Welcome to the Huberman Lab podcast where we discuss science and science-based tools for everyday life. I'm Andrew Huberman and I'm a professor of neurobiology and ophthalmology at Stanford School of Medicine. Today my guest is Dr. Rhonda Patrick. Dr. Patrick is known to some of you as a podcaster and one of the premier educators in the landscape of mitochondria, metabolism, stress, and other aspects of brain and body health. Her podcast Found My Fitness is one of the premier podcasts in the world for disseminating knowledge about how the brain and body work and how we can use behavioral tools, microtutrients, supplements, and other protocols in order to maximize our immediate and long term health. Dr. Patrick did her formal training in cell biology, exploring the links between mitochondrial metabolism, apoptosis, which is naturally occurring cell death, which is a healthy form of cell death that occurs in our brain and body throughout the lifespan and cancer biology. She then went on to do postdoctoral training with Dr. Bruce Ames, investigating the effects of micronutrients, meeting vitamins and minerals, and how they affect metabolism, inflammation, DNA damage, and the aging process. She has published landmark review articles and primary research, meaning original research articles in some of the premier journals in the world, including science, nature cell biology, trends in cell biology, and facep. Indeed Dr. Patrick is an expert in an extraordinarily broad range of topics that impact our health. For today's episode, we focus primarily on the major categories of micronutrients that are essential for brain and body health. I have to confess that before the discussion with Dr. Patrick, I was aware of only one of the categories of micronutrients that we discuss. And so you'll notice that I am wrapped with attention throughout the discussion, and I think that you'll want to have a pen and paper handy because she offers not only a very clear understanding of the biological mechanisms by which other micronutrients operate, but some very clear and actionable tools and items that we can all embark on if we are to optimize our brain and body. We also discuss behavioral protocols. Dr. Patrick is well known for her understanding of the scientific literature on sauna and the use of heat and cold for optimizing things like metabolism, longevity, cardiovascular health, and I'm delighted to say that we discussed that as well and how behavioral protocols can interface with supplement based and nutritional protocols. I'm confident that you'll learn a tremendous amount of information from Dr. Patrick, much of which is immediately actionable. And if you're not already following and listening to her excellent podcast, you'll absolutely want to do that. It's foundmyfitness.com is the website where you can get access to that podcast. It's also on Apple and Spotify and YouTube as foundmyfitness. Dr. Patrick also has a terrific newsletter that I recommend signing up for. It's foundmyfitness.com slash newsletter is where you'll find it. And it includes research on fasting, micronutrient sleep, depression, fitness longevity, and far more along, of course, with actionable protocols. I'm pleased to announce that the Hubertman Lab podcast is now partnered with momentous supplements. Our motivation for partnering with momentous is to provide people one location where they can go to access the highest quality supplements in the specific dosages that are best supported by the scientific research and that are discussed during various episodes of the Hubertman Lab podcast. If you go to livemomentous.com slash Hubertman, you will see those formulations. I should mention that we are going to add more formulations in the months to come. And you will see specific suggestions about how best to take those supplements, meaning what dosages and times of day. And in fact, how to combine those supplements with specific behavioral protocols that have been discussed on the podcast and are science supported in order to drive the maximum benefit from those supplements. And many of you will probably also be pleased to learn that momentous ships not just within the United States, but also internationally. So once again, if you go to livemomentous.com slash Hubertman, you will find what we firmly believe to be the best quality supplements in the precise dosages and the best protocols for taking those supplements along with the ideal behavioral protocols to combine with those supplement formulations. I'm pleased to announce that I'm hosting two live events this May. The first live event will be hosted in Seattle, Washington on May 17th. The second live event will be hosted in Portland, Oregon on May 18th. Both are part of a lecture series entitled The Brain Body Contract, during which I will discuss science and science based tools for mental health, physical health and performance. And I should point out that while some of the material I'll cover will overlap with information covered here on the Hubertman Lab podcast and on various social media posts. Most of the information I will cover is going to be distinct from information covered on the podcast or elsewhere. So once again, it's Seattle on May 17th, Portland on May 18th. You can access tickets by going to HubertmanLab.com slash tour. And I hope to see you there. Before we begin, I'd like to emphasize that this podcast is separate from my teaching and research roles at Stanford. It is, however, part of my desire and effort to bring zero cost to consumer information about science and science related tools to the general public. And now for my discussion with Dr. Rhonda Patrick. Rhonda, welcome. There's been a long time coming. Even longer than you know, because even before we discussed you coming on this podcast as a guest, I've been watching your content for a very long time. So I want to start off by saying thank you. You were the spearhead to break through from academic science to public education. So I consider you first in and the rest of us are just in your wake. So thank you for that. That's been. Oh, that is so kind. Thank you. Thank you so much. That's absolutely true. I am so excited to be here having a conversation with you. Thank you. It's absolutely true. If anyone does their research, they will realize that the statement I just made is absolutely true. And there isn't even a close second. You know, any other public facing educators that have formal science training and do regular posting your content came in several years after you initiated it. So we're all grateful. I have so many questions, but I want to start off with a kind of a new but old theme that you're very familiar with. So temperature is a powerful stimulus as we know for biology. And you've covered a lot of material related to the utility of cold, but also the utility of heat. And as I learn more and more from your content and from the various papers, it seems that there's a bit of a conundrum in that cold, can stimulate a number of things like increases in metabolism, brown fat, et cetera, et cetera. Hopefully you'll tell us more about those. But heat seems to be able to do a lot of the same things. And I wonder whether or not the discomfort of cold, deliberate cold exposure and the discomfort of heat might be anchoring to the same pathway. I'm sharing with us a little bit about what happens when we get into a cold environment on purpose and what happens when we get into a hot environment on purpose. And I'm hoping that this might eventually lead us to some point of conversion understanding. So if you would. I would love to let's take a step back. I think you brought up a really important point here. And I think that point has to do with the intermittent challenging of yourself and whether that is through, you know, temperature changes like cold or heat or through other types of stressors, like physical activity or perhaps even dietary compounds that are found in plants. These are things like polyphenols or flavanols. Humans were, you know, we evolved to intermittently challenge ourselves. And before we had Instacart where you could basically just get your food delivered to you. Before the industrial revolution, you know, occurred. We were out hunting. And I say we not us humans. We were out, you know, gathering, we were moving. And we had to be physically fit. You couldn't catch your prey if you were a sedentary slob, right? You were moving. And you had to like, you know, pick your berries. You had to move. And so physical activity was a part of every day life. And caloric restriction or intermittent fasting was also a part of it. This is another type of challenge. You know, we didn't always, you know, have a prey that we caught or maybe temperatures were such that, you know, there was nothing for us to gather, right? So food scarcity was something common as well as eating plants. So getting these compounds that I mentioned. So this is these are all types of stress intermittent challenges that activate genetic pathways in our bodies. Often referred to in science as stress response pathways because they respond to a little bit of stress, you know, physical activity is strenuous. Fastings a little bit stressful heat cold. These things are all types of little intermittent challenges. And there is a lot of crosstalk between these stressors and the genetic pathways that they activate. And these genetic pathways that are activated help you deal with stress and and and they do it in a way that is not only beneficial to help you deal with that little stressor exercise or heat. It's it stays active and it helps you deal with the stress of normal metabolism, normal immune function happening, just life aging, right? So this concept is referred to as hormesis, right? This is a little bit of stressful challenge that activates these stress response pathways in a beneficial way that is a net positive that actually, you know, has a very profound antioxidant anti-inflammatory response or, you know, or whatever the response is. It could be the production of more stem cells. These are cells that help regenerate different cells within tissues or something like a topogy, which is a process that can clear away all the gunk inside of our cells, pieces of DNA, protein aggregates. So you'll find that these stress response pathways are activated, like by a variety of stressors. So for example, one pathway is called heat shock proteins. And as their name would apply, one would go, oh, they're activated by heat. Well, correct. They are activated, very robustly by heat. And we can talk about that. But, you know, you can eat a plant like broccoli sprouts, which is high in something called sulfur, a fan. This is a compound that is sort of like a Hormetic compound or as David's clear likes to say it's a Xeno-Hormetic compound. I love that. I love that term. And it activates heat shock proteins, among other things. It also activates a very powerful detoxification pathway called NRF2, which helps you detoxify things like carcinogens that you're exposed to. Well, guess what? He activates that. So what I'm getting at is there is overlap. Like cold also activates heat shock proteins. You're like, really cold. Yes, it activates. These are stress response pathways. And they are activated by various types of stressors. Now, you know, you're going to more robustly activate heat shock proteins from heat versus cold, but there is overlap. So I think that sort of forms the foundation there. Yeah, that's very helpful. And, you know, it brings to mind in the context of the nervous system. I was so people, you know, you only have a small kit of neurochemicals to work with. There isn't dopamine for Netflix and then dopamine for relationship and dopamine for work, et cetera. There dopamine is a generic pathway by which motivation craving and pursuit emerge, et cetera. It just like adrenaline is a generic theme of many different behaviors. And it seems that it is the job of biological systems to be able to take a diverse range of inputs, even unknown inputs like we don't know what technology will look like in three years. But you can bet that some of those novel technologies will tap into the very systems that I'm talking about now. And there certainly will be other. Stressors to come about that will tap into these pathways. I have two questions related to what you just said before we talk a little bit more about cold and heat. You mentioned plants as a route to creating intermittent challenge. There's a lot of debate mostly online about whether or not plants are our friends or plants are trying to kill us. The extreme version from the carnivore types pure carnivore diet types is that plants are trying to kill us from the plant based diet folks. It seems like it's more about what's healthy for the planet animals and maybe for us. But if we set aside that argument and we just raise the hypothesis that plants have compounds that are bad for us, but maybe by consuming them in small amounts, they're creating this hormisist type scenario. So then I think we conceivably solve the problem we could say yes, plants are bad for us, but in small amounts, they provide this hormetic response and they're good for us. So in the same way that heat is too much heat is bad for us. Too much cold is bad for us can kill us can kill neurons, but appropriately do in an intermittent challenge type of scenarios can be good for us. Is that how I should think about plants in these compounds? Do you think of them as good for us or as bad for us? They're a very sharp blade and we want to use them. I actually think that it's almost impossible. I mean, you'd have to eat nothing but the same plant all day, every day in the large. The bioavailability of these compounds in the plants, they are attached to a food matrix, it's not like taking it in a supplement form as well. It's such that it's very difficult to make it toxic. Now, there are some cases, for example, if you eat cabbage and I think there's some group in Africa somewhere that's like that's all they eat is cabbage and there's a goitrogen in cabbage. It's not so for a few minutes, another compound, but that's all they eat every day. Nothing but that and they get yeah, and they're like iodine deficient on top of that. So, you know, I do think there's there you can of course make I mean there are types of plants that are toxic in small quantities, right? That's a hamlock exactly. So, don't play this game with them. But you're not going to get poison from eating, you know, you're serving a broccoli at dinner, right? So, I mean, it depends on the plant. I don't these generalizations are kind of they're just not useful. And I think that a lot of people online in the blogosphere, they gravitate towards them because it's easier and it's a lot more sensational. I plants meat and starches. I'm one of those rare omnivores out there now. I feel like a rare or it's rare to be an omnivore. But I think once you step out of the social media as you said the blogosphere, the most people, I would say 99% of people on the planet are probably omnivores. Right. And someone will probably correct me. But I doubt the number falls below 90, 98. I think if you look at data, you know, and when we have carnivore data, I can't wait to see it. But like right now it's a lot of, okay, well this is a lot of anecdotal evidence and there's, you know, there's a good. There's a lot of good starts with anecdotes, but like people change a thousand things at once and they don't realize that, but they do. And so anecdotal data is only so good, right? It's a starting point. And so we don't really know long term what carnivore diets are going to do. They may be beneficial short term. They may, you know, be beneficial for reasons of elimination of other things like who knows, right? Lots of possibilities, but I do think with respect to plants, you know, that there's, that there's so much evidence like, for example, sulfur, is one that I really like because there's just evidence that sulfur, is a very powerful activator of the NRF two pathway. And this is a pathway that regulates a lot of genes and a lot of genes that are related to like glutathione production. And so genetically, these are studies that are genome-wide associated studies for people listening that aren't familiar. People have a variety of versions of genes. And we have a gene that's able to make heterocyclic amines to basically detoxify it so it's not as harmful. And so people that don't have a certain version of that that's doing it well are very prone to like colon cancer and increased cancer risk. But if they eat a lot of broccoli and cruciferate vegetables that negates that risk because they're getting sulfuric pain, which activates a lot of the glutathione transfer, and it's now in transphorase and synthase genes. So glutathione's a major antioxidant in our brain and in our, in our vascular system and our body basically. So, you know, there's evidence that that that eating things like, you know, compounds that are like sulfuric pain or broccoli or broccoli, broccoli sprouts, which have like 100 up to 100 times more sulfuric pain than broccoli are activating glutathione in the brain. There's human evidence of that. I mean, that's amazing. Yeah, sorry to interrupt. I just want to make sure when so broccoli sprouts are different than broccoli. And you just told us that they have much they're much richer in these these compounds. So note to sell if I should have broccoli sprouts, not just broccoli. Can we cook the broccoli and still get these nutrients or do we have to eat raw I confess eating raw broccoli is really aversive to me. So the sulfuric pain is formed from a compound called glucoraphanin, which is in the broccoli and the enzyme that converted into sulfuric pain is myrocinase and it's heat sensitive. So you do somewhat lower the sulfuric pain levels when you when you cook the broccoli. However, there was a study a few years back that showed adding one gram of mustard seed powder ground mustard seed powder, which also contains the myrocinase enzyme. Two of your cooked broccoli increases the sulfur of pain by fourfold. So this is great because I confess I like broccoli if it's cooked to the appropriate density, not too mushy, but definitely not raw. The idea of eating raw broccoli to me just sounds horrible, but I like the way mustard seed sounds. So just a little bit of mustard seed powder added to the cooked broccoli can recover some of these compounds. Yes. So what I do is I will, you know, lightly steam my broccoli and then I add a little bit of my carry gold butter and then I add some mustard seed powder on the top of that. And it's got a little little kick like it's just a little spice, you know, and if you don't taste that, it's expired. Like it should have a little kick. And because I know people will want to know how often and how much, you know, are you eating this every day or most days of the week? Well, I had shifted to supplementation with sulfur of pain. I've admitted I'm admitting right now that I've been terrible about it the past like, I don't know, six months or so. The supplementation or the broccoli? Yes, yes, the supplementation. And so there's another way to get there's another compound and it's actually called Marine gas. And Dr. Jedfei, who's really the expert on sulfur, he's a good friend of mine. He's been on the podcast a couple of times. He, he basically thinks and, you know, has done a lot of research on Marine gas as well. That it's like a cousin and it activates the NRF two pathways similarly to sulfur, and so I've been buying this coolie, coolie, Marine gas powder. I don't have any affiliation with them. Coolie, coolie is a brand. Coolie, coolie is a brand that you have no affiliation. I know affiliation. Okay. But Jedfei, he like has researched it like like that specific brand. And so it's like legitimate, it's legit, you know, it's like science back. Yeah. In terms of actually containing Marine gas and activating NRF two. And I added to my smoothies. So that's what I've been doing. What are some of those ranges? So of course we give the usual recommendations that people should talk to their physician, et cetera, et cetera. But if people are going to what do you take? That's always the, let's take the table. David Sinclairian approach. What do you, where he'll talk about what he does as a way to deal with this. And of course everybody's different and should in all seriousness should. And