417 – Vagus Nerve - Transcript

With Steven Bruce and Professor Owen Epstein

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Steven (00:00:02):

There has been a lot of chat about the vagus nerve over recent months, or I should probably say over recent years, whether that's about the brain gut axis or vagus nerve stimulation or even its anti-inflammatory role.

(00:00:56):

And of course, there's that ongoing debate about the validity of Stephen Porge's polyvagal theory as well. My guest this evening is a consultant gastroenterologist who is at the forefront of a number of noninvasive surgical techniques, but has devoted enormous effort to exploring the role of the vagus nerve, including looking at its relationship to chronic physical illness. So Professor **Owen** Epstein, welcome to the academy. Thank you for making the trek all the way up here from London for this evening. Some people might be wondering why, if we're going to talk about a nerve, I'm not talking to a neurologist rather than a gastroenterologist, so perhaps we better explore your background in this first of all.

Owen (00:01:34):

Yeah, sure. I mean, the first thing to say is that you've probably heard of the gut being the second brain, and so gastroenterologists should actually be thinking neurologically as well. They don't always, but really my own interest in gastroenterology diagnosis management, it really grew out of my observation over my own training and later years that gastroenterology has steadily but surely become obsessed with the mucosa because we are all defined by endoscopy. If you go along to your GP with a problem, they'll refer to the outpatient clinic, and inevitably you'll have it either an upper or lower GI endoscopy. And so therefore, if you believe that what there is is what you see, then it's not difficult to understand that the prism through which most GI problems are viewed is in fact through the endoscope or through the mucosa, and that's wrong. So to answer the question, I think we have to have a much more holistic view of an organ, which is a much more interesting organ than just a mucosa. And we can perhaps explore that a little bit More if you wish to.

Steven (00:02:53):

Yeah, sure. There's so many areas we could go down with this evening's discussion, but why is the gut regarded as a second brain rather than the heart say, which many would say is equally important.

Owen (00:03:06):

Yeah, I'm not sure who coined that phrase originally, but it's a long organ. It's 26 feet long.

Steven (00:03:14):

I Guess we're more conscious of what it gets up to than the heart.

Owen (00:03:17):

Yeah, there's a lot of monitoring that goes on in the gut. Of course, it's one of the only organs that's actually exposed to outside environment.

(00:03:26):

So it has to have a radar system in a way to inform the organism, and this isn't just humans, but it's all organisms, of the safety of what you're eating. And it's also the way we get our fuel in. I mean, food is really fuel, that's what it is. I mean, it can be very tasty, but essentially it's taking fuel. And therefore it's important to know when you fill your fuel tank when it's empty, you need to know when you're running on reserve. And of course, there're the waste products that go through the exhaust pipe, which you have to know about as wellYou've got a tube 26 feet long with four different organs, really: you've got the oesophagus, the stomach, the small intestine, which is 20 feet long, and the large intestine, which is about five and a half feet long, and each of has got a different function, you need a lot of radar, if I could use it that way of describing it.

Steven (00:04:22):

So then where does the interest in the vagus nerve specifically come into all four of those sections?

Owen (00:04:30):

Okay. Well, perhaps to start at the beginning, all of us learned about the cranial nerves, and One of the first things they did in anatomy was to learn about the 12 cranial nerves and the mnemonics that helped you remember it, most of which were rude. But one of the interesting things about the 12 cranial nerves is that there is one cranial nerve, which is quite different. 11 cranial nerves feed the head and neck essentially. So there's optic nerve, the lingual nerve, the auditory nerve, and so on and so forth. But there's this one nerve that comes out with the rest of them that actually travels to every organ in the chest, in the abdomen. And in fact, long ago when this nerve was actually dissected, it was called the vagus nerve because it's the vagabond nerve, is the vagus nerve, is the vagabond nerve, and it touches on all the organs in the Chest and the abdomen. And that's what makes it so different. And it's really not just a nerve that we think of as being motor or sensory. That's the way that we tend to think of nerves. It's a much more complex and interesting nerve, which is really where Stephen Porges came into my thinking in a particular time, which we'll perhaps get into at later stage. But this particular nerve must be special because it is special. It's unlike any of the other nerves.

Steven (00:06:06):

And you mentioned Stephen Porges there, and maybe this is the wrong time, get into this, but I'm curious. He brought up this polyvagal theory, what about 1990s? Was it?

Owen (00:06:16):

Yeah, these research started in the 1980s. He was interested in,

Steven (00:06:20):

So it's not actually new, but there is still a debate going on about it. Perhaps you better explain to us what is meant by the polyvagal theory

Owen (00:06:28):

First of all. Wow, that's an interesting one. I won't go into, I mean, we can go into it in more depth, but it really arose from what he noted as a very eclectic clinician. He is a developmental neurobiologist. He's a professor of psychiatry. He's a polymath. He's very empathic individual. And when he was working in the paediatric neonatal setting, he noticed what he called the vagal paradox. If you imagine that when a newborn is stressed, there's a problem in labour and there's been some complication, and the dear old foetus isn't able to find his way out of the birth canal, one would expect that the response of the foetus would be to switch on its sympathetic nervous system as a response because that's what we would do if we were in trouble. But he noticed that in fact, what happens in childbirth and it's monitored, is a bradycardia develops, and that's very paradoxical. Why should they develop bradycardia when they're stressed? And he called it the vagal vagus paradox. And I think he must have scratched his head for a long time, and eventually he came out with a theory which has I think, quite robust backing to it. And to understand it, I'd like to wind back to something which isn't particularly neurological, but to the whole idea of safety.

(00:08:12):

Is that okay?

Steven (00:08:13):

Yes.

Owen (00:08:15):

Okay. As you can imagine, and I think it's an important clinical point to remember that the fundamental requirement of all animal forms and unicellular life forms as well is to find a place of safety because that's the only way that it's possible to live a decent life. And he has stressed the fact that the most basic instinct that animal forms have is to find safety. And the way that we as warm-blooded animals evolved was to have sensing system. So for example, I'll show you a little picture over here. Our sensory information that we are all aware of are our external sensors. So constantly while we're sitting here together, our ears, nose, tongue, all those sensory organs are accruing information and that information is being fed at a very high rate to our brainstem and telling us whether we're safe or not. It is like when you're driving your car and then just out the corner of your mirror, you see some crazy guy going to pass you or a motorbike coming up. Before you've even seen the individual or heard the motorbike, your sensors pick it up and you respond very quickly. And that is absolutely fundamental to survival. So the big question that arose in his mind was, we've got these external sensors, which he calls extraception. What about her interoception? What's telling us about what's going on internally in our organs? And with his knowledge of what happens

in the neonate, and then looking at the different nervous systems of reptiles and more advanced life forms, mammals, particularly warm-blooded mammals, he recognised that the safety operation of reptiles and of neonates for that matter, or foetuses, is quite different from the newborn infants and us adults. And I suppose the first message is that the sensing organs are absolutely critical to survival. And that what is the sensing organ of our internal organs? It turns out that it's the vagus nerve.

