THE FATIGUE SUPER CONFERENCE

Why isn't my brain working?

Guest: Dr. Datis Kharrazian

Alex: Welcome to 'The Fatigue Super Conference' and this is going to be a fascinating interview, it's one I've been looking forward to doing. I'm talking to Dr Datis Kharrazian who has a very deep background in the kind of broader functional medicine world, has written two key books in the area. His first book 'Why Do I Still Have Thyroid Symptoms', which was I think the key piece in the evolution of understanding for practitioners working around thyroid, and his more recent book that we're going to focus on more today 'Why Isn't My Brain Working', which is a fascinating read that I haven't got all the way through, but I've been really enjoying getting into the last few days.

Just to give a bit more of a formal introduction Dr Datis Kharrazian is an Associate Clinical Professor at Loma Linda University School of Medicine and a research fellow at Harvard Medical School. Dr Kharrazian earned a PhD degree with concentrations in immunology and a Doctor of Health Science degree from Nova Southeastern University. He completed his postdoctoral research training at Harvard Medical School and the Department of Neurology at Massachusetts General Hospital. Dr Kharrazian also earned a Master of Medical Science degree in clinical investigation from Harvard Medical School. Dr Kharrazian welcome and thank you so much for making some time to talk to me today.

Dr Kharrazian: Thank you. My pleasure.

Alex: So you're more recent book I think is fascinating in introducing the role of the brain in a whole range of things, today we're going to look at it from the context of fatigue. I think the brain is an area that often functional medicine practitioners can somewhat under emphasize the importance of. There's a lot of emphasis around kind of gut, adrenals, those kind of pieces, as I've been discovering going deeper into your work last few days it actually is in many ways one of the key pieces to understand.

So maybe as a starting point just give us a bit of context around how brain health impacts fatigue and why it's such an important piece for us to understand.

Dr Kharrazian: Absolutely. So one of the things we know is that the brain is really vulnerable to inflammation and other things that go wrong in the body, whether it's low fuel or energy, low blood sugar, anemia, chronic inflammation, they all have a toll on the brain. So we know that the longer that a person has been chronically ill, from whatever disease, we know that there's been some assault some impact on the brain. Then over a period of time chronic disease has a significant regenerating effect on the brain and then as the brain becomes unhealthy people lose the ability to focus, concentrate, have attention, to move, to have a desire to exercise, to be coordinated, to sleep. What happens is everyone tries to fix everything else, but not the brain that's injured and the brain gets ignored and then the patient doesn't really recover and they continue to have persistent symptoms despite maybe they're adrenal glands are functioning better or their gut microbiome is a little bit healthier. The brain is still is not really received the attention it deserves so a patient still continues to have chronic symptoms. That's one of the things that I try to explain and go over my book.

Alex: One of the things that struck me is actually beyond the kind of just the role that the brain plays in so many things, it's the heaviest organ in the body, it uses the most oxygen, 30% of the glucose, like just as an organ it's pretty significant in terms of both its impacts and the demands that it has in terms of supply of resources.

Dr Kharrazian: Yeah, absolutely and it's absolutely one of the key reasons why people have fatigue. Anytime we hear a patient come in and they complain of fatigue, depression, little bit of memory issues, cognitive decline, like what's going on the brain? And it's funny it's so obvious, right? If someone comes in with cognitive decline, depression, fatigue, you would think about the brain but unfortunately people just jump to everything else and this is not going to be fixed with an antidepressant. It's gonna be fixed with a brain becomes healthier. So a critical evaluation of all the different variables and all the different factors that impact brain health become really critical when it comes to patients with chronic fatigue.

Alex: One of the things that became clear to me as I was reading your book was that I think part of the reason why functional medicine practitioners don't have such a focus towards the brain is it's almost like well that's the realms of traditional medicine and there's quite a lot of evolution in understanding around that. And one of the things that became clear to me is just how nuanced brain function actually is in the same way that, for example,

functional medicine practitioners working with the adrenals or the thyroid, they would have a much subtler understanding of that function than a traditional endocrinologist would, for example.

And I got the same kind of recognition in terms of brain function when you were talking about some of the more crude ways that traditionally a doctor might just give someone Gaba or go in with kind of certain things, it's pretty complicated in from a point of view of understanding how to work with it.

