines contract and move.

Sean: Okay.

Dr. Datis Kharrazian: And control your bowel function.

Sean: Okay.

Dr. Datis Kharrazian: But that's all controlled by brain function, right? So if you have a person who's lost their brain-gut axis, we clinically know we can't just have them take a digestive supplement to treat it, and we go into three main things we do—and I cover this in my book. One of the first things we do is we have people gargle, and this is something that was done in the functional neurology world for a long period of time—people that had head injuries and things like that.

But gargling is you take water, put it in the back of your throat and go "ahhhhg." You fire those pallet muscles, which are fired by the vagus. The key thing when we have patients do it is to sometimes understand the intensity they need to do it; they need to do it—basically, do it to the point of tearing, y'know? So it's not like, "Uhh," it's like they take the water, pull it back and go "AAHHHHHRR—"

Sean: So you're working it out.

Dr. Datis Kharrazian: Yeah. And then the area of the vagus is right next to an area called the superior salivatory nucleus, which causes you to tear. So you hit the brain stem aggressively enough, you'll start to see the tearing. So we ask patients to gargle aggressively enough until they have tearing. And if this area is a part of the brain that isn't functioning well—it's degenerating—they're gonna have a really hard time gargling, or they may gargle for three or four seconds and they just may choke and spit it out.

So you may have to start with a small amount of water and kind of build up over time, they can do it for several minutes really aggressively and they're tearing and they're tearing and they're tearing, and that's how you activate it: through an activation pathway. The other thing that patients do is we have them take—go to Amazon and buy a box of tongue blades, and induce a gag reflex.

Not in the back of their throat, so they don't injure themselves, but just to push down on their tongue. If they push down on the back of their tongue they're like "!" and gag, and their eyes will start to tear. As they do that, they're actually firing that pathway, and it's just like having weak biceps. If you have weak biceps, you have to activate it by doing curls. If you a weak vegas brain to gut connection, you have to activate it to really develop those connections, get that plasticity going.

The third thing we do, and this is really important, is we have patients do a coffee enema, but not for detox reasons. What we want them to do is we want them to do a coffee enema, and the coffee has the caffeine, and the caffeine stimulates gastrointestinal nicotinic cholinergic receptors, so it makes your gut kinda move. That's why a lot of people who are constipated do coffee enemas.

But we want them to get enough coffee and saturate it enough so that they have to force themselves to suppress their bowel movements. So if they lay on their side and do a coffee enema, they might have this urge to have a bowel movement, and if they don't have this urge we need to have them increase the concentration of the caffeine in there.

And they just hang out there as long as they can, suppressing the urge, and as they suppress their urge they're firing their frontopontine vagal enteric axis. If they keep doing that, they build endurance and they start to regain their brain-gut axis.

Sean: You just hold it as long as you can?

Dr. Datis Kharrazian: You hold it as long as you can and then you concentrate it as long as you can so that it becomes difficult. It's like kind of getting—you know, adding plates to your bench press. You have to increase the intensity to make yourself work harder. So those three things we do seem to have a really good impact on impacting the brain to gut axis.

At the same time, you want them to have a clean diet and digestive enzymes and support their intestines because we don't want the inflammation there; because the pathway goes from gut to brain as well. But the most area that's neglected with a lot of chronic digestive people is failure in their brain to gut axis. That's why I wrote a whole chapter about it in my book.

Sean: Going back to gargling, several times a day, are they doing this?

Dr. Datis Kharrazian: Right. So the key thing is to do it multiple times a day. We have some patients we say, "Listen, every time you watch—if you watch TV—every time commercials come on. If you read a book, every time you finish a chapter. Every time you use the restroom, gargle." Just so it becomes part of a routine thing. If you ask a patient to just do it sometimes, they don't remember, so you try to correlate it with something they do.

Like I just saw an athlete – college football player – and he's eating two hours a day. Every two hours, he's eating. Like "great, every two hours do your brain exercises." He had a different area than the gargling, but it was just a way to remind him to do it. But usually if they can get it in a dozen times a day—'cause they don't take that long, it'll take like a minute, right? It's not like you're working out and getting exhausted afterwards.

Sean: Gotcha. Tongue blade as well? Several times a day?

Dr. Datis Kharrazian: Yeah.

Sean: Gotcha. Coffee enema, daily?

Dr. Datis Kharrazian: Yeah, once a day.

Sean: Gotcha, okay. And hold it as long as you can. Alright. Good stuff. How common is this brain issue as being involved with the gut?

Dr. Datis Kharrazian: Depends. If you see the average patient, it may not be that common. If you see chronic patients, it's very, very common. If you see failed patients no one's been able to help, it's one of the most common things you see because it's an area that everyone overlooks.

Sean: Was I wrong about the singing thing? Was singing actually part of the treatment?

Dr. Datis Kharrazian: Yes, that's right. Thank you. Another way you can activate the vagal muscles in the back of your throat is if you sing really loudly, and it's fun for people do to that as well.

Sean: Okay, gotcha. So again, brain signals coming from the vagal nuclei, was that it? I want to do a quick review.

Dr. Datis Kharrazian: So here's how this works. we have an area of the brain: the frontal cortex, that's where your motor activity...that fires into your brain stem vagal motor nuclei, that fires into your enteric motor system. You also have brain fibers from other parts of your brain called the insular cortex that fire into somatotopic areas and autonomic areas that control your blood flow and digestive enzyme secretion, but I kind of wrote them out in the book, and I don't know if people are interested in that—

Sean: Oh yeah. They're interested in all that stuff. Get the book.