(00:11:27):

The vagus nerve is the eyes and ears and nose and tongue of our internal organs constantly feeding information to our brainstem, telling the brainstem whether things are okay, whether there's wellbeing or not. So that's the first point that I'd like to make. And that is that our most basic instinct is to look for safety. And in fact, in the diagram that I've got over here, you'll see that our sensors send 11 million bits of information per second to our brain, and that's coming from all the external organs, never mind the internal organs, and only about 1% pass through our spam filter. So as you're sitting on the chair and those who are watching this evening or sitting on a chair, you were not aware of the fact you're sitting on the chair until I mentioned it. And you can suddenly feel you're sitting on the chair, and that's because there's a biological spam filter which keeps unnecessary information out of the way. But if the chair was to get too hot, for example, it would break through and you'd say there's something wrong with the chair. So I think the starting place for us all to understand, and I think it's very important for all clinicians to understand, is that according to him, and I think it makes a lot of logic, that seeking safety is very important. You need to have a safety sensing mechanism. Sensing mechanism for the external world is very easy to understand. But boy, our sensing mechanism for the internal organs is not part of the medical paradigm at all. It's not something that's taught medical school, et cetera. So that's where we start. Okay.

Steven (00:13:06):

Why the polyvagal theory? I'm thinking it's sensory and it's motor if you like, but why is that polyvagal as opposed to

Owen (00:13:15):

I knew you'd ask that - it's not predictable, it's not that easy to encapsulate the whole thing in a sort of single frame, but I want you to bear in mind the fact that it's this element of survival and safety that lies behind it all. Okay. So it turns out that when we were medical students and when you were in the world of physical therapy like osteopathy, all the other physical specialties, one of the things we learned about the vagus nerve was that it is an efferent nerve.

(00:13:51):

So what does it do? It makes your pupils constrict. It makes your bronchi constrict, and it is important for digestion in the sense that it stimulates the gall bladder to contract bile pancreas to secreted enzymes and for the gut to move. So the whole understanding of the vagus nerve to this day in medical students and in a-level students doing their biology is that you've got your cranial nerves and the 10th cranial nerve is responsible for these phenomena. It's not the case at all. And if I could just, I haven't got many slides, but I'll just show you my next one, which I think would be quite helpful.

Not me, but neurobiologists demonstrated maybe 20 years ago that in fact, 80% of the vagus fibres are in fact afferent and only 20% are efferent. And it's very easy in animal species to differentiate on the basis of histology. And there are lots of ways that you can demonstrate that most of the information is uploading and therefore it's an intranet. It's uploading information processed in your central processing unit in the brain, and then it's interpreted. And then there's a download instruction, which is only 20% of it's function. So it has got a sensory motor component like you're suggesting. So it's not just an afferent nerve, it's very much an efferent nerve. And then the best insight has come from observations that have occurred when animals and humans are stressed. And what happens physiologically is that under any stressful situation, I'm talking about significant threats, eye threats, et cetera.

(00:15:56):

What tends to happen is that you first call on your sympathetic nervous system, and that's very high energy, very calorie consuming, only lasts a short time and it's fight or flight. But if you don't manage to find your equilibrium, go back to a safety situation, then you call on a primitive remnant of the vagus nerve, which is called the dorsal vagus. It's called the dorsal vagus because it goes to different parts of the brain, so it splits. The vagus nerve is split into two branches. One is the ventral vagus, which we can come to later, but the dorsal vagus is a reptilian remnant. It's an evolutionary remnant. And if you think of Tom and Jerry, if Tom is chasing the mouse and there's a hole to run through, that's the sympathetic nervous system. And what happens that if there isn't a little hole to escape into then a mouse or a rat or a pig, and experiments have been done in all animal species, will then revert to this very primitive response, which is to freeze because that's what reptiles do. When a reptile like a frog is under terrible stress, it'll play dead. There's a term for it called thanatos, and that's true for snakes and alligators and so on. They don't have this ability to run very quickly or disappear very quickly.

Steven (00:17:39):

I'm just wondering what you have to do to stress an alligator! To be honest, there can't be very often where they have to freeze.

Owen (00:17:48):

No. I've never thought of That, but certainly if you take frogs, and they can handle it because they're coldblooded, so they can reduce their blood pressure, their blood flow to the brain, they can markedly reduce the amount of activity in the gastrointestinal tract so they don't make any noises. Their skin can go cold. They're cold-blooded animals and they're well adapted to this sort of dorsal vagus, and they only have the equivalent of a dorsal vagus. We have that remnant, and it means that if you can't resolve the threat physiologically, the body calls on this ancestral remnant, which results in freezing, brain fogging and inability to get out of bed, fatigue, all the things that would occur if you were actually using your dorsal vagus.

Steven (00:18:46):

I'm glad you said that. You explained that because when you say freeze, I imagine simply standing still with an inability to do anything. But actually it's not that it's dithering, it's wondering not being able to decide rather than

Owen (00:19:00):

It's a patient who comes into you with a sort of slightly frozen expression with very little expression in actual fact, unable to make proper eye contact. And they'll often tell you, they'll often use the word I feel frozen. But no, they don't actually freeze physically, but in terms of the way they look, the way they feel, the way they organs are, and the problem is that warm-blooded animals really aren't very well adapted to this particular form of response. And so that's the dorsal vagus, which is ancient. The ventral vagus, which is the other split of the vagus, is the one which is carrying information from all the organ systems.

Steven (00:19:44):

Is this a physical split in the nerve? Sorry to interrupt you. Is it a physical split in the nerve, not just two elements of the same nerve?

Owen (00:19:49):

Well, Yes. Different parts of the brain accepts the afferent vagus And synapse in two different areas of the brain. And the ventral vagus is responsible for well looking after your general wellbeing and also sensing when there's threat, it can pass it over to the dorsal vagus or to the sympathetic nervous system. But the ventral vagus is all about feeling comfortable. Like we are chatting over here, hopefully your ventral Vagus is engaged. Now we're talking, we're looking at each other. We've got some expression, we don't feel intimidated. I'm looking at you and you're looking at me. And essentially the ventral vagus is saying you're safe. You can get on with life. So the polyvagal theory is really very intriguing because it starts to explain or starts to raise issues about whether wellbeing is about where you are on that ladder. If you imagine it's a ladder with the ventral vagus being general wellbeing, all of us have through the day and through the night, we have little episodes where we don't feel that well, but that if you're unable to sustain wellbeing, then in extreme situations like in war, PTSD or individuals who are in very traumatic home domestic situations, et cetera, that dorsal vagus will start dominating and you'll start to feel unwell. Your organ system will presumably start to malfunction, and that's the basis of what it is. So polyvagal is all about looking for safety and helping the body find its state of safety without thinking about it. This isn't something you can think your way through and just trying to manipulate the organism to find, it's like a shock absorber to find a nice smooth route through life.

Steven (00:21:59):

I had a question coming just a minute ago as you were talking about that from Rachel who asked whether narcolepsy is effectively a dorsal vagal activity.