so it's time you add or delete something from your consumption should consult some trusted healthcare professional trusted by you. What do you recall the dosages? I do a big keeping table spoon. So we're reading a coolie coolie Marine gas sounds like a song. It's with a K I know. You know, for people also listening to why would I do that? You know, I mentioned the glutathione the brain. I mentioned it in plasma. It's been shown a lower DNA damage in people and white blood cells. It's also been shown. There's been several different studies in China. You know, in China, there's a lot of air pollution. And I mentioned that it, you know, it's a very powerful activator and NRF two. And I know you're your friend with NRF two. But NRF two is like a transcription factor that is it is it is binding to a little specific sequence in a variety of different genes and it's like turning them on or in some cases turning them off. It's regulating what's being activated or what's not being activated or being turned off. And some of the genes are are basically these these detoxifying pathways we talked a little bit about the glutathione, but there's also ones that are involved in air airborne carcinogens like benzene. So benzene is found in air pollution. I mean cigarette smoke. If you're smoking cigarettes still like please try to quit. Hey, you're mutating your DNA. Yeah, it's just nothing of the lung cancer. You're mutating your DNA. And heart disease risk heart disease risk. But anyways, people and this has been repeated in more than one study that literally after 24 hours of taking can't remember off the top of my head what the dose of sulfur fain from broccoli extract broccoli seed extract was broccoli sprouts extract not the seed it was the sprouts. Anyways, they started excreting like 60% benzene and acroline. I mean that's something that we get in cooked food. It's coming out in their urine coming out in their urine. Yeah, well I'm not a smoker and I have to be honest it's rare that I hear of a supplement for the first time because I've been you know deep diving on supplements since I was in my teens. This is fascinating and it brings me back to this question that we have before and I appreciate that you answered it very clearly. Plants have compounds that are good for us. They're not just stressing us. They're activating pathways that are reparative. That's what that's what I'm taking away from everything you're telling me. Right and and that our bodies were supposed to be getting that stress to have those pathways activated like it is like you know right I mean this is conserved among different animals like this is this is this is something that is is supposed to happen. And in our modern day world we don't have to eat plants. We don't have to move anywhere exercise we don't have to go through periods of not eating food because we can have it at our fingertips at any second right. So I mean we've got this conundrum of we're never activating these stress response pathways that were that we're supposed to activate we're supposed to I find that fastening and again drawing a parallel to the nervous system. So what I'm hearing you say is that historically we would have to go through some stress some confront cold or confront heat or confront effort or hunger in have to exercise essentially in order to obtain these compounds and then those compounds are reparative. I feel that resembles the dopamine pathway always say you know there's nothing wrong with dopamine people think about dopamine hits as bad or dopamine is bad there's absolutely nothing wrong with dopamine the problem is dopamine especially high levels of dopamine. So I mean released without the need for effort to access that dopamine is problematic so a line of cocaine gives you a ton of dopamine with no effort except to ingest the drug whereas working for four years or more to get your degree will release a lot of dopamine and a lot of cortisol along the way as we know. So it's considered a healthy accomplishment in most cases a tremendous amount of you were approaching the spring and there'll be a lot of graduations weddings are coming up now that pandemic is kind of hopefully slowing and there'll be a lot of dopamine high levels of dopamine are great but only after the effort of having done something in order to access it. So that's what I'm taking away from what you're saying is that we need to go through this intermittent the different types of intermittent challenge and we can we are rewarded with particular compounds that are reparative both for the challenge but then it make us stronger it is or me since really is it seems a case of what doesn't kill us makes us stronger. So you mentioned can I add to that one just said because because this has been shown with for example sulfuric and animal studies you precondition give the animal sulfur and then you expose them to like you know hypoxia or some kind of the exchemic stroke condition whatever they do to induce that and the sulfuric and it basically protects that like their precondition and their their their stress response pathways are primed and so when they're then exposed to the ischemic stroke. They their outcomes are so much better so much better than the animals that didn't get the sulfur for 48 hours before whatever it was you know and this is like this has been shown in multiple animal studies with sulfur and specifically in the brain. I know Mark mattes and doctor Mark mattes and he's a lot often thought of as the intermittent fasting king but you know he's a neuroscientist and he he did publish work and talks about sulfur and as well. Really glad you brought that up be that example up because many of the questions I get on social media and elsewhere are about traumatic brain injury and TBI in you know is just one example and people always think sports it's football whenever you say TBI people always think football and I just want to just take a moment to editorialize. 90% or more traumatic brain injury is construction work at home accidents football players are hockey players are martial artists are a tiny fraction of the people who have TBI and concussion of various kinds it just so happens that within those communities many of them 75% or more experienced those so it's salient within those communities but. Cushion is prominent people are always asking what can I do in order to offset brain injury had a concussion two years ago what can I do and it's been it's been a tough question because really don't have anything for them I mean you tell them sleep well eat well exercise but it sounds like some of these reparative pathways either should be explored in the context of brain injury or I'm guessing are being explored in the context of brain injury yeah so a couple of things there one is that I mean traumatic brain injury I mean it's terrible but it's also it's so interesting because it's also like literal real time brain aging like you know like it's you're able to like accelerate it and understand so I I often think of when I think of traumatic brain injury I think of so much overlap between Alzheimer's disease and dementia and these neurogenetic diseases because there is there are there are a lot of similarities that there you know and so so that I think I personally think and I do think there's been some animal research with TBI I mean and so for a thing mostly preconditioning rather than treatment so again it's like well I mean if you're going to if you want a healthy lifestyle thing in your construction worker or your fill in the blank that's you know going to be a person or I mean you're at risk to some degree right or bicycle bicycle yeah around Stanford we have you know I would say people demonized motorcycles people demonize a lot of things but moving fast through space on a small object next to a 3,000 pound vehicle I mean we've lost we have a number of friends have died we have a number of traumatic brain injury I'm not against cycling or cyclist but it is it's a risky sport by any stretch so in things like maringa or eating my broccoli sprouts maybe cooking them a little less than I'm currently cooking them putting on the the mustard seed is there evidence that well first of all NRF 2 is expressed in neurons right so those those cells should be protected are there other cells of the body that could possibly gain protection from these pathways well lungs for one but you know just even in plasma cells I mean I think it's pretty good for the inner of 2 is pretty ubiquitously expressed liver so there's I mean there's so many animal studies that have looked at all those things I try to kind of gravitate towards human ones is a little a lot more relevant but but I think you know overall like I said I mentioned you know DNA damage lower 24 24 34% lower in human blood cells after broccoli broccoli sprout powder supplementation and I made a video on this like years ago and 16 maybe and I think I have like the references on there to exact amounts I can't remember but it was it's kind of an old video is to the 2016 but I also had jet on the podcast and he he did talk about this but you know it's also been shown in randomized control trials to help treat autism and autistic symptoms and yet again it's doing interesting things in the brain and I think if I think it does have something to do with the oxidative stress and the glutathione which would be relevant for TBI treatment it hasn't been shown empirically that that helps with treatment but I do think someone could do that study I think that it's that it should be done honestly because it's a low hanging fruit I mean if there's any impact and there is at least one preliminary study that glutathione is increased in the brain after humans are you know basically taking sulfur for free so which is really for people listening that's so important because a number of compounds that people take in supplement form don't cross the blood brain barrier or they get metabolized in ways that what's listed on the bottle almost becomes irrelevant for what your cells actually experience that's very reassuring we will get back to heat and cold in this theme that I tried to service by just find this too interesting to to diverge at this point from from these themes so what other compounds or micronutrients do you place in the top tier of useful interesting there are animal studies maybe there hopefully also some human studies we've talked about a few I know you've talked a lot about omega three fatty acids so if you had to do your kind of top three you're superstars of nutrients for the brain and body sounds like we've got one one set what would you put in alongside them omega three the marine omega three fatty acids so these are found in marine types of you know animals fish cold water fish fatty fish so so there's a there's three fatty acids there's one from a plant and that's often referred to as ALA people call it short afolinally a gassid and then there's I co I co-supendinoic acid or EPA and doca hexanoid acid which is DHA yeah I'm amazing to pronounce two of the most difficult words to pronounce right next to and spell right next to ophthalmology which if you can spell it I know people who have appointments in ophthalmology departments that don't have to spell ophthalmology a little secret there's an extra P in there so the ALA that I'm not going to attempt to pronounce it because your pronunciation was perfect of both of these two compounds and you said are marine sources so fish so sardines caught this sort of thing but what about krill I've seen krill oil and there was a few years back people were saying krill is a better source for omega-3s than is fish oil I took some krill oil capsules made me itch all over so I stopped do you have a shellfish allergy no I don't think so I don't think so I'm not a big fan of shellfish but I like you know I'll have oysters every now and again or shrimp or something and feel fine so yeah we can talk about sources so krill is a source mostly of a type of DHA and EPA that's in phospholipid form so it's a phosphatidal colon omega-3 fatty acid and that's different than most most of the well if we're talking about fish oil supplements that's a different story but if you're talking about comparing fish to krill eating krill like we're talking about the food yeah krill supplement versus fish fish oil supplement and if you if it fits in the conversation talking about great sources of omega-3s in their whole form I have a bad feeling you're going to tell me sardines um sardines are yeah they're awesome anyways except for the taste and and for the potential contaminants um mercury I think was want no show is yeah I was mercury and um Joe was telling me about like he used to eat sardines every Joe and was telling me that he used to eat sardines every day and and then he had like really high mercury levels and I was really shocked because sardines are like you know low in the fish you know groups so they're the higher up you get like sword fish and sharks like really high mercury because they're eating all the other fish right but I think some brands and if you look at like consumer lab consumer lab there's it's like a third party site that I'm not affiliated with but I'll use them because they they do a lot of work analysis of different foods and supplements and so you can look at like some of their sardines and they've like they have a list of like ones that are pretty decent but anyways um back to your question about fish oil supplements versus krill oil supplements so the one of the major differences is the fish oil supplements if you get a high quality one it's in a triglyceride form. So you're you've got like a glycerol backbone with three fatty acids and and that's attached and those are either DHA or the EPA and or if you have a lower quality fish oil supplement then you have what's called ethyl ester form and typically the reason for that is it's when fish oil is purified it's run through this column with alcohol or something they cleave it off the glycerol backbone and then it's just kind of easier to leave it like that then like re-stairifying it which costs more money so you can get it an ethyl ester form which isn't as bio available and in fact if you don't take it with food you're going to be in trouble you're not going to absorb much of it at all. Would you see this on the packaging? Is it going to say it's in this Ethyl Ethyl form? Some official brands will put it on their website perhaps on their packaging but you most of the time you'll have to dig for it on the website and or call them but I think for the most part ones that are like higher end will will market it like triglyceride form and it's not that Ethyl esters bad it just means take it with food so so so the one of the major prescription omega threes out there is both of them actually Lavaza which is a mixture of DHA and EPA as well as the CEPA which is a highly purified EPA these are both prescribed by physicians to patients with hyper triglycerideemia so high triglycerides among other things I think maybe dysregulation of lipids as well. This is amazing for people so these are prescription drugs that are essentially very high potency purified omega threes but they're given to people for lipid issues so this is the treatment of issues with fat metabolism by giving people fat just to really I just want to push home again I'm not carnivore keto or anything I'm an omnivore but but to just push home that we one thing that's so wonderful that you've done over the years that you continue to do is to move away from these very very broad sweeping statements about you know fat is bad I mean here's a case where we're saying fat is not only good it can be used to combat issues with fat metabolism and then their you know fats are not just one thing there many things so anyway I just want to put a little highlighter and a point of appreciation there and make sure that people are are sensitized to the fact that if you hear that fat is bad you have to ask what kind of fat right and here we're talking about these omega threes okay so the triglyceride form can be taken with or without food and there's the prescription forms what I can't get I don't know if I can get a hold of the prescription form unless you have high triglyceride or I have a friend with high triglyceride no it's illegal folks don't share prescription drugs or you talk to your doctor and you say I'm already taking this from I mean I don't know how it works anyways what's the dosage that you recommend people get so one way or another okay so the dosage that physicians prescribed for high triglycerides for example is four grams a day four grams of EPA of yes of the Vesipa I think Lavazas also prescribed at four grams a day and you can you can get either those from your physician my father and logist got one of them described as he was we were buying our own omega three for years and years it's like hey you can actually get this and health insurance can cover it and it's really purified form but you have to take it with food that was the bottom line I've totally gone on tangents but like I you're asking more interesting questions anyway so what normally I ask about mechanism and then I talk about protocols but in the or the why or the why but we haven't gotten there yet but I think that and we definitely will get there but I think a number of people nowadays are just really excited about what they can do for their health and so here we're just raising the importance of omega three and then we'll definitely get to the why in the underlying mechanism I think four grams is I mean and in fact like you know Bill Harris Dr. Bill Harris is he's just one of the pioneers on omega three fatty acid research and he was saying that reason FDA chose that was literally just because how much they could get people to take like it wasn't like an upper and like oh this is not anything above that is unsafe that wasn't the case I mean it was it was it was just purely like cost and like you know compliance you know so like what they can get into a pill the amount they can get and how many pills they can get people to take I'm smiling because our good friend such in panda the salt institute who's done a lot of important work on intermittent fasting and other incredible work on circadian rhythms et cetera when I was talking to him in preparation for an episode on intermittent fasting he I said why the eight hour feeding window and he said well the graduate student who ran those studies had a partner I think it was a girlfriend as I recall hope I didn't get that backward and the partner said listen you can be in lab ten hours a day but you can't be in lab 14 hours a day if you want this relationship to work and so it was eight hours of feeding window plus some measurements and time to walk into the lab park the car et cetera and so the eight hour feeding window that everyone holds so holy was actually just born out of this relationship between these two graduate students you know had they been single I was single through graduate school or most of it anyway and I lived in the lab so if it be me we'd all be intermittent fasting would mean eating 14 hours a day that was a joke not a good one but just want to make clear I'm joking but the point that you're making is a really good one that the four four gram it amount is not a threshold based on anything except the threshold of people's willingness to actually take the stop so I think that's important for people to hear because so often we hear the eight hour feeding window you know four grams of EPA you know a hundred 15 minutes of cardio and it's really a question of what you can reasonably do in a study so I take four grams a day I take two in the morning two grams in the morning and I take two grams in the evening I take my EPA in the morning and I take my DHA in the evening you split them I do I don't know if I don't think it's necessary not necessarily I'm I just happen to buy I happen to get a certain fish oil supplement that's like separates them and so you know like Lavaza Lavaza is a great one and it's all like in one it's easier what if someone doesn't have a prescription so I take over the counter fish oil I know I feel better because I've done the experiment going on and off I take the mainly for I don't have depression but I my mood is better my joints feel better I just feel better and I like to think that my platelets are slippery and and they're they're you know cruising through