Dr. Datis Kharrazian: But you know, you know. Whatever you want to talk about.

Sean: Gotcha, okay. And so, if that's not firing properly, you said that won't fire the enzymes as well?

Dr. Datis Kharrazian: Right. So, as you look at brain activation through the hypovolemic areas of the brain, through the insular cortex areas of the brain, they fire into the brain stem area called the nucleus ambiguous, and the nucleus ambiguous is an area that controls autonomic function to the gut. So you have sympathetic function and parasympathetic function.

So, parasympathetic function for the gastrointestinal tract is going to cause blood flow there, and it's going to cause digestive enzyme release, and it's going to cause motility. It's gonna cause valves functioning and doing their things the right way. So there's brain control for not just motility but digestive enzymes and blood flow and circulation issues.

Sean: Okay. Let's go back to the motility issue. The motor complex—migrating motor complex. I talked about that with Dr. Siebecker.

Dr. Datis Kharrazian: Great lady.

Sean: Yeah, she's awesome. She's super smart, and lots of energy! I think that was my longest interview, 'cause she was going! It was awesome! Now, you've kinda covered this already, but I want you to go into it again, so it really sticks. Talk about what the brain has to do with SIBO.

Dr. Datis Kharrazian: Okay. Well here's the thing: small intestinal bacteria growth is one of those things where it's becoming much more popular, and the thing with it is, the concept is, you lose your bowel function and your bacteria that's in your large intestines starts to migrate into your small intestine, and then you have this abnormal small intestine bacterial population, and then the bacteria in the small intestine is very reactive to yeast and galectins and other types of probiotics and foods, and people eat something with a little starch in it or a little fiber and they get severely bloated. Right?

But it initially starts with a dysfunction in the migrating motor complex. It starts with a function in valve control, which is all neurogenic-based. This is why I get so frustrated with the world of SIBO right now. I'm going, "Listen, guys: look at the mechanism of what causes it. It's a valve dysfunction and a migrating motor complex dysfunction! It's a brain-based phenomenon!"

Well, it's not all related to the brain failing; sometimes the gut nervous system fails, because the gut nervous system is an area where you have neurodegeneration too. Just like the brain can degenerate away, the gut nervous system can degenerate away too. So, whenever we see a patient that actually

has true SIBO and have the diagnosis, we're pretty much looking with the majority of them having the degenerative neurological gut issue, or a brain to gut axis issue.

And there are some people who have SIBO from surgeries and anatomical things, but for the most part, when it's developed without surgery, we pretty much know those are the main things. And if we would just sit back and do a neurological exam on them, or just to sit back and just evaluate them, you can see many of them have early signs of Parkinson's, some even have had traumatic brain injuries and two years later that started. And it's one of the most common missed things when you work on chronic patients.

Sean: If I remember correctly, I believe she said that there are particular drugs that help to stimulate that motor complex now. Can you get rid of those and not use those by training the brain?

Dr. Datis Kharrazian: Right. Exactly. So in the conventional world, they use prokinetic drugs.

Sean: There you go. That's the word.

Dr. Datis Kharrazian: And these drugs and there to stimulate acetyl-choline receptors or dopamine receptors or serotonin receptors as an attempt to make gut motility happen, and then they give 'em antibiotics that don't get absorbed so they can kill the overgrowth. But the effective treatment is very, very poor when you look at recurrence rate; there's almost a 100 percent recurrence rate. So, it doesn't fix it, right?

Sean: Right.

Dr. Datis Kharrazian: And then at some point, with any type of neurotransmitter-stimulating drug, whether it's an antidepressant or a prokinetic, neurotransmitter receptor sites develop resistance to it, and they just stop working. And this is what's so frustrating, it's like...fix the problem. Fix integration. Right? So simple things like gargling, simple things like singing.

Coffee enemas, we hold it instead of just trying to do a detox with it and have an immediate bowel release. Tongue blades, gag reflexes, those are really, really key things to try to rebuild that system. Here's the deal, though: unfortunately, there are some people that are so progressed neurologically that their gut has degenerated away so far, you can't do much.

That's why early treatment, early identifying and treatment is the best chance you have. Just like with all brain-degenerative disorders, you really want to see the early signs of Parkinson's with someone and immediately start doing things for them. Soon as you see a child have autistic behavior, you want to go in there and start doing stuff for them.

Because there's also what's called negative plasticity: as time goes on, you get abnormal firing of pathological pathways, and as time goes on, neurons die off and then there's less potential chance to make connections with them, so you gotta catch it early. And if you catch it too late, there is a point of no return.

Sean: I feel like we're always looking for foods and supplements that are gonna help. Are there any foods or supplements that can help stimulate the brain?

Dr. Datis Kharrazian: Yes. So, at the end of the day, when you look at anyone who's got a brain to gut axis issue, the reason they have it is usually because their brain is really the problem. The brain is really what's degenerating. Or their gut is starting to degenerate.

So let me kind of give you some of the most common examples: Parkinson's disease, for example, one of the most common diseases out there—neurodegenerative diseases—and when we say Parkinson everyone's always thinking that it's older people, but about 15 percent of—some would even say 20% of people with Parkinson's start at early-onset Parkinson's, so they're before age 35. So it happens in young and older people.

But Parkinson's disease starts in the gut. Parkinson's disease, people think of it as the area of the brain called the substantia nigra, where dopamine is failing to deplete. That's not what Parkinson's is.