Owen (00:22:11):

I'm not sure, but of course you could make a point of that. I think the polyvagal theory would suggest that all these invisible physical disorders where you don't find an actual physical cause for the problem are in some way tied up with the way the organism is being called upon by a very primitive neurological system. And sleep apnoea, for example, would be another example of that. Of course, as a gastroenterologist, and we can go right back to the beginning where we started, I was a mucosologist trained in doing endoscopy and patients come in and you'd stick tubes up and down them, but I was never satisfied that that was

really the way to go. But it makes a big difference to my practice because when I'm confronted with irritable bowel syndrome or functional dyspepsia or non-cardiac chest pain or change in bowel habit, and the hardware tests are all normal, CT MRI, all the things that we've got, which are great, it makes it a lot easier to start deconstructing the problem if you're aware of the fact that the organ, particularly the digestive tract, but it's true for the heart and the lungs as well, maybe sensed as being malfunctioning because of the fake news in a way that the body is having to contend with. And that of course leads to the question of how do you measure it and how could you treat it, et cetera. It's not that complicated, but it is, if you see what I mean. As you know, nature isn't really complicated. We complicate nature, we're complicated. Nature has got its reasons for organising itself like it does

Steven (00:24:14):

Well, it's clearly complicated enough to have people still debating the role of the Vagus nerve or the effect of the Vagus nerve at the moment.

Owen (00:24:21):

No, no, no, definitely. I mean, it's a theory and he's the first person to admit the theory, but there's quite a lot of basis to it,

Steven (00:24:29):

Not surprisingly,we've had quite a few questions come in about conditions connected with vagus nerve activity. One thing I wanted to ask before we moved on though, is on this diagram here, it shows up the vagus nerve and the facial nerve. Is that just because that's the diagram or is there a particular reason why those two highlighted on here?

Owen (00:24:47):

Okay, very good point. All the cranial nerves have got branches of the vagus nerve that run along them as part of its radar. Okay. And they're little vagus fibres that are carried along with the optic nerve, the facial nerve, the lingual nerve, et cetera. And their function is really to do this radar business to try and pick up if there's any problem. And that's why you can tell quite a lot about what's going on in the vagus nerve by looking at somebody's face, if you see an animated face and you're communicating well, that's your vagus nerve actually responding. It's not your optic nerve responding, it's the vagus nerve, which is interpreting. So that's a very good observation you've made.

Steven (00:25:37):

So getting back to those questions that came in, Caz says, you mentioned interoception earlier on, are those interoception issues linked with ADHD and ASD? Is this an issue with the vagus nerve?

Owen (00:25:58):

I think it's a very important issue. The kind of medicine that I practise, clinical medicine is completely enmeshed in hardware. When patients come to see us, and we've been mentioning this before, when somebody comes to see us, we immediately think about, oh, it

must be something that you can pick up with an ECG or an echocardiogram or an angiogram or a CT, a pulmonary angiogram. We've got all these fantastic things to do, but in fact, in all specialty medicine, all of us, cardiology, respirology, gastroenterology, nephrology, the majority of the patients who you see in outpatients don't have disorders, which you can say would be likely to cause the problem. They'll come to a urology clinic with urinary frequency, for example, and they'll have fine urine sample for bacteria, and then each one comes back as being negative, but the patient is still feeling a bit of burning and has dysurea. So the prism through which we look at our patients is through hardware. So what happens when somebody comes with long covid or with chronic fatigue syndrome or with PTSD or with ADHD, all these labels that we have, which I'm not very comfortable with, I don't like labelling anybody. I think it's much better to look at the physiology rather than the label as being the cause.

Steven (00:27:39):

Do you think it's helpful from the patient's perspective though? I think patients want to think that when they come to see you, you can put a name to what's wrong with them and they don't want it to be fuzzy.

Owen (00:27:53):

Yes, there is some of that, but the most powerful clinical interaction that I think a clinician and that includes all of you and ourselves can use is to use the word you're safe. That label is much more meaningful than you've got PTSD or ADHD, or you've got whatever else, functional dyspepsia, IBS. What patients hear, and that of course is the vagus hearing, is the word safety, the specialist telling you that you've got symptoms and I'm going to try and manage the symptoms, but overall, you're safe. You can see, and I've seen it so often, that the patient's body language changes immediately. The vagus nerves picked that up and has actually allowed the resetting of where they are in that thing. So going back to hardware and software, if we can think of it that way, most interesting at the moment anyway is chronic fatigue syndrome, long covid and of course PTSD, which now covers not only people who've been in terrible traumatic situations like war -

Owen (00:29:18):

Civilians being caught up, soldiers being caught up in warfare. As you know, PTSD is inevitable, 60 70% come back badly disabled by what they've seen, et cetera. And then there are all the functional disorders that we see in our clinics. So there are a huge range of medically unexplained disorders, which we tend to pigeonhole, which at this point in time, 2025, with the knowledge that we have, in my rather revolutionary view, I would like people to start thinking about it physiologically rather than in terms of nomenclature. I think it makes it a lot easier to understand and patients really pick up the story of seeking wellbeing because they'll often say to you, and they might never mention it before, you've got your nervous system constantly looking to put you in a safe place. And they'll say, for a long time, I've been in an unsafe place when I was a child, I was bullied at school or my parents divorced or whatever. And you would not get that out of the clinical encounter. You'd normally be talking about the physical problem. These are cues which they find very easy and you can start talking about it. And as we mentioned before we came on, this is part of the therapy really, it's to say you're safe.

Steven (00:30:47):

And I think that's probably one of, we had this discussion before we came on air, but I think it's probably one of the key things that'll come out of this discussion here is the trust that patients put in us as osteopaths, chiropractors and more so in someone like yourself with your somewhat more exalted position

Owen (00:31:04):

Can I just interrupt you before you ask the next question? I think you're so right, because my naïve view of things is that whatever therapy you do, whether you be a traditional MD or whether you be a psychotherapist or a psychoanalyst, an osteopath, or an integrative therapist or a reflexologist, one of the things that occurs in that setting is that patients feel safe. They feel that they're going to be listened to, they're in a room where they can be heard. And maybe a lot of what we're doing through all our therapy is helping the patients through that safety barrier.

Steven (00:31:45):

Yes. Yeah, I can well believe that. If I can turn back to some of these questions, again, we're looking at specific conditions here. Simon has asked if there's a link between vagus nerve and epilepsy. Now I know I've seen that there is investigation into that, but what's your view?

Owen (00:32:04):

That's a really, really interesting question because, and I'm no expert in that area, but the background to it is that in grand mal epilepsy in particular, there are patients who don't respond well to therapy to anti-epileptic therapy. And despite using all modern medications that affect neurotransmitters and so on, there are patients who have epilepsy all the time. And it was really discovered, I'm not sure how it was discovered, that stimulating the vagus nerve - invasively initially, and that is where the surgeon makes a little cut in the neck, finds the vagus nerve, pust an electrode around it, and has like a cardiac pacemaker under the skin and you switch it on at a very clearly defined bespoke electrical impulse, it has to be a particular wave form, a particular frequency, so that you only affect the afferent nerves, you don't affect the efferent nerves, so you don't affect the heart, et cetera - that you can make a tremendous impact in those settings where there is intractable epilepsy.

So quite clearly there must be a relationship between epilepsy and the vagus nerve. I wish I could go into more detail, but I really dunno enough about it to take it any further. But just for everybody to know that in severe epilepsy, vagus nerve stimulation is a very important part of the armamentarium now that neurologists have to offer.

Steven (00:33:45):

And is that now standard treatment for severe epilepsy?

Owen (00:33:52):

It would be, yes. I mean it's available. It's available in the NHS, but you have to be pretty bad before you earn it.

