

## **Huberman Lab #11 - How Foods and Nutrients Control Our Moods**

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## Introduction

Welcome to the Huberman Lab podcast where we discuss science and science-based tools for everyday life. My name is Andrew Huberman, and I'm a professor of neurobiology and ophthalmology at Stanford School of Medicine. 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. In keeping with that theme, I'd like to thank the sponsors of today's podcast.

Our first sponsor today is Theragun. Theragun is a handheld percussive therapy device that releases deep-muscle tension. I was first introduced to Theragun in 2017 while on a laboratory expedition. We were in the middle of the Pacific Ocean filming great white sharks for my laboratory studies on fear using virtual reality. We were working very hard around the clock and I - and other people on the trip - were picking up a lot of aches and pains and - just kind of - chronic soreness. A couple of bad injuries that were flaring up because of all the hard work and lack of sleep. Someone had a Theragun and pretty soon it was getting passed around and became the most coveted device on board. Everyone was using it to work on these different sites of soreness. And I really fell in love with the thing. So much so that when I got back, I immediately purchased one and I've used it almost daily ever since. I use it on muscles that are sore. I use it on areas that I'm really working on to release tension, and improve tissue quality, and so forth. The great thing about Theragun is it's really quiet. So, you can use it while you're in a conversation or while you're watching a movie - and it doesn't disrupt those activities at all. If you want to try Theragun, you can try Theragun by going to [theragun.com/huberman](https://theragun.com/huberman) to get your Gen 4 Theragun. They start at \$199. But if you think about it, a massage - which is an hour long or 90 minutes long - is typically in that range of cost. And this is something you can use every day whenever you want and even while enjoying other activities. So, that's [theragun.com/huberman](https://theragun.com/huberman).

The second sponsor of today's podcast is InsideTracker. InsideTracker is a personalized nutrition platform that analyzes data from your blood and DNA to help you better understand your body and help you reach your health goals. The great thing about InsideTracker is that it gives you data that you can make sense of. I've long been a believer in getting blood samples taken. And more recently, I've become a believer in getting DNA samples taken in order to understand what's going on at the level of hormones, metabolic factors, and other things that profoundly influence our immediate and long-term health. The problem always has been getting those samples taken and making sense of those samples. InsideTracker makes all of that really easy. They'll even come to your home to take the samples. Then you get the information back and while typically after getting information back, there's these long lists of numbers and nobody knows what to do with them. InsideTracker makes it really easy to interpret what those numbers mean. And it points to things - in terms of lifestyle, exercise, nutrition, and so forth - that can help you adjust some of the numbers that you might need to bring down or up - to put into the appropriate normal range. I find this whole process to be immensely valuable for guiding my health choices and also just for giving me peace of mind about how my body and the rest of my health are doing internally - something you just can't know without a blood and DNA test. If you want to try InsideTracker you can go to [insidetracker.com/huberman](https://insidetracker.com/huberman) and you'll get 25% off any of their programs. You want to put "huberman" at checkout. So, that's

[insidetracker.com/huberman](https://insidetracker.com/huberman) to get 25% off any of InsideTracker's plans and put "huberman" at checkout.

The third sponsor of today's podcast is Athletic Greens. Athletic Greens is an all-in-one vitamin mineral probiotic drink. I started using Athletic Greens in 2012 so I'm delighted that they're a sponsor of the podcast. The reason I started using Athletic Greens and the reason I still take it once or twice per day is that I find it very hard to know what vitamins and minerals I need to take. And by drinking Athletic Greens I get it all in one easy-to-consume great-tasting formula. I really do like the way it tastes. I mix mine with water and a little bit of lemon or lime juice - and to me, it's delicious. The other thing about Athletic Greens that I really like are the probiotics. There's so much data out there now telling us - and I certainly believe based on the data that I've seen - that probiotics are really important for support of the gut microbiome, the gut-brain axis, the immune system, and many other aspects of our biology. So, with Athletic Greens I get the vitamins, the minerals, and the probiotics that I need. If you want to try Athletic Greens you can go to [athleticgreens.com/huberman](https://athleticgreens.com/huberman). And if you do that, they'll also give you a year's supply of vitamin D3K2. Vitamin D3, we also know, is really important for things like immune system and metabolic support. So, that's at [athleticgreens.com/huberman](https://athleticgreens.com/huberman) to get Athletic Greens, the year's supply of vitamin D3K2, and they'll give you five free travel packs.