Parkinson's is what they call an alpha-synucleinopathy. This is where a protein called alpha-synuclein builds up in between nerves and the nerves can't communicate, and they start to degenerate off.

But the alpha-synuclein protein buildup that then leads to degeneration starts in two places first: it starts in the gut – so people start to get gut degeneration – and then it goes into the olfactory bulb so people lose their sense of smell. And they don't lose it completely in the initial stages they just aren't as sensitive to smell, and when they lose their sense of smell, they lose their sense of taste.

So whenever you see a person coming in and they're complaining of stiffness, which is one of the early signs of Parkinson's, and then we talk to them and they just say that don't enjoy eating

anymore, nothing really tastes good, they don't have any joy with that anymore, or they don't really know it's that but it's—they just don't like to go out anymore to eat, or do anything. And we see they have constipation and have to use enemas and things like that to get bowel motility. That's sometimes the earliest presentation of Parkinson's disease, right?

So sometimes with these disorders, what we're really seeing is an early neurodegenerative disease, and that takes an aggressive approach for a brain, other than just taking a supplement. In my brain book I cover 20 different chapters to kind of address all the different things that can be involved whenever you have a brain failing like Parkinson's, to try to get it to function better and slow down some of the process.

Other times, the brain-gut axis issue isn't because the gut's degenerating first, it's because the brain is degenerating. And this is with things like dementia. What people may not realize is when they have a hard time with directions and it's getting worse, and they can't find their phone and they can't find their keys all the time and have to write everything down, those are all early dementia symptoms. And that's the second. That's one of the other second major neurological diseases.

And as the brain starts to degenerate, the majority of the brain's output is to the pontine area where you have the vagus. So you get neural degeneration, you get less activation to the pons, and then you start to get gut functions. As a matter of fact, 90% of the brain output—not input, but output

—is to the pons, and in the pons you have your vagus. So with almost every neurodegenerative brain disorder, you start to have failure in the brain-gut axis, at some point.

Sean: What'll be like those top supplements that can help to—

Dr. Datis Kharrazian: Support the brain?

Sean: Support the brain, yeah.

Dr. Datis Kharrazian: What's most important in supporting the brain, the top supplements, you first want to...well, we start with diet, or...clinically, we start with that, but let's start with foods—I mean, supplements. Supplement-wise, the basic things are...y'know, here's the thing: it's a tough question to ask me because that's not how we think.

We kinda...the way I try to teach it to people is through my book, in the sense that in the beginning of each chapter I give a list of symptoms. So here's all the symptoms of neural inflammation, here's the symptoms of low oxygen to brain, here's all the symptoms of low blood sugar to brain, and then we kind of look at it from that perspective.

Sean: Gotcha.

Dr. Datis Kharrazian: So it's not that—

Sean: Specific to the person.

Dr. Datis Kharrazian: But if I were gonna pick one— if I was on the spot to pick one, I'd say— the vagus is an acetylcholine-based pathway. The gut moteric system is what's predominantly acetylcholine, and botanicals that can improve acetylcholine activity can have the...y'know, just the...first guess effect. Huperzine being one of them, galantamine, being the other one.

And what they do is they increase the sensitivity of the acetylcholine receptor, and they inhibit an enzyme called acetylcholinesterase, and what that does is it allows the acetylcholine to hang out in between neurons and synaptic cleft longer, and that makes the receptors more sensitive. So some people, if they're just struggling and they need to do something to get their vagus to fire more or their brain to fire more or their gut to fire more, they can take things like huperzine or galantamine.

They're over-the-counter, there's no major side effects for most people, and there's no withdrawal reflex—withdrawal response where if they stop taking it they have any problems. It's just…y'know, you can try it. But there's the dose, they have to find out.

So the dose is not based on bodyweight and it's not based on age; it's just you start with one and see if you get an effect, and then if you get an effect, you increase the dose until you get a maximum therapeutic effect, 'cause there'd be a point where if you take six capsules versus five, you don't notice any benefits. You may not really feel it at one, so you have to get to three or four before you feel it, and five is where you have the best effects. So that's helpful to support the brain nutritionally.

Sean: That's huperzine and what, again?

Dr. Datis Kharrazian: Galantamine.

Sean: There's a thing that's gonna fly off the shelves now.

Dr. Datis Kharrazian: Galantamine is getting harder to find now because it's also classified as a drug, but with the FDA guidelines has it being a natural supplement, so what's happening is many factories are just not carrying it anymore 'cause they don't want to have any FDA issues because it fits the label as a drug and it fits the label as a natural supplement.

It's the most common used treatment for dementia and Alzheimer's in the world, but not in the U.S. So in most countries they use galantamine, and it's just a botanical and it's pharmaceutical-based and that's what they give to dementia patients.

Sean: It's too bad it's not used here. I want to get to di—

Dr. Datis Kharrazian: It is available. It's harder to find.

Sean: Gotcha. I want to get to diet a little bit later. Let's get on the brain's impact on leaky gut. How are those connected?

Dr. Datis Kharrazian: So there's been some really interesting studies done with brain and leaky gut. And, you know, we call it leaky gut in the literature and they call it "intestinal permeability," that's why we have some people go, "hey, there's no research on leaky gut," 'cause they do a literature search for leaky gut and they don't find any papers, right?

So if you're doing a literature search, look for "intestinal permeability." But with intestinal permeability, there's research now and they've done a lot of animal studies—they have to be animal studies—where they induce traumatic brain injury, and they can measure leaky gut within three hours. This has been repeated with at least a dozen studies, now.