Dr Kharrazian: Yeah, I mean it's complicated but is was everything and once you get the blueprint and have it explained to if you're new to it, I think it's pretty easy to take it in. But I do agree that it's not a simple system but it's something that is in anyone's reach. People can learn about different ways to support the brain, they can learn how important blood sugar stability is, they can understand how inflammation impacts the brain, they can understand concepts like blood brain permeability and then it's really easy to make some diet, nutrition and lifestyle strategies to address those.

And really when you look at improving brain function from a health perspective meaning you're trying to optimize the health of the brain that's a completely different model of indirectly helping brain. People sometimes think if they fix the gut the brain should automatically get better or if they're just taking some fish oils and the brain should be better but that’s not how it works. Then we also know that taking a simple antidepressant is not going to fix the brain and we know that eventually if you have poor brain function and poor brain endurance and poor cognitive issues that you're on your way to neurodegeneration. As a matter of fact one of the earliest symptoms of neurodegeneration is low brain endurance.

So one of the things we do clinically when we see a patient has fatigue, first thing that we try to clinically differential diagnosis is their fatigue metabolic or does it now include the brain. So metabolic fatigue just happens for no reason, you wake up some days you just can't function, you can't get out of bed or sometimes you have an episode of fatigue hit you and then you're down. Brain fatigue is very specific and that's how you know the brains in trouble. Brain fatigue occurs when you use the brain and when the brain becomes unhealthy the mitochondrial in the brain, the areas in the cell that make ATP, that make energy for the brain, they become less efficient. So the brain endurance overall goes down. So a patient will notice they can't drive as long, so if they use their brain that's when they get tired. If they're on a computer screen they get tired, if they're trying to read a book within a page or two they get tired. And that's totally different metabolic fatigue.

So when we see poor brain endurance, we know the brains in trouble and it is one of the earliest symptoms of neurodegeneration and if it's not addressed, you can pretty much guarantee you're on your way to a neurodegenerative disease.

Alex: I think for patients experiencing these kinds of symptoms, I remember some of the patients saying to me this morning that their cognitive impairment was actually more frustrating than their physical impairment. You kind of adapt your life if you can't go for a long walks or exercise but not being able to concentrate to read and not being able hold a conversation for more than a certain period of time is also a great source of suffering. I think people.

Dr Kharrazian: Yeah, your ability to appreciate music is temporal auditory, your ability to taste food, right, is gustatory or primal or temporal, your ability to have motivation and drive is frontal dopaminergic and all the things we do as human beings and the way we appreciate life. We see the brightness of colors or here discrimination of sounds and music or of the people and then think and reflect that's all brain function. When the brain becomes impaired everyone's quality of life will go down. I mean it is significant.

So it's almost a surprise when you see so many chronic patients with fatigue and energy issues and everything besides the brain gets worked up. And it's like oh that's just your brain or you're just getting older and it's like no your brains in trouble and we need to figure out a strategy to make your brain healthier.

Alex: Well, that was one of the things that struck me as well and it was taking me back to my psychology degree many, many years ago and I was reading in your book around neuroplasticity, for example, and how the brain ultimately as we get as we get older we do have less neurons or less brain cells, but we should be cultivating and creating more connections.

So maybe also, before we come to some of the signs of brain degeneration, just maybe say a bit about that element of brain function and why using and taking care of brain is also really important.

Dr Kharrazian: Sure. So there's certain cells in the body that are referred to as cell that don't go to post-mitotic change, they don't have any further cell division. So let me explain that means. So normally your cells are dying off and you get new cells built-in. So the nails you have are different cells, your skin, your hair, your liver, your organs. Cells have died off and new cells have regenerated. That's the process of cell division. There's two tissues in the body where you no longer have cell division once you're born. That's your heart tissue and your brain and your neurons. So whatever amount of neurons you

have is the amount you have for the rest of your life. And once you lose them they are gone, you'll never get them again.

So you've actually had more neurons the first couple months of your life than you have probably now as an adult, as for the quantity. The quantity alone doesn't determine function, what determines brain function is how they connect to each other. Now the more neurons you have the easier it is to connect to each other. That's why it's so easy to learn when you're young because you can learn a language quickly, you can learn sports quickly because you have so many neurons you activate them and they'll connect to each other and you get function. When you get older you have less neurons so therefore you activate them, that's a kind of branch and finally get to it and connect and as you generate more it's harder to learn anything new and get new outcomes.