Today we're talking all about emotions. Now, emotions are central to our entire experience of life. Whether or not we're happy, or sad, or depressed, or angry - is our life experience. And yet, I think with all the importance that we've placed on emotions, very few people actually understand how emotions arise in our brain and body. And I mentioned brain and body because as you'll see today, emotions really capture the brain-body relationship. We cannot say that emotions arise just from what happens in our head. It also involves events - biological events - chemical events - within our body. The other thing about emotions is that there's no real agreement as to what's a good emotion or a bad emotion.

Today we're going to talk about the biology of the chemicals and pathways that give rise to emotions. And I'm going to equip you with several - if not many - tools that will allow you to regulate, and change, and steer your emotions should you want. But not using the typical advice. You know, everyone's probably heard of this thing, "Oh, you know - if you're feeling depressed, just smile. You know, it's impossible to be depressed while smiling." Look, if that were true, we wouldn't have any depressed people because depressed people don't want to be depressed. And it is not the case that simply smiling will reverse depression or sadness. And it's simply not the case that smiling can inhibit sadness. It just doesn't work that way. However, it is the case that certain things that are happening in our body influence how our brain functions and the chemicals that are released. And today, we're going to talk a lot about how the brain and body interact to create these things called emotions in the context of food and nutrition. And the reason we're doing that is not because I'm beating the drum about particular diet regimens or anything. In fact, I'm not going to do any of that. What I'm going to do is I'm going to review some of the most important scientific data that point to how ingesting certain nutrients - both macronutrients like proteins, fats and

carbohydrates - as well as micronutrients - can impact the chemicals in our brain that give rise to the feelings of being happy, or sad, or sleepy, or alert when you want to be sleepy, or sleepy when you want to be alert. So, this is sure to be a broad discussion. And yet, we're going to get very specific about what emotions are, how they arise in the body, tools that one can use in order to better control their emotions, tools that people can use to - believe it or not - feel happier or feel calmer. And that's because in the last 20 years or so, there's been an explosion of scientific studies exploring how the brain and body interact to support certain neurochemicals that give us these feelings of being alert and happy, or depressed, or certain that our life is going to be terrible, or certain that our life is going to be great. So, as mysterious as all that might sound - and confusing as all that might sound, we're going to make it very clear today and you're going to come away from this conversation with a lot of tools that you can act on immediately. And those tools are grounded in scientific data. We are going to provide links to several of the studies and I'm going to mention some - several of those studies as we go along. But overall, the goal today is for you to understand how moods and emotions arise, and the different pathways in your brain and body that allow them to happen, and how you can use those pathways to change those emotions, and the tools that you can rely on - in very specific ways - to shift from being - say, slightly depressed - to feeling happier. There actually are ways to do that - or from feeling too alert and anxious to feeling calmer. And these are tools that are distinct from the tools I've talked about in previous episodes.

### **Aversion / Attraction**

The discussion around emotions has a long and rich history going back to Darwin and even long before Darwin. This is a conversation that philosophers and scientists have been having for hundreds, if not thousands of years. You know, the - the idea that Darwin put forth and that was really attractive for about the last hundred years was that emotions are universal and that some of the facial expressions around emotion are universal. And other people have - you know - capitalized on that idea. And to some extent it's true. I mean - I think that the two most robust examples of that would be when we see something, or we smell something, or we taste something that we like, there does tend to be a postural leaning in. We tend to inhale air at that time. We tend to bring in more of whatever chemical substance is there. So, we tend to do these mmm's and kind of lean in closer to things that are attractive to us. And when we see and experience things that we don't like - sometimes it's a mild aversion - we just kind of lean back or look away. Other times, it's an intense aversion of disgust and we tend to cringe our face. We tend to avoid inhaling any of the chemicals. This probably has roots in ancient biological mechanisms that are to prevent us from ingesting things that are bad for us - chemical compounds and taste that might be poisonous. So, much of the foundation of any discussion about emotion has to center around this kind of push-pull of attraction to things or aversion from things. Now that's a very basic way of thinking about emotions. But if you think about it, it works for a lot of different circumstances. And in the brain - everywhere from the deep circuits of the brain to the more kind of what we call higher-order, evolved centers of the brain - we have this push-pull thing. We're either - in a previous episode I talked about "go" - the circuits that allow you to emphasize action. And then, "no go" circuits - the circuits in the basal ganglia that allow you to de-emphasize action and prevent action. We talked about how that's a push-pull. So, aversion and attraction is a push-pull too. Delight, or happiness, or