Sean: It happens that fast? Three hours?

Dr. Datis Kharrazian: It's that fast, yes. Immediate. Sometimes even sooner in other papers than three hours.

Sean: And what are they doing to make that happen?

Dr. Datis Kharrazian: Well they're actually taking a control group and looking at their gut, and they take another group and induce traumatic brain injury. And then they look at their gut within a few hours later and they start to see when they start to develop leaky gut. Their intestinal permeability changes.

They did one paper, which was the breakthrough paper, and they did this with rats. They took one group of rats and they caused a traumatic brain injury, knowing they were gonna get leaky gut. They

took the other group, caused brain injury, but they electrically stimulated their vagus, and when they had electrical stimulation to their vagus nerve, none of them developed leaky gut.

Sean: So the brain injury is causing some vagus—

Dr. Datis Kharrazian: And that was the paper that really defined that it is the vagus activation, and when it's not being activated is causing leaky gut. And it really—for us, it reaffirmed the fact that, hey, when we have people gargle and we have people activate their vagus and any of those things, it's really...we clinically see it work, but this is a great paper because it connected those, too.

So those studies are really interesting because with acute brain trauma you see connections really quickly because you have an immediate dramatic loss of brain function, and then you see what happens, right? But people sometimes don't have an immediate loss of brain function; they have a neurodegenerative process, which happens slow over time. But the same consequences happen: as the brain starts to fail and not function, it can't fire into the vagal areas, and so you get leaky gut and those types of things as well.

Sean: I can't help but think about football players. They get head injuries all the time, causes issues with the vagus nerve. That can cause digestive problems as well as intestinal permeability, which can lead to dementia and other brain issues, correct?

Dr. Datis Kharrazian: Absolutely. And that's published. And they do have human studies on that, and what they find is human subjects that undergo traumatic brain injury also have intestinal permeability and leaky gut. What they have also found is traumatic brain injuries, not only do you get leaky gut but you get immediate inflammatory reactions in the gut.

And if anyone works with traumatic brain injury people like I do all the time, they almost all have chronic gut issues. And here's the problem: they go see someone and go, "well the gut's going to fix the brain, so let's put you on a probiotic and let's put you on this," and you're like "whoa whoa whoa, we've gotta treat both!"

Sean: Right. So I want to make sure I'm clear on this one. So the vagus nerve, what does that have to do with how the intestinal lining builds itself? With the cells that are going on there, that lining.

Dr. Datis Kharrazian: Well, the vagus nerve has a motor component, which you have motility.

Sean: Right.

Dr. Datis Kharrazian: And it has an autonomic component, okay? The autonomic component is what allows you to have blood flow to your gut. Don't forget, your blood carries everything to your gut. All the digestive supplements you take, all the foods you take, all the things to heal your gut get there by blood. So if you lose the ability to get blood to your gut efficiently, you're not gonna get nutrients to your gut. So that's the first, kinda basic thing.

Also, to regenerate cells you have to have growth factors and hormones and other things get to your gut. Testosterone, progesterone, estrogen, thyroid hormones that all cause your gut to repair, as well as other peptides. So as blood flow becomes compromised from lack of vagal activity, you lose the ability to give your gut what it needs to regenerate. That's why we see so much leaky gut issues with people who have either traumatic brain injury or neurodegenerative changes to the brain.

That's what we see with autistic kids. Autistic kids have brain development issues and everyone thinks, "well it's a gut issue that's causing autism." Of course everyone sees the connection between gluten and dairy, but you see very few autistic children really have their brain treated well, you know? They kinda just get a fish oil or…you know? And unfortunately, if they can't treat their brain-gut axis, there's a problem.

And if you don't treat the brain-gut axis, then you have a gut to brain axis, because as the gut starts to get inflammation and create these inflammatory reactions, those inflammatory reactions in the gut have an impact on the brain, and this is what they call the gut to brain axis, and this is where inflammatory cytokines, inflammatory messenger chemicals, cross the blood-brain barrier and

actually stimulate cells in the brain called glial cells, and that creates a brain inflammatory cascade, right?

Some papers in the celiac world are showing that as you get intestinal permeability, you release something called zonulin, and then zonulin actually opens up the tight junctions of the brain. So what we're actually seeing is some of the research showing that leaky gut leads to leaky blood brain barrier, and gut inflammation leads to a brain inflammation.

Sean: Back up on that a little bit; I want to make sure everyone gets this part, too, about the zonulin thing. What is zonulin's role in the gut?

Dr. Datis Kharrazian: Okay. So zonulin is something that researchers figured out when they were studying the cholera, and they were looking at why people who have cholera have this intestinal permeability develop. Some researchers identified it was zonulin. And then what they started to do was they took this zonulin and they purified it into a protein and the injected it into animals, and all these animals got leaky gut.

What they found is that zonulin is a protein that binds to a zonulin receptor and opens up the intestinal cells. So when you look at leaky gut, there's two types: there's what they call transcellular, and paracellular. Trans—so you have these—it's like a picket fence. You have boards that are horizontal and you have boards that are vertical.

You can have inflammation and destruction cause leaky gut by just destroying the gut. That's what they call transcellular, right? So chronic inflammation just destroys the lining of the gut and goes through the horizontal boards like a fence, and that's one version—that's one mechanism of leaky gut. Then you have paracellular, where the board in between the horizontals, or the tight junctions, open.

Sean: And zonulin—

Dr. Datis Kharrazian: Zonulin binds to that, and then they open up.