any little obstructions in my my veins or arteries that's the image I have in my head but I don't have any data to support that part yeah I mean so I mean if you're if you're asking for like where do people get these well let's look at the bottle and it says 2 grams per serving but then I look and it's 750 milligrams of EPA right or a thousand milligrams of EPA let's say half of it is EPA then do I want to hit a threshold of EPA or threshold of what's listed on the bottle right on the on the front of the bottle and because my understanding is that we need to hit a threshold level of EPA in order to derive these important benefits I think 2 grams is is a good threshold now the international fish oil standards I F S O they have a website where they do third party testing of a ton of different fish oil supplements from around the world and they measure the concentration of the omega 3 fatty acids in the actual supplement because nothing is ever what it says on the bottle and then they also measure measure contaminants so mercury PCB stocks and things that you find potentially in fish that are harmful to humans and they also measure mercury and then oxidized fatty acids so these omega 3 fatty acids are polyunsaturated fatty acids which are extremely prone to oxidation so please keep your fish oil in the refrigerator because it's colder yeah they're extremely prone and the coverage so now I know that the shelf life's you know increased lower oxidation makes perfect sense right yeah so anyways they measure that and I typically like to look for they give you a total oxidation number it's called toe toe toe no TOT X toe toe tox is what we call it for short and I like it to be at the least under 10 ideally under 6 is really hard to find all the right mixtures of things but people can go to this website and they can browse through the products I have put together an excel sheet which I have a YouTube little screen cast that I'm yet to publish press the publish button on but it basically you have to go back and check and update because these are from different lot numbers you know the products they do have up to like 20 27 or something and so I've gone through and found my topics of high EPA brands and high DHA brands if I were to buy some the ones that I would choose because of the low total oxidation and the high concentration of either EPA or DHA now people can go and do this themselves it just takes some work no I'm glad you did the work I am going to put up a tweet every week no with you tagged until this list is published online sorry round up but I'm going to do it I know it's very sadistic of me but in service to the community and myself and I chose five brands from you and I try to choose I tried to find one in like Europe and one in Canada so there's a great selection of thank you you have that work I don't want to do that work and I trust you so yeah I try and get two grams per day of EPA yeah from supplementation I'll now put it in the refrigerator mood is better I made that decision mainly based on the data that I'm aware of looking at comparison of people doing that anywhere from two to four grams of EPA per day compared to SSRI serotonin selective serotonin reuptake inhibitors and treatment of depression and I don't want to take an SSRI if I don't have to and fortunately I don't have to but the data by my reader remarkable people that take these things insufficient doses meaning the EPA is are able to get by with much lower dosages of SSRIs for depression relief or in some cases to come off their SSRIs completely or avoid going on into depression medication now of course this is not some of the people should cowboy you know mental health issues are serious but what other reasons I'd love your thoughts on that yeah to help part and so maybe you could tell us what are some things that getting two to four grams of EPA per day is going to help with in our brain and the rest of our body so do you do you know so I actually published a paper back in 2015 about the role of omega three and vitamin D in depression by polar disorder schizophrenia and pulse of behavior but so like within that paper like the doing background research and this was a review article by the way I was just connecting dots because I know I'm going to grab but I confess I don't know the paper but I love quality reviews because the references they're in are so useful well there's a huge role for inflammation the cause of inflammation in depression and you know I think we did a short animated video on this as well like here to go back when it was you know publishing that that work where you know people are injected with lipopolar saccharide I mean this is something that we're we're generating from our from our gut mostly from you know our gut permeability which happens a lot endotoxin it's also called it's like there's endotoxin lipopolysaccharide it's basically the outer membrane of bacterial cells when bacteria dot die so like when the immune cells in our gut come into contact with the bacteria because we drank alcohol five days in a row or whatever we release endotoxin or something stressed us out we release endotoxin into our body and that causes inflammation and so you can inject people with lipopolysaccharide and cause depressive symptoms however if you take those same cohort of people give them EPA and I think it was somewhere around two grams and then injecting with the lipopolysaccharide we're establishing causation here right it totally the depressive symptoms versus the placebo so the placebo was saline control so there was this was a placebo control because obviously hugely important for depression it emulatorated the depressive symptoms of a cause by lipopolysaccharide amazing LPS lipopolysaccharide is no joke I years ago when I was working on thermal regulation we would inject animals with LPS to induce fever there's the vagus nerve registers the presidents of LPS signals to these particular hypothalamic areas and cranks up body temperature because basically it's a signal that the body is infected amazing so I will continue with my two grams per day maybe I'll ramp it up to four I'm not doing the DHA separately if there is DHA in the same supplement is that okay? yes yeah yeah and you know to kind of boy we have we got a lot of things to hit back on because you're one of your original questions was krill oil versus fish oil and DHA yeah DHA specifically is it's you know in fossil lipid form it it's more bioavailable so our our bodies you know if you're comparing exact quantity or concentration you know in triglyceride form versus phospholipid form you will get more in your plasma cells or in your plasma in your plasma with krill oil however krill oil supplements are so low dose like I mean good luck getting two grams of omega three from krill oil is also krill oil supplements are notoriously like rancid I don't know for whatever reason that's what made me itchy all over I think there's just I like I haven't found a good krill oil supplement I pretty pretty much stay away from it I mean if you smell it too I mean it's just like like it just smells like rancid so but the thing is and I also published a paper on this back in twenty nineteen or yeah something like that about DHA and phospholipid form getting into the brain in a through a different mechanism than DHA in triglyceride form and so it's going through a quarter called the MFS D2A transport and I think it's very relevant for people with an APOE for a liel so I can with an Alzheimer's susceptible right so so like twenty five percent of the population has an allil and a gene called APOE for and basically it is APOE but the four is is referred to as the the bad kind of version of it this is something in our body is also in our brain and it if people have one of these versions if they got one from their mom or their dad they have a two-fold increased risk for Alzheimer's disease if they get two which is much it's much more let's let's let's calm and I think it's like two percent of the population something has two alleles but they have like a ten or eleven full increased risk of Alzheimer's disease so there is a role for phospholipid form DHA in the brain but you also make phospholipid DHA inside your body and you can do that by taking in more triglyceride forms the two grams like the magic more two grams or more is the magic number I think so so kind of back to like the the Y for fish oil and and I personally think it is one of the most powerful anti inflammatory things dietary lifestyle things that we can we can get easily relatively easily that is it's going to powerfully modulate the way you think the way you feel and the way you age and a variety of different types of studies kind of led me to that conclusion a variety of you know observational studies so there's been lots of work by Dr. Bill Harris and his collaborators looking at what it's called the omega three index so this is actually the omega three level in red blood cells so red blood cells turnover about every 120 days so it's a it's a long term marker of omega three statics this is very different from 99.9% of any study you see or any lab that you go to to get your omega three levels tested you're getting your plasma phospholipid levels tested which is kind of like you can think of it as what did I eat a couple days before oh I had my omega three levels are great but did you eat fish like that every week or was it like you know was like you went out to dinner so it's not a great biomarker for long term omega three status it's kind of like the you know fasting blood glucose levels versus the HBA one C which is like a long term marker right of your blood glucose level so the omega three index he's done a variety of studies observational studies for people listening these are studies there are obviously flawed because they're not establishing causality they're you know you're looking at people's lifestyles but in the case of Bill Harris's work he's measuring something so he's measuring the omega three index and he's measuring omega three index and people and then looking at their mortality risk for example or their cardiovascular disease risk and what he has found is that most first of all standard American diet has omega three index of 5% Japan by contrast has an omega three index of around 10 to 11% big big difference there and they also have about a five year increase life expectancy compared to people in the US and that's do you think that's mainly due to their fish intake seafood intake so what he showed was I think it's a big part of it I mean you can't always say it's the only thing but what he showed in his data was that in and I think it was framing ham study where he he looked at the omega three index and people that had a omega three index of 4% or lower so close to what this standard American is a little bit lower. They had a five year decrease life expectancy compared to people that had an eight percent omega three index and so big difference there right five years life expectancy but here's the really interesting thing Andrew he also looked at smokers and smokers and their omega three levels and so we stratified it right and he found smokers that had no omega three were like the worst of all I mean it was like it was just like worse right we on the smoking is bad for us and we'll take take years off our life expectancy but smokers that had the high level like smokers that were taking their fish or eating fish or whatever was they were doing to get them up to 8% they had the same life expectancy as non smokers with the low omega three index right well and that's that's amazing and it's also amazing that people still smoke cigarettes but I see a lot of people vaping and I and I know a lot of people consume cannabis right people as there been any studies of specifically of vaping or people smoking marijuana and I'll call all cause mortality and I haven't seen those I haven't seen those they're not motivated enough to come in as research subjects that was that was again a poor joke it is hard to study people marijuana use unless I'm told by my colleagues that study this stuff unless you offer people marijuana in which case they'll do it but again they're actually not very good research subjects in all seriousness because they are not very motivated or consistent and they forget their appointments so that's incredible and you mentioned that the data on pollution related to the plant compounds earlier so it's almost like these things are again are acting in a reparative way the omega three's are I mean they're they are resolving inflammation they're like blunting inflammation they're they're doing so many different like at they affect so many different parts of the inflammatory pathway which is I think it plays a huge role in the way we age the way our brain ages the way we feel our mood just our joints all that and so it's it's amazing but it's not you know I love fish oil I feel better when I take it I try to eat some fatty fish a couple times a week I do want to just touch on food sources for a moment first of all are there plants that are rich in omega three's and second by I have some friends who are really into meat and I like meat a lot my dad's Argentine but I don't eat very much of it I try to eat high quality meats and relatively limited amounts by do it pretty often but I've been told by these sources of a questionable authority that if an animal grazes on really good grasses for instance that the meat can contain a lot of omega three's which in principle makes sense based on this omega three index because you're telling me that a lot of this omega three is sequestered into the red blood cells so if I'm eating high quality grass fed meat and the grasses had omega threes do the my stakes have omega threes or no so there was a study published that compared conventional meat so meat that is in the that animals are fed in a corn or or whatever which is terrible yeah but for animals and people as far as I can tell I'm sure I'll get I'll get some attacks but that's okay I won't read those comments the the again a joke I read all the comments but the it seems to me that these animals have to get either be taking fish a while or eat plants that are very rich in omega three's in order for the meat to actually contain sufficient omega threes so so the meat comparing the conventional meat to like the grass grass fed or going to pasture raised cows or cattle there were higher levels of alpha and low acid and a la is the it can be converted into EPA and dHA but the conversion is very inefficient and very dependent on a variety of factors including genetics genetics a huge you know regulator like some people can do it much better others like you're getting like 5% of conversion to EPA estrogen is a major regulator of making that more efficient and it makes sense because pregnancy when your estrogen just goes through the roof I mean these omega three fatty acids play a very important role in brain development so you're you know women are supposed to be converting any a la they can into the longer chain omega three fatty acids right so so estrogen does affect that but I would say plant sources so if you're looking for the a la plant sources would be you know walnuts flax seeds those are probably highest but if you're if a person is a vegan or a vegetarian their best bet is to actually get micro algae oil and you can supplement with micro algae oil because micro algae do it's they do make the the dHA and so that would be a better source for for people that are that are vegetarian and begin rather than doing the the flax seed oil because that conversion inefficiency you know the enzymes that convert a la into EPA and dHA again there's it's inefficient and then for people that eat fish sardines you said salmon salmon and you have to eat the skin as I understand you don't have to but it's good it's rich with the oil yeah and and the reason I say like like I I think the best would be wild Alaska salmon versus the farm raised because of farm raised again they're feeding them they're feeding them corn they're feeding them like green and stuff really and then they give them asked to xanthan so asked is anton is a crot annoyed it's the crot annoyed that's in things like krill crestations that make their red pigment yeah it's also being used now as a supplement and there's a prescription form to try and rescue some age related vision loss because of the the roll of the vitamin A pathway and photoreceptors yeah well you know actually the crot annoyed themselves so like ludenium d zanthan they're really good at sequestering singlet oxygen which is some damaging right to the yeah as we age they because the retinal cells that that cells of the irs so metabolically active they accumulate a lot of reactive oxygen species and might a condra repair and limiting reactive oxygen species is is a major theme of trying to rescue vision yeah that's a whole other podcast and story there's some really interesting data now on these of red light to try and trigger these pathways from Glen that's my good friend of many years and amazing scientists Glen Jeffries lab at the University College London I'm don't we should talk about that at some point not to study like 2020 was it now they have a second oh do they they yeah it's looking real I mean you know I they're cautious they're appropriately British and cautious about it you know I've I always joke if those studies have been done over here everyone would already know about it Glenn is a very conservative guy but they've done this stuff now in in pigs and wrote in models and now also two studies in humans it's looking pretty pretty interesting so sardines but also anchovies I'm an all by the way I hate all the food items I'm describing I can barely tolerate Sam I don't like fish at all actually I like live fish thanks when I was a kid I just don't know I find fish unless it's in sushi form I find it absolutely repulsive and I don't know why I probably have some mutation so raw fish is actually higher in mercury than cooked okay well that's good now I don't really like sushi that much anyway you're giving me great reasons to not eat fish but except I should eat these other fish sources or supplement more heavily that's the message I eat sardine my like every day my like first meal almost is like I can't sardines and avocado with like avocado is good yeah with a little bit of lemon and then some little hot sauce like you know does avocado omega 3's avocado is very good in mono and saturated fat it's really high in polyensaturated fat omega 3 really I mean it's it's it's either the DHA and EPA that's in the marine sources fish or it's plant ALA source which is like the flax seed or the wall yeah so it's rough I mean all these companies now are making these plant based products that taste like meat my wish is that they would just make a fish that tastes like a steak but that's the fish come out albino the ones that they farm raised because they don't eat any of the I'm joking I don't want to genetically modified fish that is a mistake all that you know I love the taste of say the point here is that if you don't if you if one doesn't see themselves regularly consuming these fish these fish sources of omega 3's it seems to me that the only way to really get them is from supplementation and supplementation is a good way to get a high dose and to get back to your dose point a couple of studies that that basically you know I think there was that there's some way they showed that people that are in the 4% omega 3 index range in order to get to the 8% right the five year increased life expectancy for comparing the two groups was to supplement with at least two grams it was about two grams a day and that and I think it was a little bit less if it was triglyceride form but I think two grams is a good safe number so most Americans that are not eating a lot of fish and they're not supplementing are probably around a four to five percent omega 3 index and to get to the 8% and I think that's a good empirical way of thinking about it right okay well I want to get to that 8% by the way I'm almost 16% omega 3 and I was going to ask about about testing so so where can somebody measure where and how can somebody measure their omega 3 index which again just to remind people is the essentially the percentage of omega 3's in your blood with the caveat that the omega 3 index will be heavily biased by what you ate in the