excitement are attractions to certain things and ideas, songs, people, places, foods. Aversion is a leaning out. It's a disgust. It's an avoidance. And so, we can break down the discussion about emotions into these simpler versions of themselves. But at the core of that - of attraction or aversion - is an important theme - that you might realize already, but most people tend to overlook - which is that there's an action there. You're either moving forward or you're moving away from something. And anytime you're talking about action in the nervous system, you're talking about motor behaviors. You're talking about literally the contraction of muscles to move you toward or away from things. And anytime you're talking about nerve-to-muscle and action, you're talking about the brain and the body. Because the brain can't move itself. The brain has a body so that the organism can move. And the body has a brain so that the organism - you - can move toward or away from things that you deem to be good or bad for you. Now some of these things that we're attracted to and some of them that we avoid are what we call innate or hardwired. You know, when we taste bitter compounds - I'm not saying about bitter like a little bit of bitters in your drink or something like that - but really bitter compounds, we tend to avoid those because they're associated with poisons. When we taste things that are sweet or that are savory, we tend to lean - pursue more of those. We tend to lean toward those, so to speak. And we tend to not avoid them. So, there are circuits in the brain for a version and for attraction toward things and the body is governing a lot of that.

### **Vagus Nerve**

And so immediately in this conversation, I want to raise an important point - which is about a nerve pathway that many, many people have heard of - that gets discussed all the time and that is one of the most - kind of - oversold for the wrong reasons - and undersold, unfortunately, for its real power - which is the vagus nerve. So, the vagus nerve is one - not the only - but one way in which our brain and body are connected and regulates our emotional states. Now many of you have probably heard about polyvagal theory. I'm going to talk about this today. Polyvagal theory was popularized by Stephen Porges. And it's an interesting theory. Certain aspects of it, frankly, hold up to the science. Some of it doesn't. And I'm going to discuss all of that today. A lot of the vagus and the excitement about the vagus - V-A-G-U-S - is because it somehow got into the mind of the public that the vagus is involved in calming us down. So, what is the vagus nerve? Okay, we're going to make this really simple. In particular for those that are just listening, you can just imagine this. For those of you that are watching, I'll point to the various areas. But basically, vagus is the 10th cranial nerve - which basically means that the neurons - the - kind of - the - the control center of each of those neurons in the vagus lives just kind of near the neck, right? And a branch of the vagus goes into the brain. They send a little wire into the brain. The other branch goes into the periphery - but not just the gut. It goes into the stomach, the intestines, the heart, the lungs, and the immune system. So, the - this vagus nerve is incredible because it's taking information from the body and it has two directions. The first is what we call sensory. So, it's sensing things that are happening in the gut, in the lungs. Everything - for example, in the lungs when our lungs are distended, the vagus nerve senses that and sends that information up into the brain. It also can sense things in the gut - like how distended or empty your stomach happens to be. It can sense heart rate. It can sense your immune system - whether or not you have bacteria or things invading you in your body. So, it sends that information

up to the brain. So, it's a two-way street and sensory information is going up to the brain. That's all vagus. So, it's like a superhighway. Sensory information going one way and in the other direction, is motor control. So, the vagus is not just for sensing things, it's actually for controlling things. It's got a sensory pathway and a motor pathway. So, that's the first thing I think everyone should know about the vagus. In fact, it's so important that I feel like this is as important as people knowing that walking involves flexors and extensors. And if you don't think that's important - it's as important as walking, frankly - because the vagus is the way in which you can govern the brain-body connection and in which you can steer various aspects of your mood and well-being. But most people just don't understand how to use it. So first you got to understand what it is. So, you've got sensory information coming from all these different organs of the body up to the brain. You've got motor information going from the brain back to the body. And so you've got this superhighway within you.