Steven (00:34:01):

Only a few years ago I was seeing a patient whose husband was having something like between 50 and a hundred fits a day, and it must've been unbearable for her having to look after him, but I don't recall her mentioning it then. So it must be a fairly recent intervention.

Owen (00:34:17):

But leading on from that, the two areas which formed the basis of the therapeutics of using vagus nerve stimulation, there was epilepsy, the next big area was depression because I think it was noticed that patients who are being vagally stimulated because of their epilepsy, their degree of mood change and their sense of wellbeing improved. And there were then studies that were set up in people who had intractable depression. And we know that ECT is very helpful in really severe depression and it was discovered that in severe depression, which is unresponsive to therapy, it's a very effective treatment. And there's something I read recently that there are about 60 or 70,000 individuals in the world. It was probably North America mainly, but here as well who have very severe depression, who've had vagus nerve implants provided and that their depression has really improved dramatically.

(00:35:29):

So this whole thing about being depressed and about your dorsal vagus and about freezing and so on, and then your vagus, it all starts to hang together a little bit.

And the third area is migraine. Obviously all this work has come out of severe migraine. There's something called cluster headaches. I dunno if you've ever come across that. It's supposed to be the most troublesome pain known to humankind. And essentially it was discovered that cluster headaches respond when to nothing else will respond to vagus nerve stimulation

Steven (00:36:07):

Really.

Owen (00:36:08):

So there are these sort of very obvious disease states of poor regulation of the brain basically where vagus nerve stimulation does seem to play a very important role. So vagus must play a role in that area.

Steven (00:36:27):

Well, you talked about implanted stimulants, stimulators for the vagus nerve. Does that mean that they're stimulating all the time or are they only switched on as it were when required? And similarly for cluster headaches, I mean that's not something that people necessarily get at predictable intervals, so is it something they have to recognise is about to happen or do they turn on stimulation when it does happen?

Owen (00:36:53):

Okay, do you want to get into therapy now A little bit,

Steven (00:36:56):

Yes. Yeah,

Owen (00:36:57):

Definitely. Yeah, for epilepsy and for depression and for migraine, the original methodology was really to keep stimulating at a very low level for 24 hours a day

Steven (00:37:15):

And the nerve doesn't become sensitised and just eventually ignore that stimulus.

Owen (00:37:20):

No, it doesn't develop sort of refractory problems, but there's been a major advance. And that was really again happened in the States where there was a guy who realised that the vagus nerve in the neck lies just below the skin. It runs along the carotid artery, it runs in the carotid sheath, that's the connective tissue that surrounds the carotid artery. So the vagus nerve, we know exactly where it is and it's basically running under the skin. And this guy had the idea that you could recreate the same physics of vagus nerve stimulation that you could with an implantable device, which is quite an undertaking - it is a little operation very near the recurrent laryngeal nerve. So you can affect phonation, singers, et cetera, can be affected by it.

This group, they call themselves electroCorpe, they formed the little startup called electroCore. They worked very hard to develop a non-invasive vagus nerve stimulator, which was called gamma core. And I've got one here

Steven (00:38:38):

By coincidence.

Owen (00:38:39):

Yeah, so this over here is gamma core

(00:38:43):

And it's a device which has got two electrodes, one, two electrodes over here and it's battery driven. It's got a rechargeable battery inside it. And what they did was they discovered that if you placed the vagus nerve stimulator over the vagus nerve with a little bit of gel to actually improve the electrical contact and you just increased the amplitude of the signal, then you could look at the brain's physiology using functional magnetic resonance, and there was a point where the vagus nerve areas were being lit up and they also noticed at the same time that coincided with the same point where the corner of your lip started to pull. So when they noticed that it was possible to provide gamma core. They started with migraine because I think there's a big market in migraine - apparently one in eight adults suffer from migraine. And so over the past 10 years, they've done a huge number of studies in migraine, most of which were done in the uk.

(00:40:02):

And they discovered that in fact, you can use this in two ways. Obviously you can't walk around like this - it'd be crazy. So the one way to do it is if you see the aura and you start, you immediately apply it for four minutes, that's what's used. And then you wait a period of time if it hasn't settled, you can repeat it again. And in those patients, they can manage the migraine like that. Then if somebody is getting a lot of migraine three times a week, twice a week, stops some work, et cetera, then what they do is they use maintenance treatments. So twice a day they'll treat themselves with external

Steven (00:40:44):

For four or five minutes,

Owen (00:40:45):

For four minutes twice daily or three times a day. I mean usually twice a day is usually enough.

Steven (00:40:50):

Now I'm going to ask a cheeky question here. If I were manufacturing a device like that, I'd make very sure that the research I did showed that it was effective so I could sell it. You've probably looked in more detail at the research so you can reassure us that it's Robust

Owen (00:41:05):

Very robust. In fact, this is available on the NHS in neurological clinics to people who've got cluster headaches and who've got severe migraine. And again in the United States, this is FDA approved and so on and so forth. I mean, this isn't hocus pocus, I mean

Steven (00:41:21):

No, that's good to hear. And if someone wanted to buy one privately, they presumably could. Are they expensive?

Owen (00:41:29):

It's interesting. A bit of off-piste now, if you don't mind, this is the Rolls-Royce and the reason it's the Rolls-Royce is because it stimulates the two trunks in the neck. So you're getting everything from the chest and the abdomen and the rest of the body passing through here. And you can't get it on NHS except if you've got those conditions, but you can definitely request it from electroCore in the uk.

(00:42:06):

And the model basically is that the patients are given a three month trial, which costs I think about £350 for the three-month trial. And then if they are successful, they want to continue. And if they need to continue, then there's a one year rolling subscription. So they've got a system where this thing after a year or after six months, it runs out of ability to be recharged and then you have to get a card and you have to recharge. They've got a model. But what I tend to do in settings where, and we can come back to it in a moment, where I think vagus nerve stimulation might be worth trying in patient digestive disorders or now I'm starting to

see patients, we suggest that disorders are more of a minor problem than their chronic fatigue, et cetera. If after 90 days it hasn't really had much of an effect, then obviously they can just hand it back. But there is another way of stimulating the vagus nerve.

Steven (00:43:04):

Sorry, so what was the cost of the annual contract?

Owen (00:43:08):

I think it's about £600 a year or something like that. But there's competition in the market now - an Estonian company, Estonia's very well-developed, the poor guys are on the border of Russia and are shaking and shivering at the moment because they know that Putin's got his eye in it. But basically Estonia's got a very good IT setting, but the Estonians have developed one which can be applied to the tragus of the ear. The tragus is the little cartilage thing in the front there because there is an evolutionary remnant of the vagus nerve in the concha and on the thing over here. And that's probably because we once had flapping ears, which had vagus nerve, and as they contracted down they kept this little vagus nerve and using, again FMRI, they've been able to show that you can use a clip mechanism to clip it onto the, you've got a battery operator thing like this and you can actually show an FMRI that you can actually stimulate the vagus nerve

Steven (00:44:15):

Is all stimulation the same though? I mean with this Rolls-Royce Device?

Owen (00:44:18):

Oh, there's been no head to head comparison at all. Only about 1% of vagus fibre is actually passed from the tragus, whereas 90% pass through the carotid. And of course I'm interested in the guts and this in the chest and so on, and my experience has been with this, but if you do FMRI, you can definitely stimulate the vagus nerve through the ear and you can buy it and you've got it forever and it works with AA batteries or AAA batteries. I'm not sure.