previous days no omega 3 index okay so the omega 3 I thought you said in red blood cells if I ate salmon two days ago my omega 3 index is going to go no that was plasma I misunderstood so class so most people are measuring like if you look at a lot of studies and honestly I think a lot of the reason for conflicting data is because people are measuring plasma omega 3 levels okay the phospholipids it's in a phospholipid right so your your phospholipids are carrying thing these are like the proteins like you're carrying things like omega 3 and triglycerides and stuff and shuttling them around so the omega 3 index is actually in the red blood cells and red blood cells take 120 days to turn over so if you're going to do a baseline test if you want to know before supplementing what your level is you have to wait 120 days before doing the second test after supplementing to know how much you went up because the that's how long it takes for your red blood cell to turn over so the omega 3 index on bill Harris has a company that he he co-founded is called omega quant and they measure the omega 3 index they have a variety of different index tests you can do like a basic one or a little more advanced from a blood draw it it it's a little blood spot thing yeah and you know like he uses the money to like funnel back into doing lipid research like he's like out there doing all sorts of interesting studies on omega 3 is great but I know the omega 3 index is great I think that honestly more people and more researchers should be using it because the conflicting data all it always comes down to what we're measuring the sensitivity of it you know are we even measuring anything so you know you're you're giving someone 500 milligrams of DHA and you don't see any effect well did you measure what their levels were and did you measure the omega omega 3 index to you know there's all sorts of problems with randomized control trials and I think that just we need to like as scientists we need to come together and like make some progress I mean you know let's all talk to each other let's let's let's figure things out like this this test is out there it should be used it should be used not just by Bill's group but like everyone yeah well and I'm learning so much from you and I agree we need more collaboration I've always enjoyed really fruitful collaborations in my lab at Stanford and collaborating is just so much more fun online there seems to be a bias that's creating silos as opposed to bridges but I appreciate that you bring up the need for more collaboration and knowing which measures are best and in this case that now thank you for the clarification I understand this omega 3 index is going to be best you mentioned you so basically when now I'm going to look at you I think you are 16% omega 3 and dolphins are 19% I'm almost is that your goal you're trying to get there is to do the actually they should probably do something we were trying to achieve the omega 3 ratio of the your favorite species now that we've covered a bit of how to get these things into one system depending on what one eats et cetera and some of the better measurements how is omega 3 and some of these other related lipids how are they having these positive effects in my mind and this is incredibly elementary but my understanding is that at some level they're making platelets more slippery is that true or not I hope I'm happy to be wrong how is it possibly impacting my mood is it through the synthesis of membrane on neurons that allows neurons to release more transmitter like serotonin and dopamine I mean what are some of the purported reported and known mechanisms I think some of the most well known mechanisms do have to do with the omega 3 fatty acids being very powerful regulators of the inflammatory process in some way shape or form whether that has to do with resolvins that are produced so these from the metabolites of like dha for example resolvins play a role in resolving inflammation like you want your inflammatory response to be activated when it's supposed to be but you want to resolve that inflammation and inflammatory response in a timely manner and resolvins help do that and so resolvins are one and then there's these specialized promediating molecules the SPMs that also help resolve the inflammation there's like you mentioned the leukotreins and prostaglandins and these things are being affected by EPA and they do affect platelets and platelet aggregation and they you know they do affect that whole pathway as well and so there's just and there's you know I think there's just so many different ways and inputs and so when we talk about inflammation honestly it that that's a big general term but you're talking about when you're talking about serotonin release you know at the level of neurons you know we know that these inflammatory molecules cross the blood brain barrier and I just mentioned ago about injecting people life of probably saccharid and causing depressive symptoms you know it's known that that omega-3 is actually specifically EPA is able to help serotonin inflammation inhibits the release of serotonin and so EPA is actually able to blunt inflammatory responses along with DHA as well DHA does that through resolvins and stuff and this then helps more serotonin be released because you're you're not having so much inflammation getting into the brain and affecting serotonin release right that's one mechanism and then another would be well DHA itself has been shown it's it's a very important fatty acid that makes up cell membranes many cell membranes including in our neurons and as you very well know Andrew the structure and function of receptors of transporters these membrane bound proteins on the surface of ourselves including neurons are affected by the membrane fluidity you know like how rigid and how fluid the membrane is and DHA plays a role in that and so for example in animal studies if you make an animal deficient in DHA their serotonin receptors dopamine receptors they're affected because the structure of them is affected through the fluidity of the membrane and so I think that's another mechanism and I'm talking sort of general because I'm not a neuroscientist nobody makes perfect sense I mean that we know for instance neuroplasticity and the almost always involves the recruitment of more receptors or an improvement in some feature of receptors to neurotransmitters and they literally move laterally in the membrane they kind of float around like little rafts sometimes they are in fact in lipid rafts and so it makes perfect sense that these molecules like DHA which are part of the structural fat of the neuron because of course the outsides of neurons are basically fat not just the mile in that people have heard of but the actual membranes that if getting that right it you wouldn't want it as rigid as concrete but you wouldn't want it as soft as made a come up with something here it's like gooey stuff that kids play with it's like that goo anyway there's a yeah it's disgusting and it's too soft to be a membrane for a neuron that's what I told you know someone put it in the comments and tell me what that disgusting gooey stuff is you don't want your neurons to be that gooey and yet you don't want them to be like concrete either it's about it's about yeah and in mentioning DHA I'm just going to realize I'm backtracking but I want to make sure that we close all the hatches for people we talked a lot about EPA but our food sources of DHA that you find particularly attractive either by taste or by a potency for DHA what what are just a few that we could throw out because I am I am aware that there are supplements where you can get a nice ratio of EPA to DHA or you take them separately as you do but if I want to make sure that I'm getting enough DHA what do I need to be sure I'm eating on a regular basis well the fish is packaging the DHA and EPA in the ratio okay and but I I also do eat salmon row which is very salty and it's a it's a really high source of the phosphatile colonine DHA that we talked about this is fish eggs it is yeah and actually that I like for some reason do you yeah I'll eat so I'm discovering something about myself this is was not meant to be nutritional psychotherapy but you're doing that for me anyway I'm discovering that yeah I like eating embryonic fish I just don't like eating the actual fish okay well okay so fish eggs are okay so caviar base caviar yes and and that's a good source of the phospholipid form and I was consuming that a lot because I wanted to get the phospholipid form so it's actually really good there's been some animal studies and piglets and rodents as well showing that consuming phospholipid DHA during fetal brain development it like gets like 10 times more DHA in the brain again it's makes sense based on fetal development so do I need to ingest in by beluga caviar stuff can get pretty expensive it $200 a day I don't think you need to I think it's a it's a matter of preference and you're if you're supplementing with your your two to four grams of fish oil I mean that you're gonna get phospholipid form anyway because your body's gonna make it okay I've seen some containers of what I assume to be quality fish eggs that are not at the caviar level you can find in in the better grocery stores that aren't super expensive right I wouldn't dip as low as to go eat for instance like um fishing bait like when we were kids we used to go fishing you put the fish egg on the thing that's probably not good although it's good enough for the fish you're putting it okay only half joking here folks I'm just trying to protect you from yourselves don't get any crazy ideas about eating fishing bait okay so that's great to know so we have these plant based compounds we have the omega-3s so EPA DHA and then you mentioned there's a third category what would you place in your third category of foods or supplement based nutrients that our health brain and or body health can really benefit from? I mean I think the most obvious would be vitamin D which is actually as you know a steroid hormone that we produce when we're in the sun depending on the time of year we can make it in our skin and depending on how much melanin we have in our skin or whether or not we're wearing sunscreen or how old we are it's it's a very there's a sliding scale on how efficient that process is. And as I understand there's an inverse relationship with the darker the more darkers the darker your skin is naturally the more vitamin D you need to consume is that right? Well the darker your skin is the harder it is so there was a study out of the University of Chicago this was several years ago where they looked at African Americans and compared African Americans to Caucasians with light skin, a pair of skin and how how well they could make vitamin D from sun exposure and how long they had to be in the sun to make X amount right? And it turns out that African Americans with darker pigmentation which protects them from the burning rays of the sun it's a natural sunscreen had to stay in the sun like six times as long as someone with none of that natural sunscreen. So I think the the the take home there is you know a lot of people with a darker skin living in sub-Saharan Africa or people living in India with darker skin or in the Philippines you know these equatorial regions where there's their you tend to see darker skin because it's protection from the burning rays of sun. And adaptation they are in the sun war right yeah. And they're getting more vitamin D but people that maybe move to the United States to like Minnesota or in a place where you know UVB radiation isn't you know getting to the atmosphere 12 months out of the year it's only getting their four months for example. Or even living in our modern days society where people just don't go outside anymore I mean we're inside where at our laptops in school or at work when we're keeping go whatever. So supplementation does play a major role not only for people with you know darker skin that are now outside all the time but for everyone 70% of the US population has inadequate vitamin D levels 70 of the whole US so this is everyone. And and so I think that insufficient levels defined as less than 30 nanograms per milliliter. And and that's sort of defined by the the endocrine society looking looking looking at a lot of different aggregate studies and all cosmortality for example. There's been a lot of different meta analyses of all cosmortality studies where vitamin D levels are really seem to be ideal between 40 to 60 nanograms per milliliter. And so in order to get to that level if you are not outside all the time living in Southern California where you're always outside without sunscreen on I always wear sunscreen because I'm trying to protect my skin from so many wrinkles and stuff right but also skin cancer is you know somewhat the problem is that vitamin D is a steroid hormone meaning it actually binds to a receptor and another receptor dimerizes with it vitamin the retinoid receptor and that complex goes into the nucleus of a cell where your DNA is and it recognizes little sequences of DNA called vitamin D response elements are called VDREs and it also has a lot of sequences of DNA that this complex vitamin D bound with the vitamin D receptor goes inside and recognizes and turns on a whole host of genes turns off a whole host of genes I mean this is this is important stuff like imagine 70% of the population having insufficient testosterone right the steroid hormone which might we might be headed there but probably not no I think that it's names are very important and I think that one of the issues is that vitamin D is called vitamin D. It's not called DHA or you know variant blah blah blah it doesn't sound like a hormone I also I'm glad that you're mentioning skin as the major kind of interface between the environment and vitamin D synthesis because a lot of people think of skin as just a protective sheath around us or something to adorn ourselves with earrings or tattoos or whatever but skin obviously serves those roles but the skin is an endocrine organ it has the capacity to make things that are important to you to make things that impact hormones and to make hormones this is beautiful study out this last year where this took place in over in Israel where they had people get outside for 20 to 30 minutes a day three times a week exposing a culturally acceptable yet you know substantial amount of their skin during that time and saw big increases in testosterone and estrogen and this is through a correct in a site linked pathway involving p53 they did a bunch of this was done in humans but they did some knockout studies in parallel and what the study told me or reminded me is that skin is an endocrine organ so the idea that son could trigger the activation of production of a hormone is really interesting and makes total sense so when vitamin D gets into cells and it's binding to these VDR E's what what sorts of things are they triggering so like for testosterone we know it's going to trigger protein synthesis muscle grow tendons strength etc with estrogen it's going to be a keeper neurons going your joints feeling good I was remind people that by the way because the guys are always seem to want to increase their testosterone reduce their estrogen just remind people if you reduce your estrogen guys your libido will plummet to near zero don't crush your estrogen it'll also make you stupid if you're not already stupid it will make you stupid so estrogen is vitally important for males and females when you're in a vitamin D gets into cells what sorts of things is it stimulating okay so first of all it's regulating more than 5% of the protein encoded human genome more than 5 and this was you know I say more than because when I was looking at this data really in depth back in starting in you know 2012 to 2014 it was that and then it's now grown but one of the important things that you'll find interesting that I published on back in 2014 was that I'd gone through this this big published database where someone had you know published all these genes they found BDRE's in and basically I found that trip to fan hydroxylase 1 and trip to fan hydroxylase 2 was on there and so then I started looking at the sequence and is doing some of the work and it turns out that the VDR E's and trip to fan hydroxylase 2 so for people listening trip to fan hydroxylase is an enzyme that converts trip to fan into serotonin so trip to fan is what we in amino acid that we get from our food you convert serotonin you convert trip to fan into serotonin into the gut in the gut but you also do it in the brain however serotonin does not cross the blood brain so trip to fan has to get into your brain and then you have to convert it to serotonin in your brain well the enzyme that does that in your brain is called trip to fan hydroxylase 2 and it's activated by vitamin D the one that got is actually trip to fan hydroxylase 1 some of my my published work hypothesize that it might actually be repressed by vitamin D because it has a sequence the sequence itself this 12 nucleotide sequence can determine into some degree whether it's going to be activated or turned off and so like I was able to kind of look at that and think oh maybe this and that and so since then there have been some groups that have confirmed more with in vivo and or in vitro studies is a mine was all in silicone and all that stuff but anyways so serotonin a really important one but most people I mean this is regulating our immune our immune cell immune system it's regulating our blood pressure you know all that that that's water retention you know I mean bone of course homeostasis 5% more than 5% I mean I can't tell you like so much I mean with and with 770% of the US population deficient I mean anything that this could be the linchpin and a number of really important issues so supplementing vitamin D3 is what I normally here is the that I do I take a I think I end up taking 5,000 I use sometimes 10 I use a vitamin D3 per day just done that for a long time and I've had my levels tested in their in range but I have a family member I'll just mention this I have a family member who was not feeling well just kind of feeling off a little load I had some digestive is this went on along with the time was taking on my recommendation 15,000 I use of D3 and was still deficient in D3 now takes and I'm not suggesting anyone do this is a special case perhaps but no chronic illness that were aware of needs to take 30,000 I use per day in order to bring their D3 range just into normal which is to me striking because they eat quite well they're a healthy weight etc but it and it's made a tremendous difference in terms of their mood now of course is correlative now they feel better they're doing it who knows are probably also getting outside more but I mean I think people need to get tested they need to get their D3 levels tested but where where and what is a good starting range for people to to think about D3 supplementation and again foods that can increase D3. So vitamin D3 is a good way to supplement with it their vitamin D2 would be a plant source you often find it is fortified in like foods like milk usually D2 there's been a few they still drink milk besides kids. Oh, you're is that you can't find cow's milk. I mean all the lot is that you're getting milk. Yeah, they're fortified in those as well. Oh, they are. They are. Yeah, the fortified in I have a hard time finding a milk and milk and all that stuff. Yeah, they're they're in all that stuff. Vitamin D is naturally to some degree in fatty fish like you know like you think about cod liver oil right it has vitamin D but it's not you're not going to correct a deficiency with eating with eating fish for your vitamin D like you're either going to correct it with sun exposure being in the right area having the right amount of sun and being the right age because as you get old you become very inefficient at doing that converting vitamin D making vitamin D3 in your skin. Well, that's probably what was going on here because this person is getting up in there. There's a lot of single nucleotide polymorphic morphisms we talked about apoi for previously but there's a variety of genes that people very common actually in fact I've had many people that have to do done that exact same thing. So measuring your vitamin D levels before and after supplementation is