Now what actually regulates the vagus? Oftentimes, you'll hear things like, "Oh, you know, this particular behavior - you know, rubbing your face at a particular location - or breathing in a particular way - or, you know, a warm bath or something - stimulates the vagus." Well, right now, I want everyone to know that quote-unquote "stimulating the vagus", broadly speaking, is a terrible way to think about the vagus. Because - did you know what? If you have a contaminant inside your body, the vagus senses that and projects that information to your brain and you start to generate a fever. You start to try and kill that contaminant in your body. So, I don't know that you want to stimulate the vagus - just as a general theme. Today we're going to get specific about how you can activate particular circuits certain pathways from certain organs to the brain in order to feel better or relieve certain conditions. But you certainly don't want to just stimulate the vagus.

### **Polyvagal Theory**

Now, excitement about the vagus, in part, is because of what quite honestly was a fairly pioneering theory about the vagus - which is this polyvagal theory. So polyvagal - the word "poly" means "many" - is cool because it acknowledges that the vagus has a lot of different branches. It's not just one thing. And so, I really like that. I like the naming "polyvagal". The idea that Porges put forward was that there's a dorsal vagus - which is kind of on - runs the back of the spinal cord - which is involved in alertness, and activation, and kind of fight-or-flight type stuff. And that there's a ventral pathway and that that's involved in more - kind of - empathic behaviors. That is not quite in agreement with the modern anatomy, but he was doing the best with what he had at the time. So, okay. The problem I have with the polyvagal theory is the way that it's discussed. People often say, "Oh, you know, if your dorsal vagus is too active, then you tend to be someone who's a little too keyed-up. And people who are - kind of - in a state of freeze or - kind of - flaccid and - kind of - you know - like just not really active and they're just lethargic. Well, then that pathway is hypoactive. It should be more active." So, there are a lot of theories about how psychology maps onto the vagus that - as far as I know - don't map to any real physiology. Now, the other problem with this - kind of - the way that the polyvagal theory is discussed - probably not by the real experts, but by a lot of people - is that people start to diagnose different psychological and physical manifestations through the vagus. They would say things like, "Oh, you know, this person is hyperflexible at the joints and therefore, their dorsal vagus isn't active enough" - or something like that. And it's really - kind of - gone way

outside the lane lines. So today, we're going to clean up a lot of that. Let's make it really simple about how the vagus actually works - at least as we understand it today in 2021.

First of all, as I mentioned, you have sensory information. The same way that you detect light with your eyes or you hear sounds with your ears, you have sensors in your gut that sense how full or empty your gut is. It can also sense how acidic your gut is. It can sense various things within your gut. Your heart is doing the same. It's informing the brain how fast your heart is beating, how full your lungs are has been communicated, and then the status of your immune system. So, the way to think about the vagus is the same way I would think about the eyes. The eyes are looking at colors, they're looking at motion, they're looking how bright it is, and each one of those things - those features - is telling the brain something different so the brain can decide when to be awake or asleep - whether or not it's looking at somebody attractive or unattractive. The vagus nerve is also analyzing many features within the body and informing the brain of how to feel about that and what to do.

## **Sugar**

So, a really good example that I think is an exciting one is as it relates to sugar. So, we all know that sweet things generally taste good. I'm not particularly a fan of very sweet things. You know, I'd much rather have cheese, or pizza, or hamburger, or steak. I like savory fatty foods, but I do like sweet foods. And most people find sweet foods to be attractive. They want them. They might - or they might not be able to regulate their behavior around them, but they want them. And what's really interesting is that for hundreds of years people have thought that that's because of the way that sweet tooth - foods taste. So, that makes sense, right? You eat something that taste sweet. You want more of it. Well, it turns out that it's much more interesting than that. When you eat something sweet, within your stomach, you have cells - neurons - that sense the presence of sugary foods - independent of their taste - and signal to the brain. So, those sensors - those neurons - send information up the vagus to your brain - goes through a series of stations. And then, you release dopamine - this molecule that makes you want more of whatever it is that you just ingested. In fact, this pathway is so powerful that they've done experiments where they completely numb all the taste and feeling in somebody's mouth. They're blindfolded so they don't know what they're eating. And they're eating a food that's either sugary or not sugary. And what they find is that even though people can't taste the sugary food, they crave more of the food that contains sugar because of the sensors in the gut that sense sugar. So to put this differently, you actually have sensors within your body that make you crave sugar - independent of the sweet taste of those things. Now, that's incredible. And what it does and what it tells us is that we have circuits in our body that are driving us towards certain behaviors and making us feel good even though we can't perceive them. Now for those of you that are really interested in gut intuition and - kind of - gut feelings, this is a gut feeling - except this is a chemical gut feeling. This is a particular set of neurons detecting that something in your body has a particular feature - in this case, the presence of sugars - and sending information to the brain essentially to control your behavior. And I find this remarkable because what it means is that what we call attractive isn't always coming from our thoughts about that, or our feelings, or even our perception. We are drawn to particular foods and we're drawn to - perhaps also to particular people, places, and other things - because of