But the great thing about the brain is you have that potential, you have this potential for whatever neurons you have they can connect so that's the concept of neuroplasticity. So even though the brain, the time seems hopeless because you're like, oh my gosh, I'm going to lose my neurons and the ones I've lost I'll never get back that's so terrible to think about. But on the other side you can be really optimistic and go well it's not about how many neurons you have it's how they connect and despite the amount of neurons I have if I can activate them and have these neurons branch into each other I can get function. So that's what's so amazing. So when we're looking at optimizing brain health, you're trying to look at all the dietary lifestyle and environmental factors that are causing neurons to die. And then you're trying to optimize all the various things that support plasticity and that's how you regain your brain health.

Alex: Yeah, we're going to come to that in more detail. Before we do though let's talk a bit about what are some of the early signs of brain degeneration. One of the things that actually struck me as I was reading is actually part of the challenge is of course if one has degeneration in other parts of the body one's brain is what helps them recognize that happening. That when there's brain degeneration, particularly if its rapid, it's actually quite hard to self-identify because the very kind of tool that we would use to do that is the thing which is being impacted.

But yeah so talk a bit about what would be some of the clues, some of the things that one would look for? And you did touch on it briefly a bit earlier.

Dr Kharrazian: Sure. So as far as symptoms go the first earliest symptom is loss of brain endurance. So not being able to read as long, not be able to concentrate as long, less attention span, difficulty focusing, concentrating.

That's the earliest sign of neurodegeneration followed by depression. So when the brain loses its activity or its firing rate especially in the frontal there's just a sense of depression and lack of motivation and drive. So whenever we see someone with very poor brain endurance, loss of focus, attention drive, then we know that their brain is in trouble.

Other things that we see is just handwriting can change, that's another thing you'll see so people will notice the handwriting has gotten much worse over the years and if you see someone that has stated that in their history and especially the hand writing has got really bad we want to know in what time frame. If they say their handwriting got really bad in six months we know that it's pretty fast degeneration. They say well it's over the past couple years we know it's much slower than let's say six months. And then just a simple test I'll have patients do as they come in as a write a sentence like today's a nice day, today is a sunny day, whatever the word is and just have them repeat that 10 times on a piece of paper. If you can see that decompose, you know the brain is in trouble, that it's a brain endurance test.

So you can see it with things like handwriting, sometimes you just do a medical history with the patient and as they're talking they start slurring their words or there's bigger gaps between questions and answers. You can see the brain slowing down right in front of you, they can also tell that it's slowing down. Those are all big clues that brain is in trouble and that it's on its way to a neurodegenerative disease, if it's not already there. I mean many, many chronic patients that are so frustrated with fatigue exhaustion and then they finally diagnosed and already have Parkinsons, they already have dementia and that needs to really be addressed.

Alex: One of the things that jumped out to me was that you said if the brain fatigues the whole body does and so it can also I guess, from what you're saying, be the case that fatigue in the body could also be a symptom of something that's happening in the brain.

Dr Kharrazian: Yeah, absolutely. So, for example, if the brain fatigues, let's say there's an area of the brain that's degenerating faster than another or let's say there's an area of the brain that's injured, maybe someone had a car accident, they hit their forehead, now they injured the frontal lobe and then this area the brain is now inflamed then as years go by this area the rain starts to neurodegenerate faster. Well if this is the area of the brain involved with focus and concentration as soon as they're endurance drops, gets a little bit low, a little bit inflamed then their focus and concentration goes down. Compared to if their motor strip was involved and that was injured now that's heavier, it's harder for them to move their arms and their hands and if it's their medial temporal lobe that was injured now recalls a much more difficult

issue and if their auditory cortex was injured now when the brain gets fatigued, they can't hear anything, they can't hear anything with any background noise. So all these regions of the brain have specific symptoms. So sometimes if you know neurology really well you can quickly go, well that sounds like temple lobe degeneration, that looks like motor strip degeneration, that's the pre frontal cortex, you can kind of work your way through but that's how it clear and obvious it is. It's just a matter of looking for it.

Alex: Yeah, right and I guess that's part of the thing right and I know that's part of your kind of call to action to I guess patients but also typically practitioners to see this as part of the wider picture and as we'll come to in a bit practitioners are already well equipped in terms of many of the things that can be done to work with this it but they need that focus.

Dr Kharrazian: Yeah, and I think for me in my efforts has been I tried to create programs for health care professionals to teach in the stuff. I have an education service called The Kharrazian Institue and then I wrote the book directly for patients to have some answers and that's 'Why Isn't My Brain Working' and then I created an online program for some patients with brain issues the book was too hard to get through. In Dr. K news I made a six-week course 'Save Your Brain' where people learn how to look at these lifestyle changes.

