Introduction and Neuromodulation Overview

We have a very serious problem right now in the United States. I think it's a ticking time bomb. We've all seen the reports about autism rates that are skyrocketing.

But I also think that schizophrenia, which usually doesn't exhibit itself until 15 to 25 years later, I think that that's a ticking time bomb that is going to affect us in another decade or so.

We're gonna see schizophrenia rates rise dramatically. You heard it here first, I'm predicting it. This is Dr. Tons. Welcome to another episode of the Reverse Inflammaging Summit, Body and Mind Longevity Medicine.

And I'm your host, Dr. Robert Lufkin. We've heard a lot about the nervous system and how we modulate it with lifestyle and supplements and other approaches.

Today, we are going to talk to an expert in neuromodulation, but actually how you can directly manipulate and modulate the nervous system with technology.

I'm so delighted to have JP Erico today with us, who is the co-founder of a company that makes devices specifically for vagal neuromojulation and is an expert in this area and in many affiliated areas.

JP, welcome to the program. Thank you for having me. I appreciate the opportunity. It's so great to have you here. Before we get into the details, maybe you could sort of set the stage and tell our audience how you came to be interested in this fascinating area.

So it's a very eclectic background. And I appreciated the opportunities to explain it. An engineer by training, I went to MIT and studied aeronautical engineering.

becoming a patent attorney very briefly. And I was invited by my uncle, who is a world renowned spine surgeon, to work with him to develop a new set of products for spinal surgery.

We ultimately were a very inventive team and licensed products off. They've done about 20 billion in sales. Along the way, I had the opportunity to very well-respected neurosurgeon who did deep brain stimulation for treating Parkinson's disease in a central tremor back in the late 90s.

And I was fascinated by the effectiveness of the therapy and the safety of it. I knew that if I had the opportunity, I wanted to move into the field of neuromodulation and do something creative and innovative in it about Four or five years after that first opportunity to learn about it, I was given the opportunity start a new company and I knew that it was going to be in the neuromodulation space, but I didn't know what area we were going focus on.

And I had the opportunities to read an article that was basically an animal study in which they had taken dogs and they sensitized the dogs to an allergen.

JP Erico's Background and Vagus Nerve Origins

And when they did that, they created the opportunity to cause an anaphylactic reaction. And, when the did, that they then cut the vagus nerve in the animals and the animal survived.

One of the things that that neurosurgeon had told me was, anytime anybody has ever cut a nerve, and as a result of cutting the nerve gained a clinical benefit, there's an opportunity to potentially stimulate the nerve instead and to gain the same benefit.

And so in 2005, a group of us went to Columbia University and reproduced those results using a vagus nerve stimulator instead of cutting the nerves and were able to save the life of an animal that would have otherwise died of a anaphylactic reaction.

That is what started me on the journey of understanding and working on the parallel paths of the autonomic nervous system as well as the innate immune system, because it's of course the inate immune that's involved in those sorts of allergic reactions.

Yeah, it's such an interesting area and I know you've spoken about this before and maybe you could take a moment and just elaborate a little bit for our audience about your views on the innate immune system versus the adaptive immune systems and may be the proactive immune also that you have spoken.

Yes, I think most people, especially in the post-COVID era, are aware of the various different aspects of The Immune System. We have the innate immune system, which is the very basic first immune System to have evolved.

It is sort of has the first job of going after pathogens and bacteria and viruses and injuries to heal. We have the adaptive immune system, which when we hear about antibodies or T cell, memory T cells or other things, they're the cells in the arm of the immune that are involved in remembering what's happened to the body and being prepared for the next time that that challenge comes to pass.

There's also the central nervous system and the Central Nervous System really evolved in part to protect us from injuring ourselves or being in situations where danger lurked.

And so I refer to the brain as the proactive immune system or the nervous system is the Proactive Immune System because it allows us to prevent ever coming in contact with danger or injuring ourselves and other things.

So there's really three arms to the immune system. And the justification I have for using that type of language or description is the fact that about 15% of the brain itself is immune cells.

There's tissue resident innate immune cell called microglial cells and the role that they play in development and in maintaining tissues all throughout the body, but also in the.

Brain and. The effect that. They have. on ultimately degeneration is so critical that to assume that the brain was anything other than an immune organ is challenging, at least to me, from the perspective I have.