Sean: Opens up. Okay, cool. And then it also does that in the brain as well.

Dr. Datis Kharrazian: It does it in the blood brain barrier—

Sean: Creating the leaky brain. Okay.

Dr. Datis Kharrazian: And what's really fascinating now is there's numerous papers coming out showing that people who have inflammatory bowel syndrome have white matter lesions in the brain.

Sean: What does that mean?

Dr. Datis Kharrazian: What that means is, the gut inflammation is causing brain degeneration, that the gut inflammation is starting to cause destruction of myelin in the sheath around the nerves. This is a degenerative process.

Now, you know, in the functional medicine world they have the saying, "fire in the guts, fire in the brain." It's been a common thing everyone's known, but now in the literature they're showing very, very high statistical rates and they do logistic regression studies and evaluate people who have IBS, they have severe MRI brain changes.

Sean: How does one test for that? For leaky gut?

Dr. Datis Kharrazian: For leaky gut? So, the way we test for leaky gut is, for me, personally, I like to check both transcellular and paracellular ways, and we do that through Cirex.

Sean: Cyrex. Which?

Dr. Datis Kharrazian: Cyrex Labs, it's called Array #2. If occludin/zonulin antibodies are elevated, then we know it's paracellular, and if it's transcellular, actomyosin antibodies are elevated. And some people have both and some people have one version.

Sean: And that leaky gut test gives you a good idea of if you have leaky brain.

Dr. Datis Kharrazian: Right.

Sean: Right. You also mentioned in your book, GABA. If you take GABA and you get an effect from it, it could be leaky brain?

Dr. Datis Kharrazian: Right. So talking about this gut-brain connection and leaky gut/leaky brain, we talk about in the brain book, a chapter on this, and we talk about how we use GABA. In the past in the leaky gut world, the way they used to test for it was they did atest called the lactulose mannitol test. And the lactulose mannitol test was we have two sugars: lactulose, which is very large, that shouldn't be absorbed and then mannitol, which is a very small sugar, right?

Well lactulose is so large that it shouldn't go through a healthy intestinal tight junction, so what they used to do was they used to give people a load of lactulose, and they would check their urine, and if there were high amounts of lactulose in the urine they'd go "wow, that large particle got through, now it's in your urine. So you have leaky gut." That was the older test.

The Cyrex test is much more advanced now, much more reliable than that. But that led us, clinically, before we were able to test the blood brain barrier objectively, was "how do we do that with the blood brain barrier?" So we realized that clinically, we realized that all of our patients would take GABA and some would not really notice anything and some would.

And GABA aminobutyric acid is an over-the-counter supplement, right? So GABA, the molecular weight is large. It's huge! What should cross the blood brain barrier are nanoparticles. So if someone takes GABA and it actually has an effect on their brain, then it had to have crossed the blood brain barrier, right?

Sean: It's too big. It shouldn't be able to fit through. Gotcha.

Dr. Datis Kharrazian: It's too big. And there's no transport mechanism with GABA into the brain. There's a transport mechanism with GABA out of the brain, but not into the brain. So that was our test. We were trying to mimic the lactulose test with leaky gut.

That's what I was trying to do because I was trying to figure out what's going on with my patients. And then we started teaching it and other people started doing it and it was a really cool way to do it. So what we do is we'd have a person take 1,000 milligrams of over-the-counter GABA, and then see if it affects the brain. And if it affects the brain and they feel really sedated and calm, relaxed, sometimes people get a paradox response and get hyper.

But either one of them means it had an effect on the brain, so there should be no effect with 1,000 milligrams of GABA. And if you take GABA and it makes you relaxed and calmed down, you probably have a leaky blood brain barrier.

In recent years, Cyrex Labs, under the work of PhD researcher Aristo Vojdani, had papers published on this. Now there's objective ways to measure blood-brain barrier antibodies, so Cyrex has a blood brain barrier antibody test. Array #20. Now we can check leaky gut with the lab, and we can measure leaky blood brain barriers, and we see a pretty high correlation with the two of them.

Sean: Taking GABA, is that a good way to check your progress?

Dr. Datis Kharrazian: Right, and here's the thing we do: if we see someone that does the GABA challenge instead of the lab test and they feel it has an effect, we don't want him to continuously take it, even though they may feel great and relaxed taking it. We want them to put it away because we don't want to sensitize the receptors in the brain, and then after a few weeks we'll have them try it.

So here's a great example: gluten sensitivity people usually have leaky guts and leaky blood brain barriers. They find out they have gluten sensitivity, they fail the GABA challenge test because they take it and they feel totally sedated for a few hours. We have them on a gluten-free diet for six

weeks, we have them do the GABA challenge test, they have no effect anymore. So then we go "hey, your gut and brain are doing better."

Sean: Cool. I want to rewind again. You talked about inflammation firing up the glial cells in the brain, and if I recall correctly from your book—'cause read it two or three times!—you said the glial cells are hard to turn off?

Dr. Datis Kharrazian: Right!

Sean: Talk more about that, and is it possible to turn them off with supplementation or something?

Dr. Datis Kharrazian: You know when we look at the immune system, we have an immune system that's different in the brain than the rest of the body. The rest of our body, we have T cells and B cells and natural killer cells and all these variations of cells. But in the brain, there's only one immune cell, and that's the glial cells. There's subtypes—the astroglial and microglial, right—but for the most part, there's just glial cells and that's it.