But there has been as much attempt I can to hit practitioners and patients directly to give them the information because there is definitely a void and the sooner they understand what the mechanisms are involved with brain in their symptoms and make some lifestyle changes, it can be life changing for many patients, which is really important to get out there.

Alex: Absolutely. I want to touch on something else that perhaps we'll probably come around and come into a bit more detail when we look at some of the ways people can address these things. But maybe say a bit about the role of the vagus nerve and how it's the connection between the brain and the gut, because I think this is a really important piece of people understanding the kind of interconnectedness between these different kind of pieces.

Dr Kharrazian: Sure. So just like we talked about earlier we know that when the brain starts to become inflamed, starts to degenerate, becomes unhealthy, we have fatigue as the main issue, especially brain endurance issues related fatigue, second one is depression. And the third one is actually poor digestion is what you bring up. So what we have to understand about the brain is that the brain has all these different regions and all these different receptors that are constantly firing to the brain. So the brain is constantly getting stimulus

from gravity, from sound, from light, from touch, from taste, all these things are activating the brain. So they're all providing input to the brain.

Well then the brain has output and the primary output center of the brain is the brain stem and within the brain stem we have a very important group of nuclei, a cluster of nerves, called the vagus, the vagal motor complex, the nucleus ambiguous. But anyways, the vagus, these different centers they fire into the gut and they're responsible for us to have proper intestinal motility and the ability to produce digestive enzymes and many times when we see a brain that's unhealthy we'll actually see poor digestive function. We'll see a person that can't make digestive enzymes so when they eat they get bloated and distended and they have this dependency to take digestive enzymes or apple cider vinegar when they eat, so don't get so distended and bloated. We also see motility issues. So as the vagus nerve in the brain fires into the gut and causes the smooth muscles in the gut to contract, it's the vagal motor response. When the brains unhealthy that becomes inefficient, so people end up with constipation and then as they get constipated and they don't remove food well the bacteria populations change, the get dysbiosis and they get yeast overgrowths and they have this chronic gut issue that's really bring based.

And sometimes they'll go to a practitioner and they'll try to fix their gut because they'll do let's say a comprehensive GI panel on they'll see dysbiosis and bacterial overgrowth and markers for poor digestion and they then change your diet and give them supplements to change those things but doesn't matter, nothing changes, because they haven't really addressed vagal activity. So red flag is always poor motility, constipation, we always want to consider the vagas. In an exam scenario we actually have a patient open their mouth and say, ah, we look at their palate see if that moves that's test for the vagas, listen to their abdomen. And with many people that have significant brain impairment and brain inflammation and brain degeneration that whole vagus complex isn't working and the gut is compromised.

And now we know all this research between the gut and the brain, this gut brain access, and when you start making dysbiotic populations in the gut they release their own end product called polysaccharides, they change brain function and now you have this vicious cycle of inflamed brain and inflamed gut all creating this neurodegenerative, neural inflammatory process and then the patient is exhausted with fatigue and when they go and see someone that just treats everything but the brain they can't break out of it.

Alex: Yeah I think this work on the vagus nerve is really interesting because I think it's been a good few decades now that people have been aware of the impact of gut health on the brain and cognitive function, but seeing it as that

circular kind of process I think is a pretty important breakthrough in terms of how to get lasting change in these areas.
Dr Kharrazian: Absolutely. I have a practice where I see chronic patients and I can't tell you how many chronic patients over the years we've worked with that really had poor vagal function. So I think one of the things that I see as a practitioner with chronic patients is so many of these chronic patient with chronic GI issues really had vagal issues and poor brain health. And I after helping patients improve their brain function, improve their vagal responses and seeing they gut function change. It's almost frustrating to have this information not get out there so thank you for sharing that and we do talk about some of the strategies in the book and those mechanisms in the book and it is a major cause of poor gut function, so the whole picture of fatigue, depression, poor gut function, really many times go back to really an unhealthy brain and those are all red flags. And if those red flags are not managed neurodegenerative is almost certain.

Alex: So we'll come back and when we start to look at some of the ways we can address these I'd love to touch bit more on the vagus nerve there. But before we come to that you mentioned some of the ways, just briefly, in terms of how someone would diagnose poor vagus nerve function. What are some of the ways that you can start to spot early brain degeneration? You touched on some of symptoms earlier, are there particular test that you like to use or that you rate or is it primarily clinical picture that you're working with?