Steven (00:44:46):

Well, Jason sent in a comment earlier on a question earlier on saying that he's seen lots of adverts for neurostim. Is that what you are referring to or is that something different and is it worth buying?

Owen (00:44:56):

There are a few of them. There is Nurosym, which is the best publicized - nurosym.com.

And they purport to have some research, but I've looked quite intensively at their research and it is not the robust controlled trials. You can do very easy trials because you tell one person that they're going to use it here and the other person they're going to use it here. And you can do good control trials. There isn't anything like the robust trials, but it is quite reasonable and patients will often say, look, I'd rather buy something and use it. And I think, well, why not try it? Absolutely. I'm not against nurosym at all. It's just this is what I'm really used to. Nurosym costs, I think about 600 euros and you have it for life. You also have to

use it for 30 minutes twice daily. And that people tell me that one of the problems is that your ear, the tragus gets quite painful after you've been using it for three months because of the clip that you're placing. But sure, if you look at the website, you'll probably find that it's okay and there is some scientific basis to it, but it's not the most robust.

Steven (00:46:27):

This is possibly a daft question, but I'm assuming the brain can cope if you switch your clip from side to side or the stimulation will not lose it for efficacy while the brain gets used to it again.

Owen (00:46:37):

No, that's actually an interesting question. Basically vagus nerve stimulation is always applied to the left side. And the reason for that, it's theoretical - it probably doesn't make any difference - is because most of the efferent fibres to the heart go down the right side. Right, okay. And although it's of interest that vagus nerve stimulation has been shown to be very helpful in people with arrhythmias and in heart failure. There has been a reluctance for very theoretical reasons of using the right side, just use the left side. I personally suggest to patients that they do what's on the box and use the left side. But I do say to them that if you're finding that it's easier to use it for two minutes on the left and two minutes on the right, why don't you do it that way? But the reason for doing it on the left side, the left ear or over the left carotid is really because of the cardiac fibres are going down the right side. And there's just this slight concern is completely theoretical. It's like saying that you shouldn't use it for pregnant women et cetera, just because

Steven (00:47:53):

You don't want to be connected with any adverse events

Owen (00:47:54):

Be connected or associated. It might be a spurious association.

Steven (00:47:59):

Okay, so it wasn't such a daft question after all.

Owen (00:48:12):

Can I just mention that in the United States there's now an over the counter version of Gamma Core because of the competition from nurosym. There are a few other ones as well. It's called TruVago. I think it's T-R-U-V-A-G-O, which is over the counter. It costs about $400. It's the same as this basically. And it's coming to the UK and it's over the counter.

Steven (00:48:45):

But you mentioned just then the connection between vagus and the heart, but you didn't mention whether it is used for arrhythmias in the heart. Is that the case? Would you use it on the left hand side and hope that you will have an effect?

Owen (00:49:01):

Yes. I mean there are really good studies done, firstly in heart failure. It seems as though the vagus nerve is cardioprotective. The vagus nerve is all about protection and wellbeing.

(00:49:14):

In some ways Cardioprotective probably because the vagus is very important immunologically, it has a very important immunological function. It tends to be an anti-inflammatory responder. There's some interesting stories around if we have time to discuss that. So in chronic heart failure, it's been subjected to good controlled trials. And in atrial fibrillation it seems as though you can slow atrial fibrillation and I think you can reduce some of the subjective symptoms. But if you spoke to a cardiologist tomorrow, your favourite cardiologist tomorrow, and you said to them, what about vagus nerve stimulation? They probably wouldn't have heard of it for the use in the cardiac situation because it's really just not yet part of that paradigm of care.

Steven (00:50:03):

Well, I can think of at least one member of our audience who will be very interested in that connection. John has just sent a question in saying, could manual stimulation of the tragus be effective, do you think?

Owen (00:50:13):

Yes, I think so. I mean I think

Steven (00:50:16):

You'd have be doing it quite a lot, wouldn't You?

Owen (00:50:18):

Yes. I mean I think that the lifestyle things that affect the function of the vagus are very well documented. One of them is stimulating your tragus and I think one of the acupuncture points for gut problems is the tragus interestingly. So there is this thing of diving into cold water.

Steven (00:50:45):

Well indeed. Another question came in a few minutes ago saying, is cold water therapy beneficial in this regard as well?

Owen (00:50:50):

Yes. I mean cold water is a very powerful vagus stimulant and there are other things: humming yoga, singing in a choir, doing all those lifestyle things which basically boost the Vagus but not on a regular basis. You can't go to choir practice twice a day and so on and so forth.

Steven (00:51:12):

But you can hum twice a day.

Owen (00:51:14):

You Can hum. And people do hum twice a day.

Steven (00:51:16):

Yes. Interesting. Kim has asked, well, she's sent in a question about her own son. He has learning difficulties and severe torticollis, not responding to treatment is now having serious bouts of choking. Would this have any benefit, do you think, in his case?

Owen (00:51:37):

Okay, so I'm going to take a slightly different angle now and what I'd like to talk about for a moment, it might be the right place to talk about it. It's possible to evaluate the vagus nerve.

Owen (00:51:54):

As I said, you can kind of get some ideas to what's going on because the functional disorders have probably got to do with the vagus nerve, but I mean that's very subjective. But the vagus nerve is now relatively easy to evaluate, not directly because it's impossible to stick needles into the vagus nerve and see what happens when you give drugs or you hum, for example. But the vagus nerve is fundamental in controlling what's called heart rate variability. Now what's heart rate variability? Heart rate variability is the very subtle changes that occur in heart rate between inspiration and expiration. So that as we're sitting here, when you breathe in, you've got oxygen in your lungs. There is an afferent impulse which is vaguely controlled, which goes to your cardiac centre in the brain, which says that your lungs are expanded, properly full of oxygen and therefore get as much out as you can to your tissues.

(00:53:03):

And there is an increase in heart rate in inspiration. When you breathe out, the opposite occurs and you have a slowing the heartbeat just for efficiency. Now this is microseconds. You can't really feel it on the pulse, but you can very easily measure it with the ECG. So if you look at the, what's called the R interval, those big spikes and you measure it, you can see that between inspiration expiration, there are these changes in heart rate. It's called heart rate variability and everyone has it. And they're very well established patterns of normal heart rate variability. It's been very extensively studied. So heart rate variability is like a window to the efficiency of the conductor of your orchestra or the intranet. And how do we do it? And I've got one here. Okay, so this is the device that those people who are interested in measuring the vagus nerve have come to use. It's made by a Finish company called First Beat. If you want to look, you look at firstbeat.com, and they've been at it for about 20 years and they are the Rolls-Royce again of a measuring heart rate variability.

You can do it on a smartwatch, an Apple watch, but it's useless because it's based on the pulse. It's not based on the R interval.

And what this really does is as follows, I'll open it up a little bit. This is like a little mini dedicated chip computer fits in like that. It's got a little press stud for an ECG electrode sticky

to be placed there and over here and it's worn under the clothing. This bit goes under the right clavicle, this bit goes under the left breast. And so under the clothes very lightweight, you don't feel it when you're wearing it. And of course you can take it off when you bath or you shower, you go for a swim or whatever. And the, it's called bodyguard three. What it does is over 72 hours or longer, you can use it for up to five days at a time, day and night is constantly accruing the data of your heart rate variability.