information that's coming from our body. And we're going to talk about one - what one can do with this information. I know many people are thoughtful or concerned about sugars these days - thinking, "You know, we all ingest too much sugar. There's sugar snuck into all the things we eat." And indeed that's true. This should completely reframe the way that we think about the - sort of - so-called hidden sugars in foods. What this means is that even if a food is very savory - like a piece of pizza, or a piece of bread, or even like a salad dressing - if there's sugar snuck into that and you can't taste it, you will still crave more of that thing without knowing that you crave it because it has sugar. In other words, you might find yourself wanting certain foods and not knowing why you want those foods. So, I find this to be a fascinating aspect of our biology. And yes, it relates to mood and emotion. And we'll talk about how that is in a moment.

### **Locus Coeruleus & Lateral Hypothalamus**

So, let's just back up a bit and ask the question: Why do we eat certain things? And why do certain foods make us feel good and other foods actually make us feel anxious? I think some people may be familiar with this - other people might not - but most people don't realize that as you approach eating, there's an anxiety associated with that. It's an alertness. Remember in the previous discussions - or even if you don't and you haven't seen those - all of your moods and feelings of well-being are anchored on this continuum of alertness versus calmness. And we hear so often about "rest and digest" - that - you know that, "Oh, after we eat, we feel really nice and full." Hopefully comfortably full and not too full. And we're relaxing and we feel satiated. It's associated with serotonin - this molecule of satiation. That's all true. But what most people don't know is that there's an area of the hypothalamus - so, deep in the brain - kind of - in the middle, deep portion of the brain - called the lateral hypothalamus. And the lateral hypothalamus is really interesting because it controls feeding, but it inhibits feeding. It stops us from feeding. And there's another area in the brain - if you want names, I'll give them to you - if you don't want names, just ignore them - delete them from your memory and awareness - called the locus coeruleus. Now, the locus coeruleus sits back further in the brainstem and it releases norepinephrine - which is essentially adrenaline. It makes us feel alert. Now, locus coeruleus has a lot of different functions in the brain, but when we are going to eat - let's say we walk into a restaurant, we sit down, or we're preparing a meal - locus coeruleus is known to release noradrenaline in the brain. It's creating a - kind of - alertness. This has ancient utility, but it's creating this alertness. And for many people, they experience that - as they approach food - as stress - as anxiety. But what's interesting is that as we approach food, locus coeruleus is releasing all these molecules that make us feel more anxious and alert. Sometimes, it's felt as excitement - and that has probably to do with how we feel about food generally. Are we happy with our relationship to food? Are we trying to restrict our relationship to food? Are people coming over for dinner? All that will play in, of course. But there's a certain stress and anxiety on approach to food. And as we approach food - and we feel that anxiety - locus coeruleus activates the lateral hypothalamus in a way that inhibits feeding - that makes us not want to eat. So, a lot of people who have kind of pre-meal anxiety - or anxiety around food - and they can't seem to just calm down and have a good meal - to access that later "rest and digest" - a lot of that is because of this heightened stress upon approach to food.



And a lot of the tools that are out there - both for eating disorders and for just kind of the general public who isn't suffering from eating disorders - things like mindfulness around meals - you know - they always tell you - you know, "You should never eat when stressed." I'm sorry, but my life is not organized in a way that I can't do that. I would never eat, right? Because I eat when I'm awake and I'm - I don't know if I'm stressed, but I - I don't think I am - but I tend to run around a lot during the day. I don't generally take time to do two or three deep breaths before I eat. I generally will just keep - will eat. That can be healthy or unhealthy - depending on the quality of your - of your digestion. And I think using digestion as a guide is good. But a lot of people aren't aware that the - this interaction between locus coeruleus and lateral hypothalamus is a basic mechanism where we are supposed to get a little bit alert and anxious around mealtime. And then as we eat, the mechanisms for calming and satiation are supposed to kick in. And those mechanisms involve - as I mentioned earlier - two things.