Dr Kharrazian: So in a functional neurology model we just do a standard a neurological exam and have someone touch your nose and when someone misses their now constantly, has a little bit of tremor before they touch the nose, or if someone is trying to stand still they start to sway in fall those are all test of function. In a conventional neurology model we have to see those be extreme, meaning if someone closes their eyes they're going to just fall to the ground, then you would do an MRI, but in a functional model if you see someone close their eyes and they're shaking all over the place and the balance is off that would show that they're distinguished cerebellum is degenerated, right. If someone comes to me and has a hard time closing their eyes and touching their nose, we know that the parietal lobe is not functioning.

So we basically, in a clinical model, just do standard neurological exam and that's kind of hard to do as a patient maybe reading it but in a clinical setting it is a key way of identifying. It's hard to identify neurodegeneration without that, other than the symptoms that a person may have. But your biggest clue as a patient is really just, you know your brains not working, you know you have problems with focus, attention, concentration, you know that you have problems with maybe your handwriting, maybe your physical activity is a bit

less. And you don't have all of them because your physical coordination may be a different part of your brain than your focus and concentration and your recall but if you notice symptoms associated with brain, then you know that the brains in trouble.

So I think it's almost shocking when you see people come in with brain symptoms and they get diagnosed with something else. It's like I can't think, I can't focus, I can't concentrate, I'm exhausted, I can only read a couple pages before I get exhausted and it's like adrenal glands. I'm like it our brain sure, the adrenal glands could be a factor they can impact glucose to the brain, but it's not just adrenal, I'm at that point the brain is fault.

Alex: There's something else, just before we come to things that we can do to improve brain health and support it that jumped out to me that it's more of actually a practitioner-to-practitioner question, but I think it's going to be interesting to others as well. I was fascinated by something that you were saying around when neurons being close to the threshold that that could be a cause of sensitivity and you were talking about how, for example, supplementing certain things such as Gaba even a tiny amount that people can actually have a significant negative reaction to that and what it got me thinking about is, I'd love to hear more about that specifically, but also what it got me thinking about is sometimes there are crashes that people have which don't seem to be originated in the mitochondrial function or ATP production or in the adrenals, hormone kind of side. It almost seems to be something kind of crashes in the brain, which then that's the cause of and that's something that no one has really been able to explain to me before so I'd love to get your thoughts around that?

Dr Kharrazian: Yeah and this is really important. This is really more progress, what you're bringing up and what I tried to illustrate in the book was the concept of neurons close to the threshold. So every neuron has what's called the resting memory potential, which is some degree of electrical activity and then the threshold. And then in order for a neuron to fire this resting memory potential has to peak up to threshold. So for example, if you look at sound, we can't hear a dog whistle but a dog can because a dogs auditory pathways are closer to threshold so they can hear something less than us. Now when neurons fire at a threshold what's actually happening is they're getting an electrical charge they're getting this calcium influx into the cell, which not to get too deep with the chemistry of it, but it's really dependent on mitochondria. So normally when we activate a neuron calcium floods into the neuron gets to threshold and then we have to have energy within our neurons the mitochondria, ATP, to push it out. And if the mitochondria are unhealthy in neurons to push out that sodium influx, calcium/ sodium influx that comes in, they can't push that sodium out then this neuron now is now close

to the threshold but the mitochondrion doesn't have ATP so there's no endurance.

So one of the things we'll see when the brain gets really in trouble and starts to really significantly degenerated in the mitochondria, these energy producing cells in the brain really become impaired, is that whatever region of the brain is involved becomes extremely vulnerable to stimulation. So some people are extremely sound sensitive, some people extremely light sensitive, some people can't handle motion or movement. You can take literally some patients and put your finger like this and go doo-doo-doo-doo look at this and I'll be like, oh my God, I get dizziness, I get vertigo I'm gonna throw up. That's like, okay well now stabiles cerebrum is close to threshold. So what else, you can snap next to their ear and they get really anxious, and you're like it's just a snap but for them it's causing anxiety. Those are neurons close to threshold.