(00:55:31):

And so it's got an accelerometer in it that can measure breathing and it can also evaluate when you're lying down when you're standing. So heart rate variability, which is what you want to see, is a sign of wellbeing. Good heart rate variability is optimal when you lie down. And that's why when you're unwell and you need to recover, you probably lie down. But you're measuring heart rate variability, and I'll show you a slide in a moment to demonstrate this to you, the change of posture, and it's probably because you wouldn't lie down unless you were safe, the idea of being lying down tells your physiology that you're okay, you're safe. So what happens is that the patient or the client will wear this for usually 72 hours, usually two work days and one Thursday, Friday, Saturday or something like that. So you've got a bit of change. They don't take any alcohol. Alcohol has amazing effect on heart rate variability on the vagus nerve, just a glass of wine.

Steven (00:56:39):

"Amazing" makes it sound as though it's a beneficial thing.

Owen (00:56:42):

Amazingly bad! Okay. You see that if somebody is having a glass of wine in the evening, it messes up the whole recording and so on. So you tell 'em not to. But basically it's three-day monitoring. All the information is stored on here. This is paired with a smartphone app. At the end of the procedure you press a button and that information goes to the cloud where there's a platform where it's analysed and then we can look at the analysis. I've got an example of one which we could look at if you want, if you're Interested.

Steven (00:57:18):

So again, is this something that a person can buy over the counter and then on the cloud someone will analyse it and tell you where you Stand?

Owen (00:57:26):

No, you basically, you get accredited, there's an online course you can become accredited. It's not difficult, but it doesn't go into the kind of depth that we are talking about.

Steven (00:57:38):

But a patient doesn't just go and buy one of those over the counter?

Owen (00:57:42):

No, what happens is that you send the patient a link, they click on the link, it takes them to the UK branch of the Finnish company. They then send this in the post with all the instructions.

(00:57:55):

And you have a year's worth for the amount you pay, which I think is £250 or £300. In terms of the interpretation, I think I would say you have to be accredited. I don't think any Tom, Dick or Harry would really be able to make meaningful sense of what you see, but it is not too difficult to gain accreditation through first beat, through this company. They do an online course where you can have it done. So me and my team did this years ago. We actually got some, it's not very difficult at all, particularly if you're in the medical field. Can I show you? Yeah, please do. Now I'll come back to that. Okay, so I've got three recordings over here. I've got a recording on the left side, the right side, and down here. Now the one on the left is normal and this is a 24 hour recording

Steven (00:58:55):

Taken from this device. Yeah,

Owen (00:58:57):

Taken from this device. And so you can see the time along the lower line. It doesn't matter if you can't see it exactly, but that's basically a timeline. You can see a moon over there. That's the point where the individual who's using it puts in their electronic diary, which is an app, that they're lying down that they've gone to bed.

Steven (00:59:36):

Yes.

Owen (00:59:36):

Okay. And then beneath it, you can't really see it in these things over here. The electronic diary also records events during the day. So if you're bloated or if you've got a lot of body pain or if you're relaxing watching television or if you are out for a meal,

Steven (00:59:57):

These are things that you enter into the app yourself.

Owen (00:59:59):

Yeah, and it's got a time relationship. And what you'll see over here is the normal: red indicates sympathetic dominance because during the day our parasympathetic and sympathetic nervous system are constantly working in equilibrium with each other. Stop-start driving during the day to try and keep moving forward. And essentially the red indicates, which is normal, sympathetic dominance. This is not measuring psychological stress. This is physiological stress.

Steven (01:00:32):

I can see here it says where this green bit starts, it says that they were having a nap.

Owen (01:00:37):

I was going to come to that've done it -. I was going to test you. Okay. And as you can see over there it says where the green, but the patient is having a nap.

(01:00:47):

They put it in their diary and the timeline allows you to correlate these two. But the most interesting thing is that you can see that as they get towards evening time and when they lie down, it turns green. And green is parasympathetic dominance. This is where the heart rate variability is at its maximum. And this is all done through some mathematics, which I will never understand. It's called Fourier transformation. They can work out which is sympathetic dominance and which is parasympathetic dominant. And you'll see this is a normal pattern and physiologically it's amazing to see that as soon as you lie down, your parasympathetic nervous system or the vagus nerve switches on, so you can rest, restore, and recover from the day's work where you're consuming energy.

The diagram at the bottom is an individual where you can see the pattern slightly different during the daytime there's quite a lot of red, there's blue, dark blue, which is exercise. It's picking up pulse rate as well as heart rate variability. And that'll come up to indicate that the individual has got a pulse rate greater than 130. And you can see this individual has been doing some exercise there

(01:02:01):

And there are things you can extrapolate from that like muscle oxygen uptake and so on. But if you look at the moon over there, that's where the individual decided that they put in the fact they're lying down, you can see they don't switch to the green. And there's a prolonged period of perhaps a third of the night where even though they lying in bed and probably sleeping physiologically, the body is behaving as if it's daytime consuming energy. There's no parasympathetic activity at all. And then it starts to kick in. And you can see there are a little areas where daytime physiology is poking through a bit of sort of staccato effect.

And this is an extreme example of somebody with chronic fatigue syndrome and where you can see there's basically a little bit of napping during the daytime. For some reason green, that means parasympathetic recovery. It's between six in the morning and eight in the morning, but the rest of the 24 hour period, it's all energy consuming, very little heart rate variability. And this is indicating that the conductor of the orchestra is conducting the orchestra out of tune.

Steven (01:03:15):

These are fascinating. I just want to ask one question about them. We intend to share these, they do have a patient's name attached. Is that okay? Well, I can take it out before we share them if necessary. There it gives a patient's name on those two and it does on that one that I chop it off. I

Owen (01:03:30):

Can take it out.

Steven (01:03:31):

Take it out, okay. I don't think anybody's going to be able to read it at this range at the moment.

Owen (01:03:34):

No. In fact, these are for the Finnish patients.

Steven (01:03:41):

And it is actually the same patient in all three.

Owen (01:03:43):

No, no, there's three, this is a patient who's normal. This is a patient who's got some abnormality, and this is a patient who's in the freeze situation. Literally in the freeze situation where the normal ventral vagus basically isn't showing itself at all

Steven (01:03:59):

That's misled by, it's got the same name on all three.

Owen (01:04:05):

I'll tell you, it comes from their brochure,

Steven (01:04:08):

In which case they've put in a fake name or something. I imagine. Which Makes a lot of sense. Yeah. Okay. So getting back to Kim and her son's choking and talking

Owen (01:04:16):

So I don't know. I don't know. But you could do one of two things. I think one would be to say, well to hell with, let's just try vagus nerve stimulation with either the gamma core or the neurosym. You need to do it for three months because the plasticity of the nervous system demands that you wait for a period of time, or the symptoms often improve quicker than you see the changes. Or you can say, well, let's have a look at the vagus nerve more objectively with first beat and see whether there is any abnormality. And if there is, at least we've got a rationale for using it.

Steven (01:04:58):

Getting to the practicalities of that, you said that the stimulator there might be prescribed for epilepsy, severe epilepsy, or

Owen (01:05:06):

No, that's the implantable one.