How do these microglial cells relate to macrophages and other types of immune cells elsewhere in the body? Macrophage is a wonderful cell type. In fact, I think they're probably the most important cells in a body.

It starts all the way back just a few days after conception when the very first cells to move into the nascent embryo. I mean, at that point, the embryos is maybe three layers of cells.

There's a wave of cell that actually come from outside the Embryo into it, and they're macrophages and macophage progenitors. And they build our organs.

They literally build the vasculature, they built the brain, They build liver, build heart, built skin, our bones. The role that they play in building those organs is maintained after we're born and during childhood helping us to grow into adults and then as adults helping to maintain us and ultimately their failure through challenges and inflammation and other things that derail their normal function.

lead us to degenerative conditions, everything from frankly osteoporosis to Alzheimer's disease. And ultimately it's their failure that leads to us dying.

Innate Immunity, Inflammation, and Stress

So understanding how to control them and keep them doing the homeostatic tasks, the housekeeping things that keep us healthy as best as possible is the goal of longevity science and medicine.

Yeah, it's interesting. A couple of our other speakers have discussed nitric oxide and the role that it plays. Interestingly, not only with the blood vessels and endothelium of the vessel lining, but also interestingly with macrophages and also neurodegeneration.

It sounds like that may be related to the microglial cells and roles that the macrophages the immune system plays that nitric oxide may be somehow involved in that as well.

Absolutely. And nitric oxide is one of a series of different molecules that have an effect on the immune system and on. On the nervous system, and can in short order can actually cause pain, can trigger migraines.

It can be involved in cardiovascular problems, blood vessel constriction, as well as in the longer run, promoting inflammation and being involved. In the inflammatory process.

So controlling these molecules and using them, sometimes you need them sometimes, you don't, but having the immune system and the nervous system functioning together to make certain that everything is moving along in synchrony and in harmony is what we need to do.

And that's where the, the Nervous System really comes into play. And so, so both the nervous system and the immune system are about inflammation and all.

So what, what exactly, let's just step back. What exactly is inflammation? What's going on there? How does it work? and how it relates to the nervous system, sure.

So inflammation is a response that cells have, both nonimmune cells as well as normal cells, to either damage or to pathogens. In fact, there are receptors on the surface of all cells that are called DAMPs, Damage Associated Molecular Pattern Receptors.

So if they sense damage or molecules that associated with injury, they'll become activated. There are also PAMPs which are pathogen associated molecular patterns and there are receptors that're associated those.

Bacterial infections have a certain character to them that these receptors will respond to. And when those receptors are activated and they're very ancient, long preserved in evolution.

When these receptors become activated, it causes inside the cell a cascade of different molecular interactions to lead to the expression of cytokines, which are chemicals that the immune system uses to communicate, things like TNF-alpha, IL-1 beta, IL6, which are interleukin-6 and inter-leucin 1 beta.

These molecules cause the cell to change its behavior and change it's energy usage. So we'll also get a chance, I hope, to talk a little bit about the effect of inflammation on mitochondria.

and also mitochondria's effect on inflammation. Inflammation itself has really wide ranging positive and negative benefits. And the case of short-term injuries, it's critical for us to stem blood flow or to attack viruses or infected cells.

That's all part of how the immune system functions, especially the innate immune systems. But when that inflammation lasts for a long period of time, I think of it as like a farmer.

A farmer might be called up to go serve in the Army. Well, if he's only gone for two weeks on reserve duty, he can come back and the farm is still functioning normally, and he could go back into normally functioning and serving the community with the Farm.

However, if he's called away to war and he has gone for years, that farm will fall into disarray because the farmer

isn't there to coordinate the activities.

Animals will roam away, the farm itself won't grow good food, and when the farmers comes back from that war, he may be suffering with PTSD. He may suffering from other problems.

The same thing happens in the immune system. Short stints of inflammation are healthy. Longer stents of chronic inflammation lead to a disruption, not only of the tissue that's supposed to be supported by those cells, but also those themselves become disrupted.

They become either primed or otherwise injured. And we see this in, for example, concussions or traumatic, chronic traumatic encephalopathy. The injury you see associated with football injuries or people coming back from war where they've been injured in traumatic brain injury settings.

Yeah, we've heard that from our other speakers too about stress and that stress, acute stress is good, healthy for the body and chronic stress bad. It sounds like you're saying the same thing that inflammation can be good if it's acute and a healthy response to an insult, Acute meaning short term versus chronic which means long term spread out over a long period can harmful.