the only way you're going to figure that out right very important if you don't measure it like you don't know like you know you can't know what you don't measure so. So there's a variety of snips that basically make that conversion inefficient and in fact there've been a lot of these Mendelian randomization studies so these are studies where people scientists will look at common. Snips people that have these common variations of a gene that's a little more than 1% of the population so it's not a random mutation it's actually found in a size will present the population. And then they've looked at various outcomes and a lot of times they'll look at genes that are also involved in some kind of lifestyle factors so vitamin D and snips that basically make the conversion of vitamin either vitamin D precursor into D3 or in D3 into 25 by Droxy vitamin D or into the active steroid hormone which is. And there's a variety of different snips that show people and so you're not looking at vitamin D levels at all you're looking at just the snips and you know if they have it they have low vitamin D OK so it's really a way of. Doing a beautifully randomized control trial with an observation study because your you're not biased you know vitamin D levels are also associated with health people that are have higher vitamin D are either outside more they're more physically active or they're aware of their health and they're supplementing right so. You always have to worry about that when you're when you're doing an observation super when dealing around the station is beautiful for that reason where you now just random people are randomly have these genes and it's not like there's no health status like if you have the snip like your friend like your family member was healthy and all that you know they were healthy and yet they couldn't get their D levels up right so these these Mendelian randomization say so found that people that can't convert. Into the precursor the 25 hydroxy vitamin D which is usually what's measured it's the most stable form of vitamin D in the body they have a higher all cause mortality if they can't do it so people with you know that don't have it have a lower all cause mortality they have a higher respiratory related mortality they have a higher cancer related mortality so. To me now why did I get on this rant oh because your your family member so basically they also are more likely to get multiple sclerosis this has all been done with Mendelian randomization and so it really does hammer home the importance of measuring your vitamin D levels and being being very proactive about that I mean you can you can get it done anywhere your doctor will do it you ask them to do it you know so supplementation wise typically if you don't have one of those snips for for the most part taking one of the most part of the time you know that's the most important thing is that you can get it done. In the presentation wise typically if you don't have one of those snips for for the most part taking 1000 I use a vitamin D will raise blood levels by around 5 nanograms per milliliter so let's say you're deficient your 20 nanograms from milliliter and you want to get to 40 you're going to need at least 4000 I use if you are normal don't have any of these snips that change your metabolism a vitamin D right doesn't matter when you take it relative to sun exposure time of day with or without food or food. time of day with or without food? I've seen some not so great preliminary evidence suggesting maybe time of day is important. I don't think it real. I can't seem to find anything that really suggests because the fur to actually be converted into the hormone, I mean it's stored. The steroid hormones are slow. Yeah, it's not like a immediate thing. So maybe we'll get some new data that's otherwise, but I just don't. It simplifies the problem anyway. So for people who are going to be stubborn and not get their D3 levels test or their D levels tested and simply say, oh, I'll just take some D3. That was me, by the way, until I got tested. I threw 5,000 I used into the mix and figured, well, it's not going to kill me and it'll bring my vitamin D levels up. I realize that's a bit of a course way to approach it, but I feel fine and I'm still breathing in ambulatory. So is that reasonable, 1,000 to 5,000 I use for most people will be reasonably safe? Again, we're not making it just assuming that people are going to just jump to it without the blood test. Of course. I think that if we look at the scientific literature, it is extremely hard to get hypercelsimia, which would be the major concern with really high levels of vitamin D3 supplementation. I mean, we're talking like hundreds of thousands of IU a day for a long time. So hundreds of thousands. Yes. Yes. Now, the upper tolerable intake was set by the medicine institute to be 4,000. It was just like the safe. It was kind of like one of those things where it's safe. I personally take 5,000 I use a day as well, and my levels really hover around 50 nanograms per mil and I do out. I don't put sunscreen on all the time. I do put on my face and I wear a hat, but some of my skin is being exposed. So I do make it from the sun as well. I'm glad you brought up the fact that you keep arms exposed because in these studies that I mentioned before looking at sun exposure on skin and increases in other hormones, testosterone estrogen mainly, it became clear from looking at those data that the amount of skin that you expose is important, which makes perfect sense once you hear that. But I think most people are thinking, oh, I'm out in the sun, but are you wearing shorts and a t-shirt or are you wearing a sweatshirt and it's a hoodie or are you all covered up out in the sun? Well, that might be great for setting your circadian rhythm by way of light to through the eyes, because that's the primary mechanism for that. But it seems to me that the more of your body surface that you can safely and appropriately, please, folks, appropriately expose to the sun, the more vitamin D you're going to create. So laying out on your back deck in shorts and a t-shirt with arms exposed and legs exposed is a very different stimulus than walking around in jeans and a sweatshirt. Absolutely. Yeah. Okay. Especially if you have sunscreen on your face. You know, it almost seems like trivially simple, but I'm not sure that people are used to thinking about their skin as a interface to create these hormones. Yeah. So surface area matters. And by the way, you know, there have been studies looking at people that are deficient in vitamin D. In this case, it was African-Americans that were given a 4,000 IU a day vitamin D supplement to bring them back to sufficient levels. And this was a smaller study than I would like, but it reversed their epigenetic aging by like three years because again, it's a hormone. It's regulating more than 5% of your protein encoding human genome. There's been studies looking at vitamin D receptor knockout mice. And I use this a lot in my presentations when I'm talking about vitamin D and longevity. But if you look at these animals, the vitamin D receptor, as I mentioned earlier, vitamin D binds to the receptor and then it complexes with a retinoid receptor and they go into the nucleus of the complex and turn on and turn off genes. Well, if you get rid of that receptor, which is what you can do in animal studies, you can just sort of determine like what effects there will be with no vitamin D, right? Like, how do you study no vitamin D? And so what was found was that these animals, and in fact, I don't think it was a complete knockout or, you know, because I think it might be embryonic lethal. But somehow, some hypermorphous. And just basically geek speak for a gene is very vastly reduced in its function, number in function. Number people know what I mean. But it isn't eliminated completely. Right. Well, these animals, if you look at them after the age of four months, I mean, the mice look like, I mean, they're accelerated aging. They're wrinkle. They have no hair. I mean, they just, I mean, they're lifespan shorter. I mean, they just, you can look at this animal and not know anything about mice or work with them and be like, that animal looks like it's, you know, of course, my life spends really like two to and a half years, but like 500 years old. Right. It looks like it went to graduate school twice. Yeah. Actually, graduate school is a lot of fun. I like to think I age backwards in graduate school, which is not true. I look at the photos. I definitely aged forward. You on the other hand, look exactly the same way you did 10 years ago. I'm not saying that to flatter you, but it's absolutely true. I mean, the data or the data, it's remarkable. So I think it's, I'm definitely going to try and get my mega three percentage up there. I'm not going to, you know, hinge it all on that, but clearly you're doing a lot of things, right? So if I'm taking vitamin D three, I still need to get out into the sun. Correct. Absolutely. Okay. I think a lot of people don't know that or at least I have family members that have been a little bit resistance. Like I take my vitamin D so I don't need to get outside as much. I think people are really afraid of getting out into the sun because they're worried about melanomas. And I'm as, to be honest, I'm as scared of sunscreen as I am of melanoma. Like that some of the things in sunscreen are really spooky. Mainly the compound. And here I'm not one of these conspire, I drink tap water with some folks. I like people cringe with it. I drink tap water. I have the occasional croissant or donut. I'm not, you know, I'm 90% of the time I'm doing the right things the right way. I think, although I'm now going to improve on them with this new knowledge, but I don't like what I see in most sunscreens because if you look at these compounds, they cross the blood brain barrier. I don't want compounds crossing the blood brain barrier. Titanium dioxide. Dioxide, some of the tricholacines that are also in these cleansers. I mean, it's, once you know a little bit about neurons, folks, you realize that the neurons you got are basically the ones you got for your entire life. You know, there's a reason why there's a blood brain barrier, a blood ovary, and a blood testes barriers because the genetic material resides in the testes, the ovaries and the brain those neurons don't turn over. There are a few new neurons, but not that many unless you're a mouse, frankly. So protecting those is very key and a lot of the things in sunscreen are downright dangerous. So I think there are sunscreens that are safe, but it's very hard to figure out which sunscreens are free of these compounds. I'm amazed that they're still on the market, frankly. I've always geared towards the ones with the minerals that are like reflecting it. It is somewhat difficult to penetrate things all the way through the skin into the blood stream, but I don't know maybe some of these compounds get in there easily. I have seen the evidence with some of those things. Yeah, there is a, some of them say go transdermal and they get in. Okay, well, I know that there's some of them react with the sun and while they do protect from the UVA and or B, they like form massive reactive oxygen species and curcinogen. I mean, it's like the very thing you're trying to protect yourself from might actually cause. We don't know. I mean, it's completely speculation, but there is like, I think some more and more evidence coming out with some of those compounds and I can't remember all of them off the top of my head, but a lot of high end ones also have have, you know, it's the chemical sunscreen ones, the chemical ones. We should do, I'm proposing that we do a journal club. A journal club folks is where academics get together and read papers and they get together and they pick apart the papers. There's a strong correlation between being an early graduate student and being the most critical because once you've actually published some papers, you realize that, you know, most studies people are doing their best within the context of what they can do, but it'd be great to do a journal club at some point about sunscreens because I'd love to really figure out what's in these compounds up. I mean, people are using them like crazy and I'm not one of these people who's like, oh, I won't use commercial toothpaste or anything like that. I, I'm like I said, I drink tap water, I use commercial toothpaste, whatever. When it comes to sunscreen, it freaks me out because some of these compounds do go transdermal and some of them cross the blood brain barrier and I'd like to keep my neurons free of that stuff. Anyway, we're speculating now. Where are that? Where are that? But get out in the sun and get your D3 levels up. Okay, so we've, we've talked about these plant-based compounds, the omega-3s and D3 unless there's something else that you just absolutely must throw into the mix. I probably will return us to the conversation that I opened up with, which is about cold and heat, which admittedly I pulled us off that path. So I want to take full responsibility for that. But before I do that, I just want to offer you the opportunity. Is there, are there, is there anything that fit to supplement-based or food-based compounds that you, you know, you think are especially useful for brain and our body health? I do think magnesium is important in there as well. I mean, I think, you know, again, about 40% of the US population doesn't get enough magnesium. It's an essential mineral we're supposed to be getting from our diet and it's involved in everything. It is. It's also involved in vitamin D metabolism. And in fact, being deficient in magnesium may make it more difficult for you to actually make vitamin D hormone, so that 125 hydroxy vitamin D. So one of those other factors, again, talking, we talked about genetics, but there's also magnesium status as well. Considering 40%, that's a big number. Now, you know, magnesium is also involved in making ATP, the energetic currency of ourselves. They're, you know, basically all of our cells need ATP to do anything. And it's also involved in utilizing ATP as well as DNA repair enzymes, these are enzymes that are involved in repairing damage to our DNA. I personally think that magnesium insufficiency is a insidious type, causes an insidious type of damage daily that you can't look in the mirror and see like when you're deficient in vitamin C, you're like, my gums are falling apart. I have scurvy, right? But like you can't see DNA damage. You can't see it, but it's happening. It's happening right now in my body. It's happening in your body. It's happening normal metabolism is happening, you know, every day. But we repair that damage. We have repair enzymes in our body called DNA repair enzymes. They require magnesium. Magnesium is a cofactor for them. What that means is, you know, a cofactor means enzymes need it to function properly. And so without that cofactor, they're not doing it properly. And I like the way I like to think about magnesium, it's easy because people call it food shiite, right? Naturally, that's an next question. Well, magnesium is at the center of a chlorophyll molecule. Chlorophyll is what gives plants their green color. So dark leafy greens are high in magnesium. That's one of the, and basically what is the 40% insufficiency in the US tell us? People aren't eating their greens. They're not eating their greens. They're eating their packaged food, they're eating their processed food, standard American diet isn't really high in dark leafy greens. So dark leafy greens are how I like to get my magnesium. I think it comes along with all these other important, I mean, you get calcium in them. You get that vitamin K1. You're getting a lot of other micronutrients. And you're getting other compounds that we don't know about and ones that we know about, like sulfur, right? As with broccoli, do I need to eat the dark leafy greens raw? In this case, I'm a little more open to it because I actually like the taste of dare I say kale. And kale is a dark leafy green, right? It's dark. It's obviously I'm not looting into the natural. Yeah, no, I'm going to try a chromat meaning I'm not colorblind, but I just want to make sure it falls under the strict category. Yes. I'm like, oh, I eat my vegetables. I like avocados. If you were, I mean, avocados not vegetable. I love vegetables also. But so kale, what are some other examples? Kale spinach, charred, like Swiss charred, rainbow charred, romaine lettuce. Is the bitterness and important component to this? For magnesium, no, but for sulfur, sulfur, for cruciferous vegetables, that would be the brassica family. But your question about cooking them. So magnesium is, it is bound to the food matrix and it can be somewhat less bioavailable. But you know, so cooking it can somewhat release the magnesium, but it goes into the water too. So like you have to like either steam it or kind of, you know, like get your water in it with it. Yeah, you know, I personally don't worry about it. Okay. Just don't worry. I think like, well, if you don't worry, I'm not going to. I also like, I too supplement with magnesium. I do take around a, so supplementation with magnesium. I mean, we could go on and on. Let's keep this the shortens week because we're going to get back to the other stuff. But, you know, it can cause GI distress at like high doses. I personally like to take around 130 or 135 milligrams. That way it's not like a huge ballast to my gut. I think it depends on the form of magnesium too. Yes. Yeah. Magnesium 3 and 8, for example, and you know, isn't as affect, you know, it doesn't affect the gut as much. Magnesium citrate. Citrate is what I think. Yeah. Is the pretty, I take pretty potent gut stimulus. I mean, I feel like it's a little bit harder to man. Well, I take 100, 135 milligrams should be pretty good. In citrate, actually, boy, do we want to go here? Sure. I mean, it's up to you and we can, we don't have to. I personally, I've been supplementing with magnesium for a long time. Yeah. I use 3 and 8 and biscliscinate and malate for different reasons. So I, yes, I would love to go there if you were willing. I would say malate would be the best. And that has to do with the short chain ad fatty acids being good for the gut and a lot of work done by a former colleague of mine and good friend Mark Schickenaga showing that the short chain fatty acid trait malate lactate. But specifically malate really in lactate are the major ones that get into the gut epithelial cells and are energy source for the mitochondria and the goblet cells. So anyways, whole other problems. That's okay. Yeah, I take malate because I was told that it would be helpful. I, first of all, it doesn't make me sleepy like some of the other forms of magnesium, which act as a mild sedative for me. They do tap into the GABA or chick pathway, neurotransmitter folks that in general, broad sweeping generalization here can have somewhat of a sedative quality, which is why I take magnesium 3 and 8 and for biscliscinate before sleep, 30 to 60 minutes before sleep. Definitely enhances my transition time to sleep and the depth of sleep. No question in my experience. There's some data that 3 and 8 can be cognitive, can be neuroprotective, although those are still, those studies are still ongoing. I'm getting a sense that maybe you're a little more skeptical of that. Yeah, I know I've seen the studies with the 3 and 8. I think looking at the actual data from the one clinical study, there wasn't statistical significance until all three of the pieces of data were pulled together, but that really could just be because their sample size was too small. Right. Yeah, I'm thinking that that paired with the, there's some work. The general stuff. Yeah, the Gorson Luz work on, so in that this is getting kind of inside ball of neuroscience, the quality of the labs matters, folks, and that's something that's not accessible to people outside of fields. And you know, Gorson Luz and some of the other folks at that time at MIT, I think very highly of their work. And so the animal studies are indeed just animal studies, but I was pretty impressed by what they did in those studies. Very pioneering thing when you think about this being done 10, 12, 15 years ago. And then yes, we need more human clinical data. But I, for me, I figured that given the safety profile of Mac3 and 