For some people just standing on an elevator and going up and down has now made them totally want to throw up. Those are neurons close to threshold. So when the brain really gets unhealthy in the mitochondria, the brain really are not working and they can't produce ATP then as neurons fire they can't regain the resting memory potential and any trivial stimulus makes them fire and then exhausted. So like in my office I'll have a lot of patients that that are in that scenario. They're really completely exhausted and fatigue and we'll have to turn off the lights and do an exam, we'll have to give them breaks between one exam thing to another, we'll to make sure they eat small meals throughout because if the brain is not functioning well your body has to use all the available glucose to make these collateral healthy neurons work. So the intensity of the blood sugar dropped really quickly. So we'll have to kind of work our way through it and it's a real thing and if a persons in that stage they are definitely in the neurodegenerative gray area.

Alex: Yeah, it's really fascinating because I could think of a number of patients over the years that at a kind of acute phase of severe chronic fatigue/ME can become highly light and sound sensitive and we have patients which are you know darkened rooms with eye masks or sunglasses despite being in a darkened room, with ear plugs that are only able to tolerate short periods at a time a day. And although at their peak we've seen people like that gradually over time through working from a functional medicine, psychology combined kind of approach gradually come out of that and regain that function there's never for me being a truly satisfactory kind of biochemical explanation of what's happening there and I think this is really fascinating.

Dr Kharrazian: What's happening there is the mesencephalic area there's a superior inferior tectum. The superior tectum is where you have visual perception, the inferior tectum is where you have sound perception. Those

areas of the mesencephalon are inhibited by the basal ganglia indirect pathway so those are presynaptic frontal striatal projections. So when the brain in the frontal lobe become impaired, they can't gate and dampen them and then you get to severe line sound sensitivity.

So in a clinical exam finding what we'll do is we'll put on heart rate monitors or pulse ox on the finger and then you'll just get the resting heart rate and then you can just put like a tuning fork next to the ear and you see the heart rate spike. Or you can just take a pen light and just flash their eyes a little bit with it and you'll see the heart rate spike and then you know they've lost the ability to head in that pathway. It is very, very common that, is absolutely indication that the brain is in trouble and the brains healthy because 90% of the brain is to inhibit the other 10%. And the sound and light pathways are a critical part of our survival function because we have to hear or see things in a visual or auditory pathways to run away and not get eaten up by something as an animalistic brain perspective. So if the brain gets unhealthy and it can't dampen it those primitive reflexes become really heightened and like you said, you'll see many of those patients in clinical practice like you're saying.

Alex: Fascinating, really fascinating. I'd love to come a bit more to some of the things that people can do. So as people are listening to this and I'm sure people are seeing themselves in different elements of what you're describing. What are some of the, maybe to open this up, some of the key principles you look at and maybe we can touch on some specifics. But when you're encouraging someone either through self-care or ideally if you're working with a practitioner what are those key building blocks to regaining brain health?

Dr Kharrazian: These are the things that we cover in our 'Save Your Brai'n course, which is an online program we developed at Dr K news but I'll give you an example. One of the key things is to go to get oxygen and glucose to the brain right away because in order to have energy and function they have to take place. So let's talk about let's say glucose. So we really look for drops of blood sugar, I mean if someone is hypoglycemic it's really hard to ever fix the brain. So if someone is getting shaky light headed, irritable throughout the day. Or a big sign that a person's hypoglycemic is that when they eat they feel energized, that's not normal. When you eat it's not be hungry shouldn't have your energy and your function come back. So people that have hypoglycemia will get like anxiety, you know, they get hangry, that's the term they use, they eat and then they come back, that's all the sign of low blood sugar. Normal response is just to be hungry and not have eating change your energy.

Or someone who has insulin resistance, they're almost pre-diabetic, the opposite way, that they're overeating they get fatigued after they eat, have too much sugar in their diet, unofficial activity, they get really tired after you eat.

So first thing we try to do is just really control blood sugar levels and that helps us with the glucose part of it and then the next thing is oxygen. And oxygen seems obvious, because we're breathing, but oxygen could make sure the patient clinically would be to make sure the patient's not anemic. Make sure that the patient's proper lung function they don't have any wheezing issues or any asthma and then just circulation. When you see really bad circulation, it's a really difficult to change your brain. So just like taking someone's hand touching the forearm and then comparing it to their fingertips you can get a good clue of their circulation. You can just see how the distal circulation is. And if someone has really cold hands and really cool feet that means their peripheral circulation is impaired which then means their brain circulation is impaired because remember the brain is peripheral too. So if you can't get blood flow to your hands and feet which are actually gravity is helping you, the brain is going up, so when this peripheral circulation that's impaired you know the brain is not going to get nutrients and oxygen, it needs oxygen to make energy.