How is stress an inflammation related? Excellent question. And in fact, I think of them as really two sides of the same coin. When I talk to people about the effects of inflammation, and I often talk about that stress as well as sleep deprivation can lead to exactly the cellular response.

So you can see an increase in those cytokines that we talked about, things like tumor necrosis factor alpha. You can those levels go up. in stressful circumstances, and you can see them go up in sleep deprivation circumstances the same way you would see then go out if you had a viral infection or a bacterial infection.

So there really is two sides of the coin. And we don't think of them that way when we think about, well, you could manage stress and that's not going to make you sick.

But how many of us have experienced becoming ill as a result of stress? It's because it's triggering the same response in your body. And I bring that back to that whole proactive immune system associated with the central nervous system and our cognitive processing actually becomes disrupted from both stress as well as inflammation.

You can see cognitive dysfunction. I mean, brain fog is something that people talk about associated, with conditions like fibromyalgia and long COVID.

where their cognitive processes aren't functioning very well. And it's a function of the fact that inflammation has been chronic for a long enough period of time that it is actually disrupting the brain's ability to form long-term memories and for those microglial cells to do what they need to build the network of new neural pathways to learn.

So what you're saying is that the brain actually thinking or psychological effects can have direct effects on stress and the immune system and manifest with chronic diseases just from psychological affects through these types of mechanisms.

Is that right? Sure. I mean, we all are aware of how psychological abuse, emotional abuse can lead to depression and can led to measurable changes in neurotransmitter expression in the brain.

For example, depression is often associated with serotonin. Serotonins is a neurotrasmitters that's produced in in brain, it's also produced but the brain has its own areas that produce serotonin.

And inflammation can actually disrupt seratonin synthesis as well as serotonin reuptake. So one class of drugs that's oftentimes given to people with depression are called SSRIs.

They're selective seratonins re-uptic inhibitors. So their job is to block serotonin being pulled out of the synapse, because you want to preserve as much seratonin as you can in those circumstances.

Inflammation is exactly the opposite. I joke that TNF-alpha, which is that pro-inflammatory cytokine, is the equivalent of a selective seratotin reuptake enhancer.

It actually builds more of those CERT receptors that pull serotonin out at the Synapse and it disrupts seretonin production. That has a downstream effect on melatonin because melotonin is a product of serotonins.

Serotonine is the product that tryptophan, which is an amino acid. Melatonins is critically important chemical found throughout nature because of its role not only in sleep, but also in how mitochondria function.

If you disrupt seratonine synthesis through inflammation and stress, You will also disrupt the energy balance within cells and disrupt mitochondrial function.

And in a short term, that's okay. But in the longer term chronically that leads to mitochondria dysfunction. It leads a lot of other degenerative conditions that are associated with that.

Yeah, let's dive into that. That's fascinating. Maybe you could elaborate on just the basics of what mitochondria are and their role. And then also the relationship between mitochondrion and inflammation, as you said, and maybe mitochondry and stress as well.

Sure.

Mitochondria, Acetylcholine, and the Vagus Nerve

So mitochondria are fascinating little creatures and I actually call them little creature because evolutionarily it's very likely that they were actually an independent life form.

They have the ability to take the waste product, if you will, of glycolysis, which is the first step in creating energy for the cell. Let me step back for a second.

The primary energy unit or the currency of energy in cells is ATP, and ATP is formed in the cells as a result of breaking down glucose. Typically, it's glucose that's being broken down.

And glycolysis is carried out by pretty much all cells in body, but it is a very inefficient process. It leaves a lot of really highly energetic waste products.

Mitochondria have the ability to take those waste product and produce oodles of energy. So as you can imagine, early on in evolution, there were a group of cells that could only do glycolysis.

And then there was this other group that had the ability to create lots and lots of and energy and they were eaten, if you will, by the cells who didn't do it very well.

They created this symbiotic relationship and it has evolved over more than a billion years, for now, all of our cells have mitochondria in them, and mitochondrion are the energy power plants, if you will, in the cells.

Inflammation has the ability to disrupt theability of those mitochondria to function properly. And so one of the downstream consequences of inflammation is mitochondrial dysfunction.