8, given that it helps me sleep better and sleeping better is just better for everything. Frankly, that's why I take it. And biscliscinated and 3 and 8 seem to be somewhat interchangeable, but there's, I don't know of any reports that biscliscinate can be neuroprotective. But malate, I take during the daytime, it, for me, again, this is subjective. It has a tangible effect in improving the recovery time from exercise. So I don't know that I've been sore from a workout since I started taking malate, and I used to get very sore from even trivial workouts. So I don't know what's going on there, but I keep taking it. Malate, again, the short-chain fatty acid. And I mean, when you do intense exercise, you release endotoxin from your gut. I'm just going back to the interesting work, because the malate being the short-chain fatty acid and Mark Schrogganoge is showing this is all in animal research, by the way. But I mean, it was like, you know, feeding these animals malate, I mean, it really protected the gut, endotoxid release, and it affected metabolic syndrome and all sorts of things. But I think malate, malate's awesome. And I always try to eat green apples, they're really high in malac acid. Oh, good to know. And tart cherries, tart cherries are really high in it as well. It also tastes really good. But I was really interested in the magnesium, 3 and 8 stuff. I take a supplement called magnesium by Moonjuice, and it's like a little powder. It's got a little bit of monk fruit, but it tastes good. So I do it a little bit before bedtime as well, probably several more hours though, because I don't like to drink tons and tons of fluids before I go to bed. And it has magnesium, 3 and 8, and a variety of other versions of magnesium in it as well. And I really like it. But I thought that magnesium, 3 and 8 stuff was super interesting. I would love to see more clinical data as well, but I think, you know, once we get it, it'll probably be like, oh yeah, it's getting into the brain and it's awesome. So, you know, why wait? Right. I know along those lines, I once put out a post that said, you know, I feel like there are a number of different categories of health information consumers online and understanding which one you're in for which topic can alleviate a lot of the strain and stress of finding the information. There's some people that are perfectly comfortable with data from a mouse study. It's like, if it's done in mice, great, I'll try it. Other people say, no, it has to be done in humans, double blind placebo controlled studies, you know, randomized clinical trials, et cetera. And other people are just say, you know what, I don't even care about any of that. Just tell me what you do. And then other people are say, you know what, I don't even care what you do, just tell me what to do. And then there's this other category which are if it's in pill form or powder form, they'll take it. And so I think a lot of the battles of people picking apart people's posts and things have to do with that that people don't realize that people are showing up to the table in one or some combination of those stances. We know people that will try anything and we know people that won't take anything. So the idea here is to create an array of possibilities for people. And I think the animal data are very impressive. We should have you back on to talk. I take it with the hope of because I feel like the animal data is very promising. And so I'm like, it probably is. So why not? Well, and obviously you're doing things right. So cold and heat. Converge on some common pathways related to what you called intermittent challenge, which I love. I think if intermittent fasting, cold, heat, exercise, I mean, maybe even intermittent sleep deprivation. I keep waiting for the intermittent sleep deprivation movement. I will say I pull a few all nighters per year, just for work demands and procrastination and deadlines. The worst combination of academic because I'm both a procrastinator and a perfectionist. So you end up pulling some all nighters. The sleep I get the next night is pretty amazing. I must say it's the sleep of gods. I don't recommend anyone who's sleep deprivation for that. But I could imagine that we also evolved having some sleepless nights. So this idea of intermittent challenge is a really attractive one. And I want to make sure that we credit you with the phrase intermittent challenge. No, no. No, Dr. Mark Matzen. Okay, Dr. Mark Matzen. Who is published and he has used those words of that phrase. Yes. Okay, great. We'll make sure. Just like Dr. David Sinclair, I love the Xenoharmesis. He was in like one of his publications just so many years ago. I just love it. It's brilliant, brilliant term. So Mark Matzen. That's incredible, guys, they're pretty smart. You know, I mean, it's a good school, I guess. Of course, it's a good school. We will credit the appropriate people. Thank you for that clarification. So you've talked a lot about the use of deliberate, what I call deliberate cold exposure only to this thing which is from cold that you might just be accidentally exposed to. But it's sort of obvious when we say cold exposure. There are some amazing data on cold. The other day I saw a post from you and you've included this in talks before I did not know this until I learned it from you. So credit to you that even 20 seconds of immersion in, I think it was four degree, 49 degree Fahrenheit. Okay, I was translating this. I was saying 49 degree Fahrenheit water. So cold water can lead to long lasting increases in epinephrine adrenaline. And I have to presume other neuromodulators and neurochemicals as well. What are some cold protocols that you find particularly interesting or attractive from the standpoint of, I don't know, pick your favorite metabolism, neuro-slash mood effects, brown fat stimulation, which of course we've backed to metabolism. We could do an entire episode all about cold, but what I'd love to know is, what sort of activity or stimulus do you think is a reasonable and particularly potent one to use in terms of cold? So today I did three minutes at 49 degrees Fahrenheit. I have a cold tub. So you get in up to your neck? Well, I try to keep floating up. And so I'm like, it's like really hard. So the, like, I would say like maybe most of my shoulder, I mean, really, I'm floating up. I was telling my husband, I was like, there's too much water in here for me. I can't. Or too much salt in there. Is it like the Dead Sea where you float on top? Is there salt in there? I don't know. It's stuff that, you know, it's the plunge. Uh-huh. Yeah, they may, by the way, the podcast nor I am sponsored by plunge, they did give me one. That thing is fantastic. Also, because it circulates the water, which makes sure that you break up the thermal layer and it's even colder. It is even colder. It sucks. Anyways, so look, I'll give it a, I'll be honest here. I wish I did more cold than I do. I do cold when I'm going to go on a podcast. I definitely do cold when I'm going to do a podcast, when I'm going to give a talk or when I'm anxious. I need to make it more of a ritual. I love doing this on a, I hate the cold, I hate it. Unless it's summertime, it's a lot easier for me to get in the cold in the summertime. But what I do love about the cold is how I feel after and I feel less anxious. I feel good. I feel more focused, which is why I usually do it before, pop, any type of public speaking or just when I'm just anxious. I'll just get in there. The 20 seconds at 49 degrees, I think it was 49 degrees Fahrenheit was really a good number because time and temperature at time or duration, I guess it would be a better word and temperature do matter. You can do 20 seconds at a colder temperature, which is I prefer, or you can do a minute or longer at a warmer temperature. I think there was another study showing 59 degrees Fahrenheit at one hour was like two three-fold, but who wants to do one hour? Yeah, I'm familiar with that study. I love, so this is really, it reveals just how absolutely nerdy I am and maybe why sometimes and relationships in my life were challenged. I love reading the methods sections of papers. People can come at me with a number of things about papers and I might miss something, surely I miss certain things like anybody does. The methods I relish in reading the methods and that paper is really interesting because they had people sit in lawn chairs basically in swimming pools for an hour and it wasn't chilly, it wasn't super cold. I mean, 60 is not warm but it's not ice cold, obviously, but an hour is ridiculous at some level, but the increases in dopamine were massive and lasted hours. So the mood enhancing effects that you report are, you're not imagining that. Those are almost certainly a consequence of having slowly elevating but significantly elevated dopamine that goes on for hours. That's almost a dream-like profile for dopamine because most everything else like an adorol, a riddle in, a cup of coffee and a pre-workout drink or something is going to give you a big spike in adrenaline and dopamine and a big crash. And somehow it creates this really nice contoured profile. So whatever you're experiencing there is very nicely supported by the data. Well I need to get doing it more. I've had a couple of scary experiences going from hot to cold to where blood pressure changes I think where I basically went straight from a really hot jacuzzi, I was in there for like 30 minutes. I mean, I was doing heatstroke. Jacuzzi, okay. Yeah, 104 degrees Fahrenheit. That's toasty. And then I, for 30 minutes. And then I went straight into at the time, it was our pool. It was in like, February. It was like winter time and it was 50, it was in the 50s. It was cold. And I was in there and I was like listening to Simon Garfunkel. I was like trying to stay in a long time, get on my cold and then I was trying to press Dan because he like goes in there for like, he'll stay in there for like 15 minutes. But I started to feel really like blinky, like low blood pressure or something and I got scared. It's like, got out. And then I couldn't stand like I had vertigo or something and I was so scared, so scared. And so and I've had a couple of times too, we're just going straight from the sauna to it to the cold plunge where I'm starting to feel like, I feel a little blood pressure change or something. And it makes sense. The sauna is causing vasodilation and the cold plunge is called, cold exposure is causing vasoconstriction until it's like a very, you know, just shocked my system. And so now I wait, like I wait like a few minutes before going in, but I do need to kind of like make it more, the cold more routine because I talk all about the science. I'm familiar with all the science and, you know, the, the norapeneferin or noradrenaline, you know, it's affecting brain and mood and I'm, you know, way more about that than I do. I know how I feel and I, you know, it's a neurotransmitter and, you know, it is, it is released at least in rats they've shown or it wasn't mice. I think it might have been rats, but multiple studies showing in that it's released from the cold in the brain. And now in humans as well. Oh, the brain they've shown. So in that study, that's the, we can put a link to this. It's published in 2000 European journal physiology. That big dopamine increase, they also looked at epinephrine and cortisol and it's awesome really. Yes, so this has been done in human brain. They did brain. Oh, no, no, no, no, no, no, yeah, yeah, very hard to measure, don't be directly from the brain unless you're doing micro dialysis. You know, it's unfortunately, there's, unfortunately, their skulls were intact. Fortunately for them, unfortunately for the research to me, their skulls were intact, so they couldn't measure directly in the brain. But obviously, there's a correlate there. You know, it's a very real effect. I think that, but the advantage of not doing it too often is that you're not cold adapted. Now, it's very hard for anyone to get truly cold adapted. Some people start to look forward to the cold and what I think they're looking forward to is the feeling afterward, that dopamine rush. But if you get cold adapted, then it certainly blunts the sum of the effect. But I want to be cold adapted because that means I have more mitochondria in my anapostissue and perhaps even muscle like that's been shown. So maybe it is a good opportunity to, so cold and UCP1, if you could educate us on UCP1, I find this really interesting. And I learned about it from you. So. Well, so, norup and effron actually released in the plasma does act as a hormone, Bayes of Constrictions, one thing it does. But it also regulates a variety of molecular functions that have to do with adaption to cold. One happening to be, you know, shivering is a very inefficient way to produce heat, which is what your body is trying to do when it's exposed to cold. And your muscles are basically contracting and producing heat from that. But that's just not very efficient. So the more eloquent way to do it, or elegant, I guess, a way to do it is, you know, to basically have your mitochondria produce tons and tons of heat. So the way it does this is by activating a gene called UCP1 on coupling protein 1, norup and effron is upstream of that activating it. So that what that does is essentially, so mitochondria are these little organelles inside of your cells that are responsible for producing energy. And usually that's in the form of adenosine triphosphate ATP, and that's what lets everything function inside your body from your neurotransmitter production to your heart beating, et cetera. However, you can un couple your mitochondria. Basically your mitochondria, they're like a little battery, so they have, well, they have a double membrane, first of all, their structure, but they have a negative charge on the inside, and they have a positive charge on the inner membrane. So in between the outer membrane and inside part. Like a neuron. Like a neuron, yeah. So I guess it's like a neuron. It's like a battery, negative and positive. Well, basically you can un couple that charge, and so that positive charge protons start leaking out of the mitochondria, and your mitochondria freak out. So this is called uncoupling. And they start to, it's maximum respiration as we call it. They try to make as much energy. They're like, I gotta get those, that proton back, that gradient, the electrochemical gradient. And so they just go insane, and they, in this case, it's uncoupled energy, so that energy they're making is actually heat, not ATP. But heat is, but you're essentially burning substrate, so who cares? You're burning, you're burning glucose, you're burning, you lipids, you know, you're, you're basically burning things and making heat. And so that's what uncoupling does, and that is a much more efficient way of producing heat than shivering. So as you become more adapted, maybe the longer duration that you've, you've stayed in the cold or the more times you've done it, you'll no longer shiver anymore. You will start to then just do this uncoupling type of thermogenesis, as it's called. And another type of adaptation that occurs is you actually produce more mitochondria in your adipose tissue. And that actually happens also regulated by Nora Epinephrine or Nora Adrenaline through a protein called PGC1 alpha. And what that protein does is it makes more mitochondria in your adipose cell. So per adipose cell, you're getting more mitochondria. It's a beautiful way to basically make more heat when you're, it's one of those things where it's like, it's, your body's going, okay, I'm going to be exposed to this cold next time. How can I make sure I don't die? Oh, I can have more mitochondria and I'm going to make more heat. And so you're making more mitochondria in your adipose tissue. And this is often referred to as like the browning of fat. And the reason for that is because if you look under a microscope at a lipid droplet, you know, basically a fat cell, not a lipid droplet at adiposeite, you'll find that it looks darker because there's more mitochondria in there. So it's referred to as browning fat. And so I don't want to get into the whole beige fat brown. You know, there's this whole, I'm sure you've had experts on that talk all about that. Yeah, I mean, I always think of white fat, beige fat brown fat and beige is kind of intermediate. White can be converted into beige, but yeah. Right. And beige can take on thermogenic characteristics essentially. And so you can activate beige fat so that it's thermogenic in the sense that it's burning glucose and or, you know, fatty acids and producing heat. So the more you expose yourself to cold, the more you can brown your fat. You can also be able to speak and therefore you can tolerate the cold for longer periods, which people do notice. And you can then have the thermogenic qualities of having more brown adipose tissue or beige, activated beige adipose tissue, which is, you know, you'll get a lot of naysayers out there saying, oh, brown fat doesn't regulate metabolism at all. The reality is there's like thousands of researchers trying to build, pile up brown fat and thermogenic, like they're trying to make it a pill because it does affect metabolism. You know, it's not the only thing. It's certainly a phyrobease and trying to lose weight. You're not going to like do that just by doing cold exposure. You need to do dietary and exercise changes, you know, predominantly, but it does affect metabolism. And, you know, this has been shown in human studies. So it is an interesting, it's another possible mechanism for affecting metabolism. And that's an adipose tissue, but you also make more mitochondria and muscle tissue. And this is regulated not by a Nora epinephrine, but it is still PGC1 alpha. Interestingly, not like not that anyone else really cares about me, maybe you do. I'm eating this up. So PGC1 alpha is response to Nora epinephrine and adipose tissue to make more mitochondria, but in muscle tissue, it's unclear what the regulator is. Old exposure does it. This was shown at least in a couple of studies I've seen where people that were exercising, I believe, or maybe made of men, only that were exercising that some sort of training. And then did cold water immersion, something like 50 degrees Fahrenheit, 15 minutes. And PGC1 alpha, which is a biomarker for mitochondrial biogenesis, which is the generation of new mitochondria. By the way, that's awesome. You want more mitochondria in your muscle. It's associated with improved muscle mass, improved endurance. I mean, mitochondria are essentially either the making energy in your cell and we, you know, we don't make more mitochondria normally. Like you have certain inputs, high intensity interval training, exercise can do it. And actually make more mitochondria. Yes. Yeah, and that's been shown in people. And I mean, weight training or just high intensity interval training. I haven't seen weight training. I've seen it in high intensity interval training and endurance training. But that doesn't mean that it hasn't been shown. I just haven't seen it or that it hasn't been looked at. But you know, I'm always looking for reasons to finally do more hip type high intensity interval training work. I do weight training and I do low intensity cardio. There was a brilliant study by, at the time he was a postdoc, Matthew Robinson. And he's now gone on to start his own lab at the University of Oregon Health Science Center or something like that. And he did a study where both young and older people were, they had this whole high intensity protocol, which I can't remember what it was, but their protocol for X amount of time. I'm sure it was at least a month. They then measured biomarkers of mitochondrial biogenesis in their muscle tissue and the amount of mitochondrial biogenesis in old people specifically. It happened in both young and old from hit from the high intensity interval training was, I mean, it was like enormous. At least 50% I think. So it was just like, whoa. And so like, why would you want that? Well, you know, mitochondria, you're, you're mitochond, you don't make your cells, your cells are turning over, you make new cells, you replace old ones where you're mitochondria. You don't really do that for the most part. You can mitochondrial biogenesis does happen, but you have to stimulate it to happen. And the way you're mitochond, like