And glial cells don't shut off. There's no turn-off mechanism. In the rest of our immune system we have cells called T-suppressor cells that, once we fight the infection, T-suppressor cells come in and they go "hey, fight's over, calm down, you don't need to fight anything anymore," and our whole body stops becoming inflamed and we're cool. But in the brain, there is no T-suppressor cell. There is no off switch. So once the person gets brain inflammation, you get a cascading event.

Whether it's traumatic brain injury—and they call this in the sports medicine world post-traumatic inflammatory encephalomalacia, that they get an injury and the inflammation then leads to a domino effect—or it's chemical issues like IBS, that the inflammation from the gut turns on these glial cells. Those glial cells keep going until they die off. But before they die off, they recruit other cells, and then they recruit other cells, and then they recruit other cells—

Sean: This sounds like really bad news. How do we shut it off?

Dr. Datis Kharrazian: So here's the thing: if you do a literature search, there is no drug that shuts them off. But there's natural supplements in the literature that shut them off. Resveratrol has been shown to shut it off. Turmeric has been shown to shut it off. Luteolin has been shown to shut it off.

So there's a list of these, and in the brain book I go through and cite the major studies on it, and show the references. So, this is one of the areas where if you really have the brain degenerative process, first of all, the pharmaceutical world—whatever it is, there's very little options, and natural medicine has unbelievable options. This is what's really upsetting, because people aren't getting the science.

They're getting a mainstream pharmaceutical model, and this is what really pisses me off about the average neurologist. Like listen, your job is to read the literature on everything related to neuro, and you're too biased to look at natural supplements and food, so you're not serving what you should be serving as an expert. This is what's so frustrating, because the evidence is all there and no one's doing it.

This is something that people can do very easily; it's very inexpensive, they can go and start taking it. When people do get brain inflammation, what happens is nerve conduction goes down, so the brain speed goes down. So the most common thing we see with people who have brain inflammation is they just feel brain-foggy and they can't find words and the mental speed is reduced.

One of the diagnostic things is, if you have a brain inflammation issue is when you start loading up on turmeric and resveratrol. If your brain speed immediately changes and the world lights up, that's kind of diagnostic that you probably had some glial activation issues. Because everything's a working diagnosis until something actually changes it, and then you go "oh, that's more likely the diagnosis."

Sean: This is great information. Talk about the connection between the brain, the gut, leaky gut, and automimmunity.

Dr. Datis Kharrazian: Okay. So this is a very, very important question that you bring up here. First of all, traumatic brain injury people, all the time, develop autoimmunity. One of the things that we

know is that the brain and gut, and gut and brain, are first of all feedback axis, that these things communicate on a regular basis. We have gut peptides like CCK and different digestive enzymes, and different proteins in the gut, and cytokines and neuropeptides of the gut that actually communicate with neurons in the brain.

So we have this neurochemical-neurotransmitter feedback, going back and forth on an ongoing basis. When one area starts to dysfunction, other areas dysfunction, and that's pretty well-known in the scientific literature. Maybe not in the clinical practice where you're either—both medicine and alternative. But in the scientific literature, it's pretty well known.

So one of the other things we see is that when this axis starts to fail—and this axis can start to fail from either the gut failing first or the brain failing first, so if the brain fails first, then you don't get vagal activity and you get low motility and you don't get blood flow to your get and you get a leaky gut and you get an inflammatory reaction, right?

Now that inflammatory reaction in the leaky gut makes the person overzealous, and now there's multiple papers in the literature that show that in animal models, if they induce leaky gut they can develop autoimmunity. Also most of that's done with zonulin and type 1 diabetes. But on the other hand, if someone has a bad diet, and they're sensitive to gluten and they eat the standard American diet and they're eating fast food—if you eat the standard American diet, you have a leaky gut-promoting diet.

So if you have that, and you have a chronic inflammatory cascade in your gut, and you just have unhealthy gut bacteria, your gut starts to break down and fail and then you start to get leaky gut and the inflammatory reaction from the gut ends up turning on glial cells in the brain and the brain starts to fail and then you get this brain to gut axis web failure. So there's interloop between the two.

Chronically, when this becomes chronic, what we typically see is people develop autoimmunity. As people lose their brain to gut or gut to brain axis and they get intestinal permeability, the most common food that they react to are GMO food, soy, and hybridized foods, like gluten.

Both of those are considered neuroproteins to the immune system, so that's why people feel better on a Paleo older-type diet, 'cause these new proteins tend to be some of the most immune reactive, and as you lose your tight junctions you create this inflammatory vicious cycle. So what we typically see is whether the gut fails first or the brain fails first, you lose the axis. Then once you lose the axis and you have chronic inflammation and you have chronic intestinal permeability, that sets up the stage for autoimmunity.

Sean: Define real quickly, for those who may not be familiar with it, what autoimmunity is.

Dr. Datis Kharrazian: Autoimmunity is a condition where your immune system starts to attack yourself. In immunology they refer to it as a loss of self-tolerance, so you should tolerate yourself. You shouldn't attack yourself. Your immune system should know that your tissues are your tissues and they're not your enemy.

So what happens with autoimmunity is your immune system loses that self-tolerance. We know leaky gut is one contributor to it, but we also know that chronic inflammation disregulates things called T-reg cells and those T-reg cells failing are one of the key cells that allow us to have self-tolerance. And as people start to get more intestinal permeability, they get more inflammatory reactions, more of an overzealous immune system. They lose their chemical tolerance, then they react to chemicals around them whether it's gasoline fumes they can't handle anymore or perfumes.