But it's a bi-directional relationship. When inflammation occurs, yes, there's disruption to mitochondrion, but when mitochondrio begin to become dysfunctional, they will trigger inflammation and actually they can actually trigger programmed cell death.

When the mitochondria fail, there's two ways that they fail. One way is that, they will eject their DNA. Mitochondria have their own DNA, it's one of the reasons why we are pretty sure that there were their life form.

They can eject that DNA into the cell and the cells sees that and views that as potential damage and will upregulate

the inflammatory processes. That's the one way that inflammation can be triggered simply by mitochondrial dysfunction.

The other way that they become dysfunctional is the electron transport proteins, and there's no quiz on this, but the proteins that are involved in electron transfer can leak out of them, when the balance of ions aren't correct.

And this is one of the ways, tying it back to the autonomic nervous system, is that one way we can regulate that is by enhancing parasympathetic tone.

So there's a special receptor called the alpha-7 nicotinic acetylcholine receptor. Again, no quiz on that, but they're present on the surfaces of cells like innate immune cells, and they are also present in the surface of mitochondria.

And so when they're activated and they are activated by the release of acetylcholine, which is the neurotransmitter of the vagus nerve and the parasympathetic side of immune system, of autonomic nervous system.

When that aceticcholene is released, it binds to that receptor and it has through each of various different locations that it's present, It has this anti-inflammatory cell preserving effect.

So one of the ways that we know that can kickstart those cells to behave normally again, if they've been inflamed, is to have that release of acetylcholine and activating these receptors.

Even in our own language, we see this. We tell people, If they're stressed out, We say, take a deep breath. doing meditation or yoga, yoga breathing techniques is a very positive thing for our health and for stress levels.

And it's also true that those things are good for lowering our inflammation levels and that's all a function of activating the stretch receptors that activate the parasympathetic side of the nervous system.

So it all ties together. It's a fascinating story. Yeah, now a lot of your work has been with the vagus nerve. So tell us what is the Vegas nerve and how does it tie in with inflammation and stress and all these things that you've been talking about?

Sure. The vagus nerve is the 10th cranial nerve. So your brain stem has a series of nerves that reach out to various different places, mostly in your head and neck.

But the longest nerve, uh, is, the tenth cranio nerve it's called the vagous nerve because of this, this Latin root, which means the wanderer, because it is longest of the cranios nerves.

It wanders throughout your chest and abdomen, innervating various, different organs and tissues. What most people don't realize who are aware of the vagus nerve is that about 80% of fibers that are in the Vagus nerve, and there are hundreds of thousands of them, about 85% are actually bringing information back up into the brain stem.

It's not a nerve where, well, there aspects of it that bring information from the back down to the body, but it is the brains primary source of information about how the autonomic functions or your heart rate your breathing, your kidney function.

Frankly, even your immune system and your metabolism are related and all the information is being relayed back up into the brain stem through the vagus nerve.

Now, the functions in a way I refer to it as frequency coded. So it's not so much the strength of the signal that's important, although that is. It's really more important about how rapidly or what frequency those nerves are firing.

And so it is possible to activate the vagus nerve through deep breathing by activating stretch receptors that will change the frequency with which the nerve is firing.

You can also do it manually or mechanically. you can gargle cold water for 20 minutes. Seems like a long throw to

get to doing that. Humming. dancing, chanting, all of those things will activate it through the proximity of the nerve in your neck to your voice box and other things.

You can also stimulate it manually. There's an old technique in medicine, which was called the deep carotid massage, and it involved digging the thumb into the neck and rubbing the carotic artery.

It was actually a physician from upstate New York by the name of, I think it was John Leonard or James Leonard Corning. He might have been a member of the Corning Glass family, but he recognized that the nerve, the vagus nerve ran in that same sheath as the carotid artery, and that really had nothing to do with rubbing the vasculature or the blood vessel.

It had to with the fact that thumb was activating the vegas nerve. And it was used to treat things like supraventricular tachycardia, which is a cardiac condition where your heart's beating very fast and it hurts.

And then also status epilepticus, Which is when you have a seizure that doesn't break. So people used use this technique to fix that. Um, and he said, you know, I think maybe it's really the nerve, not the blood vessel that we're activating.

and so he was the very first person to come up with the idea of using electricity to stimulate the nerves. Now, for my benefit and for the benefit of everybody today, he wasn't such a very good electrical engineer.