Steven (01:05:10):

Oh, I see.

Owen (01:05:11):

This is only really used for the functional problems like migraine, irritable bowel syndrome, functional dyspepsia, where the studies have been done, fatigue syndrome, PTSD, those sorts of situations.

Steven (01:05:29):

So might Kim be able to get hold of one of those

Owen (01:05:32):

Yes,I think so. I think if perhaps I could give you the website address or the name of the Individual.

Steven (01:05:40):

Sure. You can share that in email and you can share it. Thank you.

Owen (01:05:42):

That'd be reasonable.

Steven (01:05:43):

You, I'm sure Kim will be quite reassured by that. Hannah, you were talking about heart rate variability just a moment ago. Hannah's asked if you could please explain why low heart rate variability is correlated with poorer health outcomes and why it reduces with age and what can be done to improve it.

Owen (01:06:06):

It shows flexibility of the physiology, essentially. It shows that the physiology is very responsive. That's what the current view is, that having good heart rate variability, particularly at night, which is why the Fitbits and these things over here aren't really that helpful, but it just shows that there's flexibility in the nervous system that is very responsive. It's listening and that can be extrapolated to wellbeing. And the corollary is that people are in the free situation or depressed or et cetera, they have very little heart rate. People with PTSD, for example have very little heart rate variability, athletes who overtrain. For your audience I think it would be very interesting because the biggest use of first beat is initially in elite athletes, because it was discovered that if you don't have normal heart rate variability in athletes, it usually indicates that they're over-training and they're much more susceptible to injury. And again, if you go to the website, you'll see that there's a whole area on exercise and so on. And I think osteopaths and other physical therapists may find that really, really interesting. In terms of prediction, it's interesting.

I'm also involved in liver disease to a certain extent. The royal free is a liver disease place, as some of you will know, and heart rate variability becomes abnormal a couple of years before people develop liver failure. So it's almost like early warning system that something's

going on. And of course my view is that all individuals who are feeling depressed and who aren't going to work and who've had covid, this should be part of that armamentarium, but it's not.

Steven (01:08:01):

Well that was one on cardiology for you. We've got one on gastroenterology, so this might be your home ground. Hannah says it may have nothing to do with the vagus nerve, but she's wondering if there's a link between autism and what she says is the increased rash of GI issues.

Owen (01:08:25):

Well, that's an interesting question. The first thing to say is that everybody's being labelled these days, 50% of kids at school have now got one thing or another. They're all on Ritalin or are they on one thing or another.

(01:08:38):

And I personally think that's why I don't like labels. I prefer their physiology. But in terms of Porges, his big thing at the moment is the issue of how does the polyvagal theory relates to neurodiversity generally, but autism specifically. And it's really, really interesting to listen to him talking on it. And also there has been a therapy that's been developed specifically for neurodiversity called the Safe and Sound Protocol. I'm not going to go into it here because I dunno much about it, but essentially I would suggest that anybody who's interested in neurodiversity and autism and the polyvagal theory that you just look on YouTube just put in **Steven** Porges and autism. And he does some terrific talks talking about what the relationship is between the vagus nerve and autistic behaviour and how it can be treated by trying to reprogram - like neurolinguistic programming, but with a better scientific basis. I think he claims, as do many therapists, that it's a very helpful therapeutic option to think Vagus when you're thinking about neurodiversity. And that's all about safety and it's all about the ability to communicate. If you're stuck in your dorsal thing, you can't communicate properly. So maybe that's why people who are neurodiverse have difficulty communicating.

Steven (01:10:20):

So going back to Hannah's question there, obviously there's a connection with the vagus. Does that therefore, given the role of the vagus, does that mean that it could be associated with GI issues?

Owen (01:10:29):

No, absolutely. I mean in autism, GI problems are a real problem. And of course I don't see that much of it because mainly in the under 18 population where this goes to the paediatric setup. But absolutely they constipation, irritable bowel syndrome, bloating, it's all part of the spectrum.

Steven (01:10:53):

Yeah. Okay. Mayoori sent in a question ages ago actually. Is there any correlation with fascia release techniques, for example, acupuncture or lymphatic drainage that have been positively related to helping patients manage pain related to the vagus nerve?

Owen (01:11:11):

I dunno specifically, but I'll just get to the basics of, how can I put it? I'm going to call it the placebo response.

Owen (01:11:22):

The placebo response is really all about feeling safe. And it doesn't matter I think too much what you do as long as you do something and as long as you make patients feel a little bit safer. I think that there is recalibration, and as you probably are aware, much of the chronic pain syndromes are basically central. They're localised centrally rather than peripherally. So you probably see a lot of patients with joints and muscular pains where all the tests, the inflammatory tests and the CTs and the MRIs really don't explain why the patient is so resistant to conventional non-steroidals, et cetera, but who respond to your therapies. And so I'm only being speculative now, but I do believe that the search for safety occurs at a formal level saying, I think you're safe. And also occurs when you say, I think it might be that if we do this particular procedure, like some lymphatic work or we do some tendon release or something, I think that's got to do with being cared for, feeling safe, et cetera.

Steven (01:12:31):

Which isn't to say that those therapies don't have other effects as well, but that placebo effect, that feeling of safety is a very important part of all of them.

Owen (01:12:38):

Placebo effect isn't a negative term.

Owen (01:12:41):

I think it's a fantastic, fantastically powerful non-drug therapy in a way that we should really applaud. We shouldn't think of the placebo response as being good.

Steven (01:12:55):

It's a nasty conundrum, isn't there? Ben Goldacre talks about this in some of his books about bad science, particularly. He's particularly hostile to homoeopathy, but he doesn't deny that it might have an effect. He insists that it's probably due to a placebo. But sadly, conventional medicine isn't allowed to prescribe you a placebo. It has to be a drug that does something.

Owen (01:13:17):

Well, it's interesting because in gastroenterology, if you give patients with heartburn, for example, if you give them omeprazole, which every Tom, Dick and Harry is taking at the moment, give them omeprazole, or you give them a placebo, about 80% will respond to omeprazole. About 55% will respond to the placebo. Now, it's not to say that there are only 30% where it’s probably doing what it says on the box, which is antisecretory, but it's saying

that there are other factors involved as well, which are very positive. And placebo responses are not something to be scoffed at in my book at all, as a clinician I feel that reflexology, immersing yourself in cold water, all these things that have an effect need to be part of the armamentarium that we use in a positive sense rather than fencing ourselves into our particular way of thinking.

Steven (01:14:20):

I think I saw some research somewhere probably in another of Ben Goldacre's articles where he said that actually even if you tell the patient that this is a placebo, it's probably still going to have a beneficial effect. It may be reduced in the overall population, but it still works. Which is bizarre.

Owen (01:14:36):

No, because in some of the trials they've said, "we want to carry on". It's a six month trial and then we'll tell you what you're on, and then we want to see what happens a year later. And the guys that get better on placebo, say, I know it's a placebo, but I want to carry on with that. So it's absolutely valid. Yeah.

Steven (01:14:53):

Pip's said, you mentioned depression earlier on and she's asked whether there's a connection with anxiety.

Owen (01:15:01):

Yes.