### **Mechanism - Nutrient Sensing**

One is how things taste. Digestion starts in the mouth, of course. We taste our food. Everyone tells us we should chew our food more. Yes, that can improve digestion. We're not supposed to drink too many fluids as we eat. That's true too. But a lot of how we feel while we eat - and after we eat - is because of this vagus sensing of what's in our gut. It's sending information all the time. Is there sugar? Are there fats? Are there contaminants? There are a lot of information - these so-called parallel pathways that are going up into our brain - that regulate whether or not we want to eat more of something or not. And there are accelerators - things that make us want to eat more - like sugar and fats - because those are nutrient-dense and they help, generally - or at least in the short term, support the survival of animals.

### **Mechanism - Amino Acid Sensing**

But also amino acids. And this is very important. There are a lot of data, but much of what comes from the data on what people eat and how much they eat is from a subconscious detection of how many amino acids and what the array - meaning the constellation of amino acids - is in a given food. And it's fair to say that the sum total of these studies point in a direction where people will basically eat - not until their stomach is full - but until the brain perceives that they have adequate intake of amino acids. Now, this is a conversation that comes up in the context of the meat-only, the keto, the - kind of - zone diet, the Mediterranean diet, the vegan diet. I'm largely going to ignore the - kind of - strict camps today. I will talk a little bit about it, because I think each one of them actually taps into something important about this brain-body relationship that the other ones don't. But I don't want to get into a discussion about the ethics of different foods of animal-based or non-animal-based, because that's not the topic today. It's really about nutrient sensing and amino acid sensing. So, we generally will eat until our gut tells our brain that we have adequate amounts of these amino acids. Amino acids, of course, are important because they are the building blocks of - sure, muscle and the other things in our body that need repair - but what most people don't realize is that amino acids are what the neurochemicals in the brain are made from. Now, this is vitally important, okay?

## **Dopamine & Reward Prediction Error**

So, we've heard dopamine is this molecule that makes you feel good. Actually, dopamine is a molecule that makes you feel good. It's released within the brain and it does feel very good when you have dopamine release. Dopamine release is caused by surprise, excitement, events that you're looking forward to and that turn out well. It is inhibited by events you're looking forward to that don't work out - when someone says they're going to call that you're really, really excited to talk to and then, they don't - or you thought a movie was going to be really great and it's not - or you expect a meal to be really delicious and it's - kind of - meh. And we actually - there's a name for that. It's called reward prediction error. So - and you can actually use this in the context of meals and plans in a way that's very useful with yourself and people you know. Essentially, if you expect something to be really terrific, it really does place a higher expectation at the chemical level. So, if you don't get as much dopamine as you're expecting from something - so you - you hear about a really great restaurant or a place that has a really - in my case, I wouldn't call it an addiction - I would call it more of an affliction for croissants. The best vegetable, of course, is the croissant. And I get really excited about the fact that - someone will tell me, "Oh, there's this place and they have incredible croissants. You got to go there." So, I get really excited and I'll go and just them telling me that it's going to be really terrific, raises an expectation - a dopamine expectation. And unless those croissants are amazing, chances are I'm going to experience them as less good - less satisfying. I will truly release less dopamine than I would had they just said, "Oh, yeah. I think that there are croissants down the street" - or if I just tried one at random. And that's because of this reward prediction error. Your expectation of something releases dopamine and the actual event releases dopamine. And if the event-related dopamine does not exceed the expectation - or at least match it - there's a much higher tendency that you won't pursue that thing again. So, dopamine is really powerful and it's not just the molecule of reward, it is the molecule of desire. It's the molecule of wanting, not just the molecule of having. And a book - since people often ask for book recommendations - I don't know the author personally, but I love the book - it's called "The Molecule of More". It's a terrific book. I wish I had written it, frankly. But if you want to learn more about dopamine, reward prediction error, and how dopamine regulates various aspects of your emotional and motivational life, it's a terrific read. Dopamine is what's going to lead us to want to eat more of something or to not want more of something. Because dopamine really is about craving. It's about motivation and it's about desire. And as I mentioned, these amino acid sensors in our gut are detecting how many amino acids, but they're also detecting which amino acids.