Brilliant scientist and physician, but he didn't have the electrical engineering capacity to make a device that would stimulate the vagus nerve correctly.

That took about 100 years for first vagal nerve stimulators to be approved and they're implantable devices that are used to treat epilepsy. But they've subsequently become approved for a number of other conditions, including depression.

And a non-invasive device that I was involved in developing is actually used to treat migraine headaches and other headache conditions. Although we did study it in a numbers of things, and of course it has stress relieving and stress management benefits, the same way deep breathing techniques do or meditation does.

So the stimulating the vagus nerve then electrically somewhere along its course will simulate the effect of deep breathing and get the stress response and also immune response as well with it.

Yes. So when you stimulate the vagus nerve electrically, there's a pathway that goes again, back up into the brainstem. It goes into an area called the nucleus tractus solitarius.

Again, nobody has to remember that, but that's where a number of really important nuclei exist in the. One of which is called, uh, the locus coeruleus.

The loco coelule is tiny. I mean, compared to the 86 billion neurons in brain, it's only a couple hundred thousand. but it has the most widely distributed network of neurons or projections into the brain.

It's the primary source of norepinephrine in thebrain, which is a very important neurotransmitter. Another area that's also activated by vagus nerve stimulation is called the nucleus bacillus of Maynard's.

And that, much like the locus coeruleus, is the primarily source for acetylcholine in And so when the acetylcholine is released, it has the effect of calming down the microglial cells, because again, aceticcholene is the neurotransmitter that's binding to those receptors that we talked about before, the alpha-7 nicotinic aceti-cholin receptors, and it down-regulates inflammation.

Vagus Nerve Stimulation Devices and Uses

It corrects any dysfunction that is going on in the mitochondria, And it sets those micro-glia cells which are innate

immune cells on the correct path of doing their homeostatic function.

We've got research looking actually at animal models of Alzheimer's. And you can see that in the Alzheimer animals, when they become symptomatic, their microglial cells in the brain are exhibiting all of the characteristics of an inflamed immune cell.

And within just a matter of minutes after stimulation is delivered, you can see changes, morphologic changes shape changes and behavioral changes in those cells, moving them back into the more normal function that you would expect of a healthy animal.

Go ahead. No, I didn't mean to interrupt. Go ahead. No. I mean, so, the same thing that's happening in the central nervous system is also happening and the rest of the body.

There's a reflex arc that was discovered by a brilliant scientist by the name, and he's, a physician, is a neurosurgeon as well, by name of Kevin Tracy.

And Kevin Tracey is the discoverer of some of what I've talked about today, but he recognized this reflex arch that exists that doesn't just affect the Central Nervous System, it also affects the Body and it down-regulates pathological inflammation, whether it be autoimmune diseases, he's looking at rheumatoid arthritis and Crohn's disease, as well as other people have looked at effects on heart disease atherosclerosis and other problems like fibromyalgia pain.

We've looked a hypertension, we've look at a number of other things in the periphery, but most of the work that we have done is really centered on the central nervous system.

and things that are affecting both early life as well as late stages of life, things ranging from autism and schizophrenia all the way through to Alzheimer's and Parkinson's disease.

Well, so the stimulation of the vagal nerve then takes those 80% of efferent fibers going back to the brain. So it's a way of directly stimulating thebrain from the periphery and then the brain stimulates the rest of body and so you get the effects throughout everything there.

Is that right? Yeah, it is bidirectional. But yes, there is a reflex arc that happens in the brainstorm. The signal going up into the outflow from the dorsal motor nucleus of the vagus nerve down into the body to cause that anti-inflammatory effect.

It's called a cholinergic anti inflammatory pathway. One of our other speakers spoke about the Vegas nerve in the context of something called polyvagal theory or autonomic dysregulation.

How does that tie into this? Is this the same thing? Very much so. In fact, I think you're referring to Stephen Porges, a brilliant vagal theorist, if you will, and a lot of his work is psychologically based and evolutionarily based.

And I, think a, lot, of the molecular work that really ties all of, his theories together is the work, that I've been talking about in the central nervous system and peripherally.

So you have that fight, flight or freeze mode that he talks about that is sympathetically driven. That's the sympathetic arm of the, of The Vegas or the autonomic nervous system.

And that's, the opposite of, The rest, digest and restore side of. The autonomia nervous, system, which is The Vagus nerve or The parasympathetic. So yes, I very, very familiar with his work and he's a brilliant, brilliant theorist.