So really first thing we try to do in the model that I use to support the brain is get blood sugar under control, make sure that the circulation oxygen dynamic is working Okay, and then that's a good place to start. And then we get into inflammation other variables, but those are the key things.

Alex: Yeah before we perhaps touch on inflammation a bit or let's also just explore gluten sensitivity. There was a quote that jumped out to me from your book which I'm just going to read because it really jumped out because you're very measured and kind of balanced in your tone and this this quote was like, wow, Datis feels really strongly about this. You said 'If you have confirmed gluten sensitivity and feel going gluten free is too difficult. It's time for you to put this book down and realize your brain has no chance and you will continue to get worse'. I was like man this guy feels strongly on this point. So yeah, let's just touch on also the kind of role of diet and food particular gluten sensitivity.

Dr Kharrazian: So when we get to inflammation and there's certain food proteins that are very inflammatory. Now not every single person has go insensitivity but if a person does have been sensitivity, which is growing, then we know that they have a significant impact on brain and we did a study we published in the Journal of Nutrients we took 400 healthy blood samples and we tested them for a gluten sensitivity and when we tested them for gluten sensitivity we checked atha gliad and Gamma gliad and glutamorphin and all the different subtypes of the immune response to gluten and we found about 17 percent of the U.S. population we tested had really, really high antibody titers.

So then we took those people and we wanted to see do these people have brain inflammation. So then we looked at antibodies myelin basic protein, myelin denrecites, icann65, cerebellum antibodies and a few other ones and then we wanted to see what the association was. Well the association was almost like one to one when they had it was like .9 R value, which is really high as you know, and we had more half of the people that had reaction to gluten have brain auto antibodies, which means not just inflammation it's now heading towards autoimmunity. This is significant inflammation, its the highest] level of inflammation.

So that plus a lot of research that shows gluten has molecular mimicry or antibody similarity to different structures in the brain means if you produce antibodies against glad meaning your gluten sensitive to make those antibodies, if you eat it your brain will be inflamed. So I'm definitely convinced more and more every year.

So it's one of those things when you see someone and they'll say yeah when I don't eat bread, I feel so much better I have so much better focus. Then you go well yeah and then you check the blood work and you see it's gluten sensitive, it's like well I can't give it up and like well it's time to live with what you got. And those people do turn into gluten ataxia's and brain autoimmune diseases if they're not addressed. So it's not just like well, I'll change it some point. There's a point of no return with that reaction.

Alex: Yeah, yeah. Let's just touch a bit more on inflammation. So you mentioned in terms of gluten as a kind of a trigger of that but brain inflammation more generally what are some of the ways that you would work to reduce that people?

Dr Kharrazian: So one thing about cell function with the brain is only 10% of the brain cells are neurons and 90% of the brain cells were microglia. And then within the microglia, I should say neuroglia, within the neuroglia we have like 20% that are their astroglia the control our blood brain barrier. We have another 20% that are microglial cells that are scavengers and then we have the remaining oligodendrocytes which kind of sheath, our neurons and so forth. So the brain is really more immune cells that it is neurons, these glial cells, and these glial cells act completely different than immune cells in the rest of the body. So once they get activated they can really get activated and it's really hard to turn them off. So brain inflammation is a unique feature and we know that there's pathways, there's four different pathways, that can turn on brain inflammation, some across, some through passive diffusion, inflammatory meters cross the blood-brain barrier, some through the vagus the inflammation in the gut travels up the vagus nerve to the brain stem that turns on brain. And we know there's pathways in the blood-brain barrier that

are open and by the hypothalamus but all these different pathways turn on brain information basically.

But when these brain cells turn on they don't always turn off and there's a concept called glial priming. So within your brain needs glial cells, they have a certain shape like arms branching out kind of sampling stuff but once they get turned on for significant inflammatory response, they change their structure and they never change back. So we know that when there's systemic inflammation that these glial cells change their structure and they get what are called prime glial cells and they may never go back to where they were. And this is what we see with let's say traumatic brain injury. So it has a traumatic brain injury these glial cells change, now they're always in an inflamed state and then five or ten years later the brain functions down and then these patients really have a serious inflammatory reaction the brain. And the only thing that really has been shown to block these if you do a literature search are dietary flavonoids. So if you were just looking at the evidence and going I have clinical scenario with brain inflammation, microglial activation, what has been shown to suppress it. With the exception of heavy steroids, which no one will use unless it's an emergency because of the effects, what you're left with is flavonoids. Green tea polyphenols and things in the vegetables and grapefruit and a lot of the things that we use like Resveratrol, Curcumin have really been shown a very powerful anti-inflammatory properties because these flavonoids these polyphenols can cross the blood-brain barrier and ensuring that these glial cells enter into an inflammatory state. So this is really where natural medicine shines and its really inexpensive and it's a great way to help calm down some of that fire in the brain and we use it all the time in a clinical setting.