Steven (01:15:03):

I was looking at some quite a bit of material before the show started and there's a whole range of things which can be affected by treating the vagus nerve, aren't there? And I dunno how well researched they all are, and I don't want to go through a whole list of them, but there's clearly, it's promising. It's promising for medicine as a whole because it is noninvasive. And have any detrimental effects being shown, any adverse side effects from treating the vagus nerve or stimulating the vagus nerve, apart from the theoretical which you mentioned?

Owen (01:15:36):

I don't think so. And I think that's probably built into the idea that the vagus nerve is essentially, if you're thinking about ventral vagus stimulating, ventral vagus is essentially the nerve of wellbeing. It's not the other way around. And if you look at the data, I think it's really, really unusual to come across any except local skin reactions, maybe on the ear or whatever that you'd expect. But if I could, just as we're moving on now, I just wanted to show you my last little slide here

(01:16:13):

Because it does relate to what you've been talking about. The anti-inflammatory effect of the vagus nerve is absolutely fascinating. And how was it discovered? By a Russian research worker in the Pavlovian times, when Pavlov was doing all his experiments, there was a Russian research worker who was interested in anaphylaxis, and he discovered that if you have a mouse model or a rat model of anaphylaxis, which apparently you can do, that if you cut the vagus nerve you would influence the incidence of anaphylaxis - they were much more susceptible to anaphylaxis. Whereas if you stimulated the vagus nerve, they had no anaphylaxis at all. And it was out of that observation that people started to ask the question, does the vagus nerve influence the immune system?

(01:17:17):

And there is very powerful evidence now to indicate that it's the first responder, so that if you get an infection, you can't wait for your lymphocytes and your neutrophils and your cytokines to start building up, you need the message to go through to say, there's a bug here or there's a virus here, whatever. And the vagus nerve, firstly, by virtue of the fact that it has a number of different sensory attachments, chemoreceptors, stretch receptors, receptors that look at particular chemicals like tryptophan and serotonin and so on. So along the gut, for example, the vagus nerve touches the gut, but the receptors are actually looking at lots of different things. So essentially what has been demonstrated is that in the immune situation, what happens is that the vagus actually tries to balance the immune system so that you don't have an overactive immune system. And a good hypothesis is that if your vagus nerve isn't actually doing that balancing act, then you land up with autoimmune disorders. And the corollary of that is that it's now been demonstrated quite nicely, I think, in inflammatory bowel disease, Crohn's disease, ulcerative colitis, which has been difficult to treat with conventional therapies, that vagus stimulation causes a significant fall in inflammatory markers and improvement in the mucosa of those individuals. And that's almost certainly because it resets the immunes.

Steven (01:19:06):

I think it's also been beneficial in rheumatoid arthritis as well.

Owen (01:19:09):

Correct. In fact, the first work that was done was in rheumatoid, and that was done with implantables,

(01:19:14):

Whereas the work that's been done in inflammatory bowel disease has been done with transcutaneous vagus nerve stimulation. So in terms of mood, in terms of messaging, in terms of wellbeing, in terms of immune system, the vagus nerve is so fundamental, our wellbeing that it should be core to the clinical approach. And the concept of saying you're safe is very powerful via the vagus nerve. In fact, I suggest to medical students that when they wake up in the morning, they should just remind themselves that when I go and do my work in outpatients, I must be sure to use the word you are safe. Even if the patient isn't safe, they must get the feeling that they are safe. You've got something or other, but don't worry you're safe because we'll look after you. That sort of thing.

Steven (01:20:11):

Patients don't like uncertainty on the part of people who are delivering their healthcare, I think.

Owen (01:20:15):

No, they feel unsafe.

Steven (01:20:17):

Yes. And we're constantly looking for all the differential diagnoses, so we're never certain that that's right. DE's asked whether you've got any advice for patients who have vasovagal syncope?

Owen (01:20:29):

Yes. POTS for example, postural orthostatic tachycardia syndrome and vasovagal syncope is a prime example of an underperforming vagus. Vagus nerve stimulation in POTS particularly has been studied and been shown to be very helpful in a proportion of patients. Of course, like all our therapies, not everybody gets better on all these therapies. And that's why I like to at least to have some basic physiology to try and filter out patients who I think are most likely to benefit. But yes, certainly. I mean, people who've got low blood pressure get out of the bath and they have hypertension, et cetera. Vagus nerve stimulation does appear to be helpful. And then there are trials to demonstrate that. Yeah.

Steven (01:21:25):

And is there a move to make this more mainstream therapy or are we still, in NHS sluggish terms, 10 years away from this being incorporated into the mainstream?

Owen (01:21:42):

10 years. And I think the reason for that is because of our education system that we Doctors basically like to look at the mucosa. And if you think of gastroenterology, think of an endoscope. And when you start to talk to them about this kind of language, they really don't get it. Patients get it in half a tick if you tell them that the symphony, the body symphony is playing out of tune, but they're safe, the patients get it. GPs get it in no time at all because they're seeing patients as a whole. But the clinicians, no, they don't like it.

I'm very involved in capsule endoscopy, where there’s a tiny little capsule you can swallow, you don't have to be hooked up to colonoscopy. And it's been very difficult to persuade clinicians to move low risk patients, who are very easy to identify, from having colonoscopies and are on big waiting lists to swallowing a capsule and having the capsule genome scope. And that's got to do with our biases.

Steven (01:23:00):

there's probably a whole other discussion to be had on that, isn't there? Because I read up on what you are doing in your practice. I was fascinated by that.

Owen (01:23:09):

Yes. And I mean, it's not only cluster headaches, but I've done my best in my own clinical situation at the Royal Free and more widely and amongst politicians to say that you can very quickly crack the waiting list for people with positive faecal occult bloods, for example, where they're in a screening programme, by delivering capsules at their home. You don't even have to come into the hospital. And to train somebody who has some biological background to read capsule endoscopy, takes about 10 weeks as opposed to five years to teach colonoscopy. And the message you get back from the politicians is, you're not in my constituency. Therefore, you need to go through your constituency. And then they say to you, well, we've just been elected to parliament and we're busy sorting our office out. And so it's very difficult for people who aren't instinctively political to get these messages. But yes.

Steven (01:24:11):

One last question. I think Ambo sent in a couple of questions, and he's probably getting very frustrated that I haven't asked either of them. Connective tissue disorders such as HEDS seem to deplete energy. Would the vagus nerve paradox explain much of this, also chronic fatigue syndrome CFS, which seems to affect so many patients who are already trying to cope with other disorders? I think you've probably answered

Owen (01:24:34):

I mean, I really think that, I don't want to sound like a sort of one dimensional clinician because I think there are lots of ways of looking at these problems, but I think that this must be part of the opportunity we give patients to look for a fundamental reason why they run out of energy, why they run out of gas. And at the moment, in chronic fatigue syndrome, they used to say, well do graded exercise. Well, there's no good evidence for that when you look at it.

Steven (01:25:07):

In fact, there's evidence to the contrary.

Owen (01:25:08):

Absolutely. And patients tell you that they feel terrible when they do a bit of exercise. But again, not wanting to be one dimensional, but I would say that these patients should have their heart rate variability assessed over 72 hours, not just a ten second strip of an ECG measure. And I think all those poor individuals who haven't gone back to work, and everyone's berating them because they should be back at work, 3 million people on financial support by the government, part of helping them, I think would be to think vagus. Maybe that's a way to conclude it.