And so to use a device like this, you just apply it to yourself. I think you may have one there, a sample one we can look at that it's at. Yes. So this is the device.

The wellness version is referred to as Truvega. It's available for purchase. What you'll do is you place a small

amount of electrode gel. so it is gel that's provided with the devices onto the electrode surfaces.

And then you palpate for where you feel your pulse. sort of technically it's between your trachea and your sternocleidomastoid muscle, but it is basically where you feel your pulse.

Place a little gel on there, rub it in on the neck there and then activating this button here will cause the device to turn on and everybody's anatomy is a bit different.

You turn up the amplitude of the signal to the point where First, you'll feel a tingling at the skin and then it'll sort of move away from the skincare and move into the muscle and you will feel the little vibration of the muscles.

And once you get to a strong enough amplitude, most people will the corner of their mouth pull down. That's associated with the platysma muscle, which is sitting right in the neck there and controls the corners of your mouth.

It happens to sit in close proximity to the vagus nerve. So we know that when your corner your lip pulls down like this, while you're doing it, that indicates that you've activated the vagus nerve.

And the moment you pull the device away, the effect goes away. But the longer-term effects of what you have done to the central nervous system and to this vaguely mediated pathway can last for hours.

In fact, in some studies, even days, we did a study talking about looking at cardiac vagal tone, which is around heart rate variability. And we were able to increase heart rate variability, increase cardiac vagal tone after a one, two minute stimulation that lasted out 24 hours.

So we generally suggest people use it twice a day, you know, sort of when you brush your teeth in the morning and in evening. And it will have sort an effect that lasts over the full 24-hours of your day.

And so what we're talking about here is a use for kind of the general public for wellness and longevity and not necessarily a pathological condition. I mean, other than inflammation, which we all have, is the pathology that we get with aging, but that somebody that regular people could apply.

What are the contraindications for this? Are there certain people who shouldn't use it? Is it pretty much available for anyone? So it's pretty available to everybody.

We're targeting adults. Obviously there's pediatric indications. The prescribed version of the device, which again is called GammaCorp, that is specifically provided prescribed for migraines and other severe headache conditions like cluster headache, for example, can be used both acutely and preventatively.

But the precautions include things like if you've had a previous surgery on your neck and there's metal in your. It's not guaranteed that it's going to cause a problem, but it is contraindicated because there is always the concern that there could be some heating effect.

of the electric coupling between the device and a metal implant in the neck. It hasn't been observed, but it's a theoretical risk and therefore we contraindicate for that.

Contraindicates if the person has had a prior surgery that's cut the vagus nerve because in that situation it is not going to be useful. Those are the sorts of things that we would contradict.

But for most other people, it's a very benign and low risk treatment. I guess inflammation is notoriously hard to measure with objective markers. Is there any effect you see on C-reactive protein or any markers like that?

What sort of results are you seeing with this? So yes, C-reactive protein, vagus nerve stimulators have been studied, including ours, looking at markers like those cytokines that we've talked about, TNF-alpha IL-1.

And there's published literature around all vagous nerve stimulators having that effect, whether they're implanted or

non-invasive like ours. But there are also effects that, we have seen on metabolic measurements, things like HbA1Cs on lowering of blood pressure.

So there is a number of different markers that you can look at. I'm interested for those gastroenterologists out there and people with IBD. We're very interested to hear about the effects it might have on fecal calprotectin levels, which is a marker that's measured in people who have inflammatory bowel disease, because there's data out they're suggesting that it has that effect too.

It will lower those levels. Which is consistent with the lowering of stress and lowering inflammation. So there are plenty of markers out that you can look at, sure.

I'm interested in the psychological effects on that. You mentioned it was used for depression for the implanted devices. What are the difference in effects of the implant ones, which is obviously a much bigger procedure versus the topical ones for psychological conditions like depression or other things?

Yeah, so all of the data that we've collected, whether it be in animal models, studying the implanted devices versus the non-invasive have all shown exactly the same effects both clinically and pre-clinically.

measurements of activations of areas in the brainstem. We've done EEG studies, we've fMRI studies. All of which seem to indicate that whether it's implanted or done topically, it has the same effect on the nerve.

Of course, Not all of those are large clinical studies. They're more preclinical studies, but there's no reason that I know of as a scientist to believe that there is any difference between the implanted device in its activation of the vagus nerve versus a noninvasive.