what happens with your mitochondria is they essentially are bobbing around inside of your cells and then they fuse with other mitochondria, exchange all their content and mitochondrial DNA and then fizz back apart. And that's how they kind of stay young-ish. But like as you age, you keep doing that with the same pool of mitochondria and you're going to get a bunch of old mitochondria mixing old stuff together, right? So why wouldn't you want to like bring up new healthy, young mitochondria into that pool, right? So in my mind, when I hear mitochondrial biogenesis, I'm like aging. Like that's the first thing I think of. So anyways, cold exposure does that. It helps other things as well. You know, and please, thank you for offering to somehow filter the level of detail. But I assure you that listeners of this podcast are familiar with getting, drinking from the fire hose of mechanism and that was really helpful. And again, this is just one example of maybe four or five other things that you've said, at least, that are going to inspire me to change my behaviors. I'm going to start doing some high intensity in real training. Dr. Andy Galpin was on this podcast recently and he told me that the subtle zone to cardio and the weight training is great, but that I really should be doing some max heart rate work per week, you know, going into max heart rate for 90 seconds and resting and repeating that maybe even mild repeats. I'm just curious as a brief aside before we talk about heat, what sort of cardiovascular or other types of training do you do? Do you do hit? I imagine you are doing high intensity interval training. If you could just give us a sense of the contour of your week as it relates to exercise and because you've been very gracious in sharing some of what you do for supplements and food, what about exercise? So I, it all depends on my week, of course, and what I'm going on with my son and my work schedule. But I typically, I do a lot of high intensity interval tabatas on a stationary cycle. I use peloton because I just like that instructor there, like telling me what to do and then me competing with everyone else. I'm like, yeah, you know, so it worked. You were revealing something about your psychology. We just learned about, so this podcast is actually just a decoy for psychological assessment of the guest, not getting. But so now we know you're competitive. Good. That explains a lot of how you got through graduate school and then do what you do. So you're getting on the peloton and what does it look like for someone who's not familiar with peloton? I know what they are, but I've never been on one. You are peddling against the instructor for how many seconds? So you're, there's a bunch of people that are online either doing the class with you at the same time or at all time doing it so you can kind of toggle on what you want and like you can try to compete against the other time really competitive. Oh, yeah. Okay. And the instructor is just there to like whip you like like you know make you there's there's a part of the brilliance with peloton is like I used to do rush with called rush cycle and I used to go in. It's basically you go in and group cycle and have an instructor there and you do all this high intensity interval training stuff. And I loved it because there was a competitive aspect to it that had me working harder than I would work if it was just me in the room like without an instructor or anyone there and it was just like I'm at a gym any gym and I'm just on a stationary cycle listening to a podcast doing something which is fine if that's your group right. But there is something about that group setting that kind of make hold to accountable to right. And the peloton made it somehow virtual. It was amazing and I remember being back at rush cycle. This is before pandemic and people talking about peloton in my class and I'm like oh, that's ridiculous. Why would I do that? Like that's never going to work. I need to like be here and then the pandemic hit and I was like all over the peloton and it works for me really well. So I tend to do that at least three times a week. Sometimes I do it more like you know, I'll do four and I do a 10 minute just 10 because it's efficient and I push my ass. I push myself really hard. It's the tabata at the 20 seconds on 10 seconds off and it's 10 minutes and on means you're pedaling like you life depend on you're maxing it and there's a lot of resistance. And so you do. Well, so you basically there's a part where you're I always do resistance. I'm like the power. I do the power for there's a part where you're sitting set cycling and you're trying to go really fast but I always crank the resistance up. I always go above what they give me and then and then there's a part where you're standing and then you really crank the resistance up which I really do and like you feel it and you're glued. Like going up a hill. Yeah, exactly. I'll crank it up and most of the time you'll have like those two parts and I love the efficiency of it. You just you get it done and people sometimes hear me go 10 minutes or really you think you work and like look like you max you do max you a tabata for 10 minutes and it's intense. Yeah, most people can't sprint for the for the gate of an airplane they're about to miss carrying a backpack. So if you think about if I think about that and then I just described myself, the other sprinting through the airport and going, all right, Andy Gallup and I got my 90 seconds max heart rate in for you carrying this thing. But 20 seconds on 10 seconds off repeating that over and over for 10 minutes. So by time you're done you're cooked. And then I because I'm competitive during the recovery that they give you at the minute at the end I'm pushing it max. Right. Right. So three times a week. Yeah, three times a week and then I always have my sauna on pre heating up takes about an hour and a half and I get it to about 189 degrees Fahrenheit. I hop right in the sauna after my my my peloton. So the elevated heart rate continues is that the last. Yeah, I mean, I literally like down a bunch of water and then I get in and then I like either read a science paper prepare for a presentation or a podcast or I hash over things in my mind and it's interesting because something about getting in the sauna, I think the stress the heat stress of it. I used to so I started doing the sauna in 2009 in graduate school. Okay. And I you're early adopter. I started doing it every day. I lived across the store. I lived in a studio apartment with the on within the like small studio part, the smallest apartment you'd ever imagine. And it's across the street from a YMCA because I was poor in graduate school, very poor, very poor. I mean, so you know, I recall I recall me. I lived in my lab. Wow. And again, I lived in my lab as a postdoc and as I admit, I lived in my lab with my bulldog as a faculty member for other reasons. Okay. But I get it. I when you're graduate student, you're poor. Yes. Yes. And so I used to go to the sauna before going into the lab and I would and I would I started noticing that I was all of a sudden able to handle stress better. Like the stress of my six month setback because of failed experiment, which is crushing. On top of the pressure from your advice, my advisor and my own pressure because I'm very competitive with myself and I put a lot pressure on myself. So I was having a hard time. I mean, I was very stressed out in graduate school. And the sauna started to really noticeably affect my anxiety and my ability to handle stress. And I was like, what is going on here? So I started looking into the literature and you know, started getting interested in the effects on the brain. And in fact, at the time, I had a friend who was not actually experimentally but theoretically looking into the opioid system. And basically, so when you get in the sauna, you release a lot of endorphins and dwarfs are the feel good home, feel good opioids that you know, make you feel good. But you also release something called dinoirfen. And dinoirfen is an endogenous opioid that binds to a receptor called the capa opioid receptor, which dinoirfen is responsible for that dysfork feeling when you're in the sauna and your hot and when you're running, doing exercise and you're like, you feel uncomfortable. Well, I think that's dinoirfen speaking absolutely. I think it is. No, I think it is. I mean, there's evidence in alcoholics that some of the symptoms withdrawal that they experience are related to dinoirfen and dinoirfen is known to negatively impact the dopamine receptor system. So basically, it's the feel like garbage pathway. Right. You feel like garbage. And so you think that that would not be good. But this is where my friend that comes in. He was looking at the effects of like treating morphine or heroin addiction and, you know, people that are using those drugs. They basically, the endorphins or the morphine or, you know, heroin, they bind to a receptor in the brain called the mu opioid receptor. And as they take these drugs, that mu opioid receptor becomes down regulated. And so you need more and more of the drug to feel as good as you do. Right. Well, endorphins also bind to that receptor. And he was looking into some of the other other drugs that are like salvin, salvinorium, or something that's alvia. It's called it binds to the opioid receptor. It also makes you kind of feel uncomfortable. Anyways, he had put some studies in front of me that showed basically binding of the, you know, either dinoirfen or, you know, whatever ligand to the capa opioid receptor basically sensitizes the mu opioid receptor to the feel good endorphins. And also changes. I think it also upregulates it or something. So basically, there's a lasting effect of feeling good. So the endorphins that you release later from hugging someone or a joke you're laughing out or whatever, you feel it for longer. Right. And so anyways, this is a, with the son, with respect to the son, it's a big sort of hypothesis of mine. I did kind of publish that part of my hypothesis in a review article. But I do, I would do wish more people would kind of look into that. That'd be amazing. But what I was getting at, I think, was I would use the sauna to memorize things. This is way back in the day and I still do it. And I wanted to talk to you about this because you're a neuroscientist that there's something about being in the sauna. And I think, I don't know if it has to do with the stress response. Like when you have an emotional trigger, like you remember things better, right? Absolutely. There is a clear and known explanation for mechanism for this. So in the sauna, I mean, you also release norup and effort. Just like you do in the cold. You have a lot of overlap. You know, you're really, you, I mean, it is a stressor. But I like use it to remember things like I'm going through something. I want to go through a presentation or a talk or a podcast or whatever. And I go in that sauna and I mean, you should try it. Like if you haven't already, I don't know if you have. I have a sauna and a cold punch now and I haven't tried prepare. I read books in the sauna in the evening. It's a, it's a time I insist on having my phone out of there mostly because I initially because I thought I'd cook the phone. But also just to get some separation from the phone and screens the evening. So I read books. The only challenge sometimes you're dripping sweat onto the books. But I'm willing to forego a few pages of a book. The, the idea that being in this semi stressful environment would aid in the learning and retention of information is, is really well substantiated by this. It's a beautiful work by a guy named James McGau. I don't know if his lab is still active, but he was at UC Irvine for a while. And then I think at University of Arizona as well. They have a great memory group at both places, very strong in learning and memory, both places. And he was the one that really defined this kind of inverted U-shaped function for the relationship between adrenaline and memory. Basically if you're too relaxed and not stressed enough, you're not going to remember any information. At peak levels of stress, you actually are a memory machine, at least within the context of whatever it is you're trying to learn. So very well, what you're describing is very well matches with that. And then of course it tapers off as you really increase adrenaline to the point where people are starting to lose autonomic function where they're just, they're panicking basically. But obviously you're keeping it in range. The other thing that I'd like to ask you about is in the sun, of course there's vasodilation. And perfusion of blood to the brain is a wonderful way to enhance cognition. There's even some really nice data showing that during inhales as opposed to exhales, people are better at learning information. But during the inhale you're taking in and absorbing and remembering more than during exhales. And these are beautiful studies done in humans, of course. So I can imagine that vasodilation, getting more perfusion of blood to the brain, plus a little bit of stress, or maybe a lot of stress from the epinephrine. And yet it's in, and then of course there's going to be the, I don't want to call it placebo, but there's going to be the context, the condition place context of it. If we had a good experience remembering something in the sauna once, we tended to positive association effect of that location is real. Just like if people go to a new city and they get robbed, like if you go to a Cincinnati, I've never been to Cincinnati, but you get robbed in Cincinnati, your purse gets taken in your wallet gets taken, you kind of hate Cincinnati as a tourist. But that could happen at any number of different cities, right? The opposite is also true. So if something good happens someplace, so I'm imagining that it's a combination of those effects. But I'll start, it would be very hard to do this in the cold. I feel like the cold is a very potent, I think it takes you too far down that curve, the McGaw curve. You have to sing songs or something when I'm in. Distractions, yeah. I sing songs. But afterward you're very efficient at learning. After I am. And with respect to the sauna, the vasodilation does occur. So there's a lot of overlap between moderate intensity, aerobic exercise and heat stress. And as you can imagine, when you're exercising, you're elevating your corbide temperature, you're sweating. And when you're actually in the sauna, blood does get redistributed to the skin, defecilitate sweating, but much like exercise, blood flow in general is improved to the brain, to the muscles everywhere. So I think generally speaking that, and this, there's studies showing that sauna use is associated with a much lower risk of dementia in Alzheimer's disease. People that use it four to seven times a week have greater than 60% reduction in dementia in Alzheimer's disease risk compared to once. I was sorry, I didn't mean to cut you off. You said people who use it, I apologize, maybe you'd tell us again, people use it four to seven times per week have. They have a greater than 60% reduction in dementia risk and Alzheimer's disease risk compared to people that use it only one time a week. People that use it two to three times a week have something like a 20, a little greater than 20% reduction in risk. There's a dose dependent effect on dementia risk and Alzheimer's disease risk. It also has a profound, there's a big link between the cardiovascular system and the brain. Obviously blood flow, a big one, right? You need to get blood to your brain. But cardiovascular mortality, so mortality from cardiovascular disease, if people use, or actually this was men, if men use this sauna, 47 times a week, it's a 50% reduction in cardiovascular related mortality compared to one time a week. Again, dose dependent manner two to three times a week is something like 24% lower, death from cardiovascular disease. There's also lower sudden cardiac death, it's like a heart attack. That's like 60 something greater than 60% lower if men use it four to seven times a week versus once again, a dose dependent thing. The thing that's so profound there, also to me, when again, looking at the methods, when I look at the data, and this is all work from Dr. Yari Lalkinin. He's in the University of Eastern Finland, and just one of the world experts on sauna use, especially with respect to cardiovascular health. What some of his data has also shown is that if you look at the duration, the time spent in the sauna, so I mentioned the temperature I do is about, I do like 189 degrees Fahrenheit. Typically I go in there, I'm pretty heat adapted. The more you do the sauna, or any sort of heat stress, whether it's a hot-tubbered or a jacuzzi, you become adapted. You basically start to sweat at a lower core, body temperature to cool yourself down. All these sort of physiological changes start to happen earlier. I stay in for like 30 minutes. So I stay in a long time. That's a lot. You have to listen to your body. Most of the studies that I just talked about were from the duration, the time spent in the sauna, when I said 50% reduction in cardiovascular disease related death. What was shown was that men that were in the sauna for only 11 minutes, even if they used it 47 times a week, that reduction was only like 8%, set of 50. It had to be greater than 19 minutes, so like 20 minutes is the sweet spot. About 174 degrees Fahrenheit. Most of the sun is in Finland, by the way, they're humid, so they put hot hot hot hot, they put water on hot rocks to create steam. So it's usually between 10 to 20% humidity in the Finnish sauna. So those studies where I would say most of the time you're going to find that their humidity is also elevated. But to me, the dose-dependent nature of it and the duration knowing, to me, that's a very strong data that this is more causal than some corollary thing. Because that's always the problem with observational studies, including these, which they corrected for a whole host of factors like cholesterol. You know, exercise, just everything, everything of the sun. I mean, they corrected for those. And on top of that, you have the dose-dependent nature of the duration, the time spent in the sauna, and the frequency. So to me, it's like, something's going on here. Plus, there's been studies, intervention studies where it's like comparing directly head-to-head, moderate intensity aerobic exercise on a stationary cycle to 20 minutes in the sauna. They're physiologically the same things happen. So heart rate elevates while you're doing the activity, blood pressure increases while you're doing the activity. But then after heart rate decreases, resting heart rate decreases below baseline, blood pressure is improved. So it decreases below baseline. This is happening the same in moderate intensity cycling versus sauna. So again, the sauna, like this heat stress, there's something about it that really mimics this moderate intensity aerobic exercise, which is really great for people that can't go for a run. That can't even get on a bike. So disabled people granted there are some safety concerns, they're pretty mild, but they do exist. So people that had a recent heart attack or have some rare kind of heart disease or problem, drinking alcohol, never do that. Elderly people prone to low blood pressure, always talk to a physician before doing the sauna. It is stressful. Pregnant women. Pregnant women. Oh, yeah, I definitely avoided sauna as when I was pregnant. But it is, I think it's very relevant for disabled people and also people that are sedentary, I've been sedentary most of their life. My mother, I've been able to get her in the sauna because she's not, I mean, I did get her on the Peloton once, but it's really much easier. She feels like it's a spa treatment and it's like she can listen to her music in there. And I care about her health, but she's mostly been a sedentary person. And so I find it much easier to convince her to get in the sauna than to get on Peloton. Ideally, you do both. The question would be, well, I exercise, I run, I do it by high intensity interval training, why do I need to get in the sauna? And the reality is, and so I published all this and I review in the experimental gerontology last year, I guess, late last year. And basically, cardio respiratory fitness, which is a marker of, it's a