And then all those things become triggering events that make the immune system crazy, and now their immune system is attacking their own tissue by making antibodies for their thyroid or antibodies for their brain or antibodies for their adrenal glands or wherever they are, and now they're in this vicious cycle of brain-gut axis, leaky gut failure and an autoimmunity on top of it. And that is very common in chronic people.

Sean: How would somebody test for that?

Dr. Datis Kharrazian: For autoimmunity? We test for autoimmunity by doing what we call auto-antibodies. Auto-antibodies are antibodies to yourself. That's really where auto—self—antibodies come from. For me, again, I use Cyrex.

I consult with Cyrex and I work with them on a regular basis, but I think they're the world's leading autoimmunology lab. They have a panel, which I use on a routine basis anytime I suspect autoimmunity. It's called Array #5. It's their multiple antibody screening, and it checks for antibodies against all the major tissues: stomach, intestine, thyroid, joint, liver, adrenal, nervous system, heart, platelets—

Sean: Is that also called the predictive antibody test?

Dr. Datis Kharrazian: Yeah, and the word predictive antibody test has come up because researchers are now finding that when you start to make antibodies, it's not benign; that it actually is predictive. So there's research showing, for example, if you have thyroid antibodies, you're gonna get Hashimoto's in your lifespan. Some papers have shown if you have islet cell antibodies or GAD antibodies in a period of five years, you will become type 1 diabetic.

So in the past, they used to think antibodies didn't really mean anything. Now here's the thing: someone can have their brain fail, their gut fail, be in this gut to brain vicious cycle, they start to go into losing their self-tolerance and they start to make antibodies.

Then whichever antibodies they make—and no one knows why you would make antibodies specifically to one tissue versus the other. There's multiple theories but no one really knows for sure—but then you start to make antibodies, and the antibodies can now be to your own gut, could be to your own brain, or could be sent to your thyroid.

Sean: It could be at your estrogen, correct?

Dr. Datis Kharrazian: Yeah, it can bind to estrogen. Yeah.

Sean: Ovaries, all the reproductive issues. I think you mentioned miscarriages in the talk that I was at, right?

Dr. Datis Kharrazian: Yeah, years ago when I was used to work with a lot of infertility patients, we'd find that a lot of them had antibodies to their own ovaries. At that point we were able to commercially test through a lab called Immunosciences - antibodies to their own estrogen and progesterone, it can lead to chronic infertility.

Again, this as brain to gut vicious cycle fails and someone starts to lose their self-tolerance, the next thing that happens is they get autoimmunity, then the autoimmunity creates its own whole complex list of symptoms, and then, for them, it may be their reproductive areas they're fighting, so then they have chronic infertility and they don't know why. For someone else it could be their brain; the brain's degenerating really, really fast, and they don't know why.

Sean: Last topic I have for you is gluten. How does that impact the brain?

Dr. Datis Kharrazian: So gluten, first of all, cross-reacts with the brain. That's one of the key things. We know that gluten is very inflammatory, but in immunology there's a concept called molecular mimicry or cross-reactivity, and this is where, when you look at the amino acid sequence of a protein you can see it has its own unique blueprint. But if three amino acids are identical in a sequence with some other protein, then antibodies from one protein can bind to another.

So gluten antibodies have been shown to be similar to areas in the brain. Gluten has been shown to directly bind to cerebellar purkinje cells, because of that amino acid sequence being so identical. Gluten has been shown to bind to synapsin, which is a protein in all your neurons. Part of the reason why gluten is so dangerous is when an antibody is bound to a tissue, it means to destroy it.

For example, if you're gluten sensitive, and you eat gluten, your immune system goes "wow, we don't like this protein. We're gonna react to it," and they make antibodies and those gluten antibodies attach to the gluten and it destroys it, and that's where you get the inflammation from, because the immune system is all revved up.

But these gluten antibodies not only attach to gluten, they actually attach to brain. The brain's cerebellum purkinje cells. That creates a severe inflammatory reaction, and then overall just the overall systemic inflammation from gluten sensitivity does create brain inflammation. And now they're showing the celiac disease literature that gluten triggers zonulin release and zonulin opens up the blood brain barrier.

So think about this: if you're gluten sensitive, and you eat it, you get antibodies to gluten, you get systemic inflammatory reaction, you release zonulin—now your blood brain barrier is open, now you get influx of inflammation to your glial cells, now you have your brain on fire. Then your brain starts to degenerate and as your brain degenerates, your gut starts to degenerate and you get this brain to gut axis inflammatory reaction.

Sean: Sprouted wheat bread. People think that that's better for them.

Dr. Datis Kharrazian: It's not.

Sean: WGA?

Dr. Datis Kharrazian: One of the other things—and we cover this in my third book coming out, *Gluten, Leaky Gut & Autoimmunity*—is, it's not always gluten. Sometimes it's wheat germ agglutinin, and sprouted types of grains have the highest amount of wheat-germ agglutinin. Papers have been published that show that antibodies to wheat-germ and gluten bind to neurons and they suppress nerve growth factor release. They basically create their own inflammatory disruptive process.

So you can have a person who may go, "hey, I've been tested for gluten and everything's okay; I don't have gluten antibodies," but they've never been tested for wheat-germ gluten and they're eating sprouted grains, and all of a sudden their brain's failing and they don't know why.

Sean: And that would be the Cyrex test, again?

Dr. Datis Kharrazian: Yeah. So we use Cyrex Array 3 and that checks wheat-germ agglutinin and the whole spectrum of gluten reactions. As we talk about brain and gut, recent researchers show there's three different enzymes for gluten sensitivity or celiac.