And for a person to use it in this topical application, what sort of things do they experience after? I mean, obviously you mentioned the pulling on the platysma muscle and all, but like after they begin to us it, do the feel effects of wellbeing or are there any other effects or there are any side effects also that we should be watching out for?

So yes, there's definitely a feeling, a lot of patients will talk about a feel of stress release in the neck area.

Clinical Effects, Cognitive Benefits, and Neurodevelopment

They'll feel just looser. We've got chiropractors who use it who say that when they're dealing with a person who has a high level of stressed, it's very difficult to do the manipulations that they do.

And within just a minute or two after stimulation, they feel as if the muscles have just turned to butter. They're much more relaxed. There's also effects that have been studied by the Defense Department and published around cognitive enhancement.

And I realized that for some people that may sound very Star Trek-y, but there was a $100 million program that DARPA, which is the Defense Advanced Research Projects Agency, ran looking at various different neuromodulation products, looking to see if any of them could actually enhance a person's intelligence.

And I'm happy to say that our device came through that work very positively and it's been published, demonstrating anywhere from a 25 to 40% improvement in learning capacity and the application of that learning and formation of memories out and tested out 90 days.

So there appears to be, and I understand why that would be the case, but there appear to at the top level cognitive benefit, a cognitive enhancement benefit associated with vagus nerve stimulation.

The flip side of that is, well, what happens in inflammation and what does inflammation do to damage neurodevelopment? And that's where we're doing some really interesting work right now, looking at the consequences of neuroinflammation or inflammation on neuro development.

And, that where I talked earlier about autism and schizophrenia at early stages of life. sort of a reversion of those innate immune cells to sort a second childhood, if you will, reverting back to doing some of the things that are really only appropriate during neurodevelopment.

but result in neurodegenerative conditions like Alzheimer's and Parkinson's disease. That's why when you talk to some of the neuroscientists and neurologists who are working on Alzheimer, one of things they talk about is anything that works for schizophrenia looks like it has benefits in Alzheimer.

And the reason for that is because it's exactly the same mechanisms that are taking place. So really exciting stuff. Yeah, it's fascinating. We had Chris Palmer as one of the speakers, a psychiatrist from Harvard using ketogenic diets for schizophrenic patients.

And those are the same ketogenetic diets that are so effective in Alzheimer's. Dale Bredesen was a guest here also. It's amazing the overlap with inflammation and all these common threads that affect our longevity that are controlled by this.

You mentioned it was effective for migraine headaches, I assume other headaches too. Yes. Yeah, severe headaches, it's been studied in severe headings like cluster headache, which is referred to as the suicide headache.

It is a terrible condition that affects largely men, about two out of three or even three out four sufferers are male, but the Suicide rate among that patient population is 20 times higher than the national average.

it is brutal disorder. If you've ever seen somebody suffering with one of those headaches it, is difficult to watch. So that's actually the very first thing we went after to get a clinical approval because we felt that that patient population was in desperate need.

Yeah. Now, understanding that, I guess, neck pain can have many, many causes and depending on the cause, but is this something that is effective for any sorts of neck Yeah, cervicogenic headaches, you know, one of the reasons why women suffer with more migraines than men is because they tend to carry stress in their neck.

The neck muscles become very, very tense, sort of, permanently locked, knotted, and that stress ends up through cervical nerve roots ends up leading to migraine headaches.

And so one of the reasons that I personally believe we were successful in getting approval and showing in our studies how effective it can be is because of that ability to relax the neck muscles.

So absolutely. There's so much promise for this, so many effectiveness across inflammation, across stress, all these different things. What sort of resistance are you encountering?

Why isn't this more widespread? You know, why isn' everyone using this everywhere? What is the pushback and what are doing about it? There hasn't been a tremendous amount of pushback from patients or clinicians.

In fact, most clinicians who've heard about it and learned about are fascinated by it, and want to try it. The issue has been largely around reimbursement.

Most people in the United States have insurance and expect to have, insurance cover things. And that's a dance that large companies have the opportunity to do very well in, in small companies sometimes have challenges.

I think that going into the space with a product that's priced at a place where people can afford it themselves is going to give us an opportunity to expand the usage tremendously.

And I'm looking forward to that. It's really only within the last few months that we've been selling the product through that channel directly to patients.