marker of health, you know, cardio respiratory fitness is improved in people that do exercise and sauna, compared to exercise alone or sauna alone. So for those healthy, fit people out there already exercising, there's a synergistic effect by also adding a sauna into that routine. And to me, that's great. And there's so many beneficial things happening with the heat stress in addition to like mimicking aerobic exercise. There's the heat check proteins that we talked about earlier. And those, it kind of brings me back to my early days of science when I was at the Salk Institute for Biolateral Studies, doing research on little nematode worms that we are someone else injected, amyloid beta 42, the peptide, the 42 amino acid peptide that is involved in amyloid plaques found in the brain, correlated with Alzheimer's disease and other, you know, brain disorders. We injected those into the muscle tissue of worms. And basically, these worms become paralyzed with age because the aggregated proteins, these proteins aggregate. Well, heat shock proteins, one of the main things they do is they basically make sure their proteins inside of your cells maintain their proper three-dimensional structure and are folded right. And so they don't, they're not prone to aggregating and forming these plaques in your arteries and also in the brain. And there's back to my, my worm studies I was doing, I would elevate heat shock proteins in those worms and it would totally, you know, correct the problem where they would no longer become paralyzed. They'd move around like they were young. So many animal studies have been done looking at Alzheimer's disease, you know, like a human-like Alzheimer's disease in a rodent and heat shock proteins protecting from it, you know. So heat shock proteins are robustly activated in humans. This has been shown to, you know, 50% higher over baseline levels after just 30 minutes at 163 degrees Fahrenheit in the sauna. So and they stay activated at least in rodents for, you know, 48 hours at least. So you know, having these heat shock proteins around, making sure they're properly taken care of our proteins so they're not aggregating in our brains and in our plaques could be another potential way that sauna is protecting from Alzheimer's disease and other, you know, cardiovascular health as well as longevity. So, you know, there's people that have SNPs in heat shock protein factor 70 that if they have one of them, so they got one from their parents where they have more active heat shock protein 70, they live on average one year longer than people that don't have that SNP. And if they have two versions, if they got one from their mom and one from their dad, they live on average two years longer than people that don't have that SNP. So it's also been associated with human longevity as well as in lower organisms. So you can heat shock a worm or a fly and they live 15% longer. This has just worked on by Gordon Lithgow at the Buck Institute years and years ago. So anyways, I guess what I was getting at was the heat shock proteins are part of that stress response pathway that we talked about earlier and, you know, they're also activated by cold as well. Cold shock does activate heat shock proteins, not as robust. So for a free and active, it activates them. Again, it's one of the reasons I think we should get all of these things because they are more robust inputs, you know, they're input activating mechanisms are more robust for, you know, different ones. So there is cross talk. There is, you know, I mean, I guess I get it'd be more accurate to say there's overlap. But, but, you know, it's also like you want to get the most robust from all of them, right? I do. So, I mean, that's why I want to do the sauna and exercise. And eat myself, you know, my broccoli sprouts and all that stuff. Oh, it's super interesting. A couple of questions came up for me. One is you mentioned these SNPs, these nucleotide repeats. Basically, genes that some people have more of a less of than others that can predict longevity in some sense. Is that the FOXO3 pathway? That's one that can. Yeah. So, the FOXO3 is, in fact, if you go back to the warm studies I was talking about, that was like one of the first things when you see it with your own eyes, you can take these worms that you basically decrease their insulin signaling pathway and their IGF1. Worms have what are called homologous genes. So they have a lot of similarities to humans. They have an insulin like receptor. They have an IGF1 like receptor and they make something like FOXO3, which we have. And basically, if you decrease that insulin signaling pathway, their FOXO3 is always active in those worms and they live like 100% longer. And not only do they live longer, I mean, they are like a very young worm. I mean, they are like, you look at this thing and you're like, this looks like the worm that was just born like hours ago. What's going on? This thing is at the end of its life. Now, as a side note, the thing that always got me on this was, by the way, this was discovered by Cynthia Kenyon and this was like back in the 90s. And honestly, I'm not sure that anything has been as exciting in the worm world since then, but I thought, I mean, it was a really big finding. The only caveat there is that the worms go through this dour. It's called a dour stage when this happens, when you decrease their insulin signaling and stuff. And they go into this like metabolic stasis. Like they're not eating as much or moving. And so it's like, okay, well, they live 100% longer, but like they go into this weird state. I know people like this sum in the longevity community. They know who they are. But they'll get the last laugh because I'll be dead, well fed, but dead and they'll still be going. So in terms of the many data on sauna and I also just want to acknowledge these finish groups that did this work is really pioneering, right? When you think 20 years ago, long before social media or any of this and they're out there up there, I should say, measuring cortisol and growth hormone and all this stuff in people getting in now, sauna. Very, very interesting. So 20 minutes seems like the threshold at 170 degrees Fahrenheit. More times per week seems to be better than fewer when you think when in terms of all cause mortality cardiovascular risk, according to what I just learned from you. Or would be a good, I think minimum effect of dose. More times a week and you combine it with the cold. I've also seen a protocol where it's a very extreme protocol. I don't recommend this to people right off the bat where they had subject, human subjects get into the sauna for 30 minutes, get out for five, 30 minutes, get out for five, 30 minutes for a total of two hours of exposure. But that was what led to these massive 16 fold increases in growth hormone. I actually have a, so I, and they had to do it very seldom. So it sounds like these protocols you're describing 20 minutes done four times per week. They are more reasonable for most people to access. But I know people are probably desperate to know what if they don't have a sauna. You know, a sauna is kind of a unique item. So I have a couple questions. Can people use hot baths? And with the appropriate warning, of course, that without getting into a description of the mechanics and the underlying biology, it's pretty obvious that the testes, if they get too warm, you'll kill sperm. That's the reason why the testes are housed in a structure called the scrotum that can move around. So just to be, you know, a biologist just talking about realities here. So if you're trying to conceive children or keep your sperm healthy, guys should probably stay out of warm hot baths. For at least six months. That's been shown. So sperm, so sperm, motility goes down and sperm production goes down. But that is completely, like corrected, if they stay out of the sauna for six months. So through six months later, it's back to normal. Great. That's very useful information. You can go to a number of people out there. So if people don't have access to a sauna, and we get this about cold too, you always say, what about cold showers? And I always say, well, the studies have mainly been done on immersion because it's hard to keep things controlled in cold showers. It just doesn't make for a very good experiment because you get a bigger person. Less of them is under the shower. And so it doesn't make for a good experiment. So it's not as good as immersion. But with heat, I could imagine that a hot bath would work almost as well. So there's been some studies looking at, for example, activation of heat shock proteins, also brain drive neurodegrofic factor increases with heat stress. And so the hot bath at around 104 degrees Fahrenheit, which is typically what studies will use for temperature, which is actually cooler than what I craved my bath hot. It's so hot. But you're very heat-adapted. I'm very heat-adapted, yeah. And it's 20 minutes from the shoulders down. And that is like a very robust activation of heat shock proteins. And in brain drive neurodegrofic factor. And then heat shock proteins are also protecting against muscle acrophy. So that's also having to do with the protein structure and the muscle tissue as well. And this has been studies in animal data as well as some recent human data as well. It was local hypothermia or local heat treatment. But essentially it showed that it protected. I mean, it was like, there was a study where they were looking at muscle disuse. And it was something like the local heat treatment prevented almost 40% of the muscle atrophy from dysus. So it's funny because I used to use this on when I was injured and stuff. I would go in this on because I didn't know at the time because I was a graduate student. But I knew just from experiments that I'm not losing as much muscle. I feel better. At the time I was reading a lot about the growth hormone and stuff back then. And I knew about heat shock proteins and so I kind of knew that data wasn't around yet. And so now we have the data. And I've always felt like I wasn't losing my muscle. Like I should have been when I was doing the son and I was doing it literally seven days a week. It was like hardcore. This is also during graduate school. Yeah. Now I'm doing the son, like a bare minimum I do three, but I try to do four because of the, it all depends on my schedule. I also like to do long runs. I really, it's like long being like three miles, not like camhains. It's not long. But I really, for me, and we were talking about this earlier, like off camera, that the runs for me are for my brain. And there I get this mind wandering effect where I daydream and I think about things, I work through problems, I get creative, I come up with ideas. And this is all happening on the runs. And so I just, I, I, I miss my runs if I don't do them and I miss it because of the brain effects I get from it. And when I exercise, it's funny because I'm a female and you think that I'd be exercising, you know, to stay fit and in shape and care about my figure. But when I exercise, literally what I'm thinking about is my brain. And I'm like, this is the best long-jogged, long-javvy drug there is. This is it right here, Rhonda. Like you, you're always wondering, you're always wanting to know, you're wanting to do the best. And so, you know, I exercise, you're missing that is central dose. And so that for me is, is, is the motivation, the dopamine seeking thing I, I'm looking for. Admittedly, I need to, I do not do enough strength training and I have to do it, I have to have to, I'm like, I'm just, I'm so after the endurance and the hit and I, I really need to add that in because muscle mass is also extremely important for aging as well, you know. So that's, that's my, that's my fault. Well, the, the brain effects are really interesting. I also run, I try and get one longer run per week and a few other runs and I do it without a phone. I don't listen to podcasts. I occasionally will listen to music, but I really try not to. I also find that my mind solves problems. I feel like it, it washes out the cobwebs, so to speak. Some of the most brilliant and prolific neuroscientists that I know who've had very long careers, Eric Kendall, Nobel Prize winner at Columbia, comes to mind for all his work on memory. Used to swim a mile a day and now I think swims half a mile a day, but he's in his late 90s and he's still sharp, which is incredible. And his lab has done some work showing that any load bearing exercise repeated, so endurance work, unlike the Peloton or cycling that's really load bearing all the year cycling really hard with the resistance, but causes the release of osteocalcin from the bones, which acts in an endocrine way, sort of like a hormone, can actually travel to the hippocampus and at least in these animal studies induce the proliferation of neurons, growth of synapses, BDNF, a number of downstream things, which kind of makes sense if we were to put a just so evolutionary story on this, a body that's active can signal to the brain that the body still needs cognition, an inactive body in some ways is depriving the brain of any signal of what the body is doing. This is obviously making this up as conjecture, but we know in ocean and various ocean animals that they'll swim around for some period of their life and then they'll have a completely stationary portion of their life and basically the brain degenerates. You don't need much of a nervous system if you're not moving. So I think there's really something there and also just letting your ideas and mind drift. I love that you and I appreciate that you shared your protocols because I think right now we're in an interesting time in public health information history where people are just kind of getting bombarded with cold is good, heat is cold, cold is good, heat is good, excuse me, I must spoke. There are all these micronutrients and of course macronutrients are important too and today you've really enriched us with the description of the underlying mechanisms and the logic behind them, but also sharing what you do is really informative because I think people need a jumping off place and obviously they need to start someplace and getting heated apted, etc. takes time, but I really appreciate that you're willing to share your protocols and that you do the things that you that you teach and educate people about as a final question because I have have have to ask red light sauna or no red light sauna. I've been a little bit vocal about my feelings that none of the red light sauna's I've ever been in got hot enough and it was frustrating. I feel like it's neither here nor there. However, I do acknowledge that red light and low-level light therapies are now known to do a number of interesting things. It was a Nobel Prize in 1908 for photo therapy for Lupus so you know it's not like a new thing. The idea that red light and light could do things positive for our biology, but do you have a red light in your sauna? Do you think it's useful? And I mention this because this is the number one question I get about sauna. Red light or no red light or some intermediate answer. So I don't have an infrared sauna, but I do have like I have a sauna that has lights. It makes red light, but I don't think it's the red light that you're talking about. Okay. It's not activating it at a specific wavelength, which is. It's usually so that the range that seems to be helpful and I have I confess I use a red light panel for other things is 670 nanometer out to about 720 nanometer. So it looks like red and very dim light dim red and bright red and the ideas that red light can travel the photon and energy is such that it can travel down through the deep flavors of the dermis of the skin. I you know I don't have a red light in my sauna. I don't know if it's essential or not. I don't think so based on all the studies I've talked about. I think that would be is is you know the potential effect on mitochondria is interesting. I do think there's a lack of really good solid evidence in you know humans, but I don't that not might only be because it's just not studied enough and that's usually the case. So perhaps you know like there's the juve right the juve that they have those pant red light panels. So Z or the two ones I know K O Z and juve there they're as far as I know I'm probably going to insult both companies at the same time but I'd rather insult them both at the same time than just compliment one or insult one. Both of them seem excellent for getting the appropriate wavelengths of red light and I do not have a relationship to either. Yeah well I personally think that the the sauna in and of itself it's about the heat stress and typically the question I get is infrared sauna or regular sauna and there are some differences as well infrared saunas maybe the infrared saunas are the ones that have the red light that you're talking about. Infrared saunas only get up to around a hundred and forty degrees Fahrenheit. So as I mentioned the studies were about one seventy four degrees Fahrenheit and so you really have to stay in a longer period of time. However there have been some studies coming out of Japan they they use infrared saunas. They have this whole protocol it's called way on therapy and they they they get people and infrared saunas and they wrap them in a towel and like they stay warm for X amount. So it's like the whole protocol ends up being like an hour long but again it's a hundred and forty degrees Fahrenheit so it's an infrared sauna and it's been shown to improve a variety of like coronary heart disease and conditions heart related conditions like there have been some improvements. So obviously there's there's evidence that infrared saunas can be beneficial for cardiovascular health. I do I've used infrared saunas many times that my my in laws they have an infrared saunas and I have to crank that thing up for a while until it's maxed and then I have to sit in there for an hour at least. I do sweat a lot and that's another thing we didn't talk about you do sweat some heavy metals and some some heavy metals are excreted predominantly through sweat and others through urine. So so for example cadmium there's like a hundred and twenty five fold increase in cadmium excretion from sweat when you get the sauna also lead is something like seventeen fold excretion is higher another one is aluminum it's about fourfold higher so infrared you do sweat a lot too and that's because the main difference is that you're heating your body up through thermal radiation versus the ambient hair air like a standard you know sauna is a heater and the heater is heating up the air and and that's how you're heating yourself up. So it is a little bit of a different mechanism I prefer regular saunas most of the data out there from the heat stress itself like that your heart rates elevating when you're in there you're feeling hot you're getting that cardiovascular I mean that's what you're feeling when you're in the hot sauna and that for me takes a really long time and the infrared sauna get at the very end but I do think there are some benefits from infrared and they are more affordable they're less of a fire hazard but again hot baths are I think a good alternative modality for heat stress compared to like a regular sauna so great that's a really helpful answer I like I said I use the red light but not in the sauna and thank you for reminding us of that um hundred and seventy four degree Fahrenheit threshold those mainly used in all these studies so we covered a lot of of territory but I just want to thank you again it was extremely thorough and extremely informative I now have my notes are always look a little bit like they were drawn out by a macaque monkey who has no knowledge of the English language but I can decipher this to tell you that there are at least ten additions to my current protocols that I'm going to add and I'll have lots of questions so I apologize in advance for that but on behalf of the listeners and just directly from me thank you so much for your time I learned a ton my pleasure thanks for having on it was really awesome conversation so I enjoyed it a lot let's do it again totally great thank you for joining me for my discussion with dr. Rhonda Patrick I hope you founded as interesting and as actionable as I did once again if you'd like to learn more about dr. 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