Alex: Very cool. I want to just touch on briefly again the vagus nerve because there are some interesting ways that that you've identified. I don't know if it's you that's devised it but you certainly talk about in the book in terms of things like singing, gargling, talk about how they can help re-energized and reactivate and why they do that.

Dr Kharrazian: So there's a principle in functional neurology that I've helped it helped patients to learn, to teach the practitioners, and the basic concept is whatever they can't do is what you do. So you activate the path twist that are not firing and that's how you get plasticity. So the vagus nerve can be activated by activating the gag reflex. So when someone says 'argh', if you ever had a doctor check your gag reflex with a tongue blade when they put that tongue blade against those muscles back of your throat that causes them to stretch ad that fires the vagus. But when the vagus fires is it's not just the muscles in the back of the throat the entire vagus firers. That's how the

nervous system works. When you fire the pathway the entire neuron it gets excited and turns on.

So one of the things we do to activate that gag reflex and that vagal response is to have patience gargle. So as they take some water and just gargle with it aggressively gargle if they use the muscles at the back at their throat they can actually start to get some bigger responses. So we'll have patients all the time if they have lost their brain gut access pathways to the vagus nerve we'll have them start gargling to really help get some plasticity in those pathways to get the function back. Loud singing can also do it. I have some patients get a just get cause a gag reflex in the back of their tongue, not their throat, so they don't injure their throat but just causing gag reflex thinking in a box and tongue blades and do it throughout the day. So those are some of the strategies that I talk about in my book of how to activate the and it does work for many, many people but there are some people that it does not work with and I think some of those people are just too degenerated to have any change or maybe the diagnosis is wrong.

Alex: And how long do you find people have to use those practices for but before they get a kind of noticeable change?

Dr Kharrazian: So it depends on each person. So if someone has significant neurodegeneration you have to kind of rebuild the area so the brain can fire to the vagus before they can have a bowel movement. And for other people they have some subtle inflammation and if you change those with a couple dietary things, maybe they're gluten sensitive, now the inflammation's gone and I start activating the vagus and within a few days they're back. That'd be an ideal scenario, but it's not always that way.

But we also know that the most common cause of Parkinson's disease starts in the gut. So in Parkinson's disease you get this build up of something cool alpha-synuclein. It actually starts in the gut ten years before it goes into the brain and then it goes up the vagus nerve and one of the first symptoms of Parkinson's disease is actually chronic constipation. So in those really progressed Parkinson's patients gargling like it's never going to come back to normal, it's a degenerative processes in their brain at that point, but it may help them have a better motility if they gargle and some people need to do that just to have a bowel movement when they're that progressed. But it's an ongoing thing.

Alex: Fascinating there is so much more I'd love to ask you but I'm very mindful of time. Dr Kharrazian for people that want to find out more about you and your work maybe talk a bit about where they can go and what they can find.

Dr Kharrazian: Sure, so I have a general website called drknews.com and I put different articles up there and on there I have different programs. One of the programs I have is 'Save Your Brain', like I talked about, and that's where people can go and enroll into an on demand whenever they want six week program and it just teaches them how to go each of the key steps we know are critical to regain the brain function. And I also have for healthcare professionals an Institute called the Kharrazian Institute and the first course is on neuro inflammation and that should be on demand and we go through all the different mechanisms that cause brain inflammation, all the clinical findings and that's really a Institute designed to teach clinicians how to do clinical work ups and treatment strategies. It's a bit intense for a non trained healthcare professional because we use a lot of terminology and terms, but certainly anyone is welcome to take it. It's just you know, I know what you're getting into if you are interested in that and then I have my book 'Why isn't my brain working?' So those are my main sources in thank you for asking me about this.

Alex: Fantastic. Thank you and just again sir to mention your book it really is fascinating and I feel like you're taking care of the reader because the end of each chapter you doing nice summary. So there were a few times when I was like am] I on track and I was like, yep, I'm on track it was is very helpful. Dr Kharrazian thank you again so much it's been a really Illuminating to every appreciate you making the time to talk to me.

Dr Kharrazian: Thank you. My pleasure.