Trans-contaminates 2, which is intestinal, trans-contaminates 3, which is skin, and trans-contaminates 6, which is brain. And now, papers are showing—like one paper recently showed that when they check people who have reactions to gluten, 20% of them have trans-contaminates 2, 70% of them have trans-contaminates 6.

Sean: Really? Wow.

Dr. Datis Kharrazian: Yeah. Other papers have found that two thirds of people who have gluten sensitivity actually have reactions against the brain and have no intestinal complaints at all.

Sean: So they're dealing with the brain fog, depression and anxiety.

Dr. Datis Kharrazian: Without question, now, researchers are saying that really, the impact of gluten is really on the brain and it's never been on the gut. It happens to be that gastroenterologists found it first, and they classified it as a gut disorder. But really, now what's really happening is it's showing that it's a neurological disorder, and you usually don't even have gut manifestations.

Sean: Fascinating stuff, man. I love this. Lastly, diet: what kind of diet do you recommend? Is it Paleo diet, or what are we talking about here?

Dr. Datis Kharrazian: Listen—for brain? For brain-gut? Listen, let's talk about the complex pattern. Brain-gut axis failure. Brain fails, so you gotta get the brain healthy. Gut axis fails, now you have sensitivities to foods. So obviously, we know non-inflammatory foods are really the way to go, and we can say foods like gluten are off the table. Wheat is off the table.

And if you make it very simple, it's Paleo, right? But here's something that we just recently did in our lab. We went and made monoclonal antibodies, and monoclonal antibodies are antibodies that are produced that can only bind to one antigen and nothing else.

Sean: When you say "antigen…"

Dr. Datis Kharrazian: Antigen is the protein that they bind to. So you have proteins, and if you react against them, an antibody sticks to them then your immune system destroys it. So, Dr. Vojdani and I, we got monoclonal antibodies for cerebellum and thyroid, and we went and checked TSH, T4, T3, TPO, purkinje cells—and we did it for the pancreas: islet cells and GABA pathways, and we found many Paleo food diets cross-react.

Sean: That's not good news. What are people gonna eat?

Dr. Datis Kharrazian: So here's the deal: we're fine-tuning now and we're taking this to the next level. This is gonna be in the next year or so. The next level is you find out which tissue antibody you have, and you find out which of those foods cross-react with that tissue antibody.

So for example, what we've mapped out now—we haven't published it yet; we just got the data back, takes another eight months to publish because we have to write the manuscript and reference everything and who knows how many revisions we have to do for the journal to accept it, right, and we can't disclose the research because then we can't publish it.

So here's the thing. Right now what we've found is, the next future model is this: you have thyroid antibodies, here are the foods that cross-react with thyroid. Now, what that means is it's more specific than Paleo. But, I'll give you one example. When we did our research, we found tuna antibodies cross-react with T3. So if you have tuna antibodies that are high, antibodies can attach to your actual T3 hormone.

Sean: T3 hormone for what. Is it thyroid?

Dr. Datis Kharrazian: The thyroid, yeah. The main thyroid hormone. And it can bind to that T3 hormone, and then cause your T3 to be destroyed. It doesn't mean every single person with thyroid has to avoid tuna, but if they have tuna antibodies that are high because they're sensitive to tuna, that reaction takes place. Interestingly enough, we checked cooked tuna, and no reaction. Another one was soy. Soy cross-reacted with the thyroid—only a processed soy, not actual soy protein.
Sean: So it's a great way to refine the p\Paleo diet.

Dr. Datis Kharrazian: So here's the future, if you're working with an expert. The future is, here's your tissue antibody. Here's the food that cross-react. Let's check you for those foods, and if you have high antibodies for those foods we've gotta get rid of them, and that's going to be fine-tuned more than Paleo. That's where our research is going right now, and we've dissected the thyroid pathway, we;ve dissected the brain cerebellar pathway, which is the most common thing for celiac, and we've dissected type 1 diabetes pathway.

Sean: When do you see that testing being available?

Dr. Datis Kharrazian: In the next year.

Sean: Very good.

Dr. Datis Kharrazian: It'll be a food allergy test. It'll just be test food allergies then we have to match it up with the research we've done with the monoclonal antibodies. And then that's where this game of just doing general diets is going to go away for autoimmunity.

Sean: This keeps getting more and more dialed-in. I love it. Very good. Your book is *Why Isn't My Brain Working?* Fantastic book. Your website is brainbook.com.

Dr. Datis Kharrazian: Brainhealthbook.com.

Sean: Brain*health*book.com. Tell us about your book, because this is coming out in November, and so your next book should be on the way then, right?

Dr. Datis Kharrazian: Right. So our next book is gonna be out before the end of the year, 2014, and it's called *Gluten, Leaky Gut & Autoimmunity*, and it's really a book where it's beyond just "hey, gluten's bad for you" and "leaky gut, take glutamine."

It's really a book on really getting into the complexity of all these things, and going "hey, here's all these different mechanisms of leaky gut, and here's why some don't heal" and "here's all the most common tissue antibodies" and "here's the vicious cycle, here's what you don't know and here's why some don't get better." It's really trying to take it to the next level, instead of just "don't eat gluten, take some glutamine and go on a Paleo diet." It's much, much more advanced than that.

Sean: I'm looking forward to reading it. Dr. Kharrazian, thanks so much. Great stuff.

Dr. Datis Kharrazian: It's been a pleasure.