The military has been one of our biggest buyers, frankly, of the product. They recognize the value and they're freely using it. And this direct consumer product, I assume that if you had a family that everyone in the family could use it, just observing sanitation stuff, you just wipe it off, wipe the electrodes off and reuse it right?

Yes. I mean, our hope is that the same way people don't share toothbrushes, they won't be sharing their Kevin doors or their true Vegas, but you're certainly right.

There is, there is option and I've seen it in my own house. So yeah, it will happen. Well, since you mentioned it, what is your personal routine, if I can ask, like, how do you use it and what benefits have you seen yourself from it?

I'm fortunate enough that I don't have a lot of the symptoms. However, when I use it, it's usually during a period of significant life stress where, you know, like most men my age, I get up in the middle of night to go to the bathroom.

And when i get back to bed, if I've got a lotta stress and things on my mind, i have difficult time falling back asleep. And what I found is that if I use it, I will be back to sleep within a matter of minutes.

So I think that's my own personal testimonial. I can tell you that it's been very beneficial for stress management for my wife as well. And the cognitive enhancement benefits have certainly helped in the house.

Some kids have used it as. Well, and I'm very pleased with how I've seen the effects on them. Cause I really truly believe that ultimately one of the key benefits of vagus nerve stimulation is going to be neurodevelopmental optimization.

I think we have a very serious problem right now in the United States. It's a ticking time bomb. We've all seen the reports about autism rates that are skyrocketing.

That's the function of maternal immune activation and maternal inflammation and early childhood inflammation. And there's plenty of data to demonstrate that.

But I also think that schizophrenia, which usually doesn't exhibit itself until 15 to 25 years later, I think, that that's a ticking time bomb that is going to affect us in another decade or so.

We're going see schizophrenia rates rise dramatically. You heard it here first, I'm predicting it. And given the fact that mental health is such an important thing for the country to be addressing, whether it be homelessness or mass shootings, mental is a really major problem.

The data is out there demonstrating that if we can reduce inflammation and infections during pregnancy, we can reduce schizophrenia rates by 30% or more.

And unfortunately, I think we're going in the opposite direction. I that there's a lot more inflammation and a more risk of pregnant women being under a high stress or under inflammatory conditions.

It sounds like this is an area ripe for prospective trials in this area. Are there any going on now or is this something yet to be done using this type of technology to reverse or diminish maternal perinatal inflammation?

Yes, in fact, I'm partnering with really a world renowned scientist, a basic scientist up in Canada, who she's got models of both schizophrenia and autism in animal models where they do exactly what we've been talking about, generate an inflammatory insult.

while the animal is pregnant. And what they see in the offspring is not only the behavioral symptoms of autism or schizophrenia depending on when the insult is delivered, but it also has an effect physiologically.

You can actually do the post-mortem analysis of the central nervous system and you see the same structural anomalies that you in autism and schizophrenia in humans.

So what we're doing is we are doing a study to look to see whether or not Vegas nerve stimulation delivered during that period has the ability to protect the offspring against that immune activation.

And there's reasons to believe that it will work because we've seen it in headache models where we have taken animals and sensitized the animals so that they become migraine ores.

And we can prevent that sensitization from occurring and from taking hold by using vagus nerve stimulation in those models. So I'm cautiously optimistic that the benefits will be there.

I'll come back next year and tell you. Well, we've covered so much interesting material here in this hour.

Future Research, Resources, and Closing Remarks

How can people, if they want to learn more about your work, how can they follow you on social media or what is your… For the device, it's easy. It's truevega.com.

That's T-R-U-V-A-G- A dot com. So that's if they want to get a device. But there's also the Vegas Nerve Society. And I'm doing a podcast with my partner, Dr.

Nawaz Habib. The podcast is called The Health Upgrade Podcast. We welcome everybody to listen in on that. Then of course, I am in the process of writing a book.

Actually, it's a companion book with a book that my podcast co-host is also writing. So the two of us will have two books that will come out together.

He's focusing on the clinical aspects and I'm focusing the more scientific aspects, and historical aspects of vagus nerve stimulation. Should be exciting.

Well, great. Well we look forward to having you back to talk more about that when that comes out. So thanks so much, JP, for spending an hour with us.

And thank you so, much also for all the great work you're doing. It was a pleasure speaking with you. As I said, I look to updating everybody in due course.

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