## **L-Tyrosine**

And there's a particular amino acid called L-tyrosine - which comes from food. You can look up online which foods contain L-tyrosine. It is in meats. It is in nuts. It is also in some plant-based foods. L-tyrosine is the precursor to a couple other molecules - like L-dopa, etc. - that make dopamine. And so, there's a misconception out there that most of the serotonin is in our gut and most of the dopamine is in our gut and therefore, our mood is in our gut. That's not quite the way it works, okay? We'll talk about serotonin in a moment, but dopamine is synthesized from the amino acids that you eat. However, the dopamine neurons that give rise to these feelings of good, or wanting more, or desire, and motivation - those reside in the brain. So, we don't want to get too

confused. We want to respect and honor the power of the gut in this vagal pathway, but it's really neurons within your brain that drive the pursuit and decision-making. So, what does this mean? Some people make too little dopamine. Some people make so little dopamine that they need prescription dopamine. They need L-dopa. People with Parkinson's take L-dopa and other compounds to increase dopamine because Parkinson's is associated with deficits in movement. It starts as a tremor. It actually starts as some other things - that are interesting - we'll talk about in a moment. But Parkinson's is a depression. It's a blunting of motivation, and mood, and affect, and it's a tremor. And then eventually in severe conditions, it's challenges in speaking and walking. So, the - some famous examples would be Muhammad Ali, Michael J. Fox - the great boxing trainer, Freddie Roach - like these people have Parkinson's and they - at least later in their life - had challenges speaking. Now, it's not just fighters that develop Parkinson's. As far as I know, Michael J. Fox wasn't - wasn't a fighter. People can develop Parkinson's and Parkinson's is a depletion of dopamine neurons in the brain. And it's not just movement challenges. It's challenges with mood. Now, hopefully most of you - all of you - don't have Parkinson's. But it's clear that dietary L-tyrosine supports the healthy production of things like dopamine and - as well as other factors within the brain. Now, some people immediately ask, "Well, should I supplement L-tyrosine?" Let's just talk about that because that's going to come up. Full disclosure, I sometimes take L-tyrosine. I'm not taking it right now. But I take it only occasionally. You can buy this in capsule form. It does increase - kind of - mood, and elevation, and alertness. It is over-the-counter. You have to check with your doctor. I'm not responsible for your healthcare and I'm not a doctor - whether or not it's safe for you. People with preexisting hyperdopaminergic conditions - like mania - should probably not take L-tyrosine. The other thing about taking L-tyrosine is there is a crash. It's not a massive crash if you take it at appropriate doses and it's right for you, but it can produce a crash in a lethargy and a - kind of - brain fog after the next day or so. And so, L-tyrosine - however - can be ingested through foods or through supplementation to increase dopamine levels. That's well known. Taken chronically, however, it can disrupt those dopamine pathways.

### **Wellbutrin & Other Drugs**

Now, there are other drugs that will increase L-tyrosine and dopamine as well, but those are severe enough that they generally tend to have addictive properties. So, things like methamphetamine - things like cocaine - are terrible because they really ramp up the dopamine system so much that people really can't achieve dopamine release through any other mechanisms. But food and the ingestion of L-tyrosine has a profound effect on our levels of dopamine. It takes a little while, but that really will impact level of mood. Certain antidepressants fall into the category of dopaminergic antidepressants. One of the most famous ones, of course, is Wellbutrin. Wellbutrin was developed because a lot of the other antidepressants tend to make people feel - kind of - lethargic or they had side effect profiles that people didn't like. So, they developed this thing that - the generic name is different, but it's generally called Wellbutrin. Wellbutrin activates dopamine and epinephrine - which is a substrate of dopamine - and both of those are involved in motivation, and alertness, and effort. So, you might say, "Wow, this sounds like a great drug." However, this drug - the side effect profile tends to be the things that are associated with elevated mood and alertness. So, this isn't like taking some L-tyrosine. This isn't like eating some tyrosine-rich foods. This is really a much

greater release of dopamine and epinephrine. And it increases things like anxiety, sweating, the pupils dilate. It has certain effects on - in particular, people with epilepsy. It's been used somewhat successfully for smoking cessation. But again, it's not for everybody and I'm not here to encourage the - the use of these things. I'm just describing the biology and the rationale for why these drugs were developed.

### **Quick Recap**

So, let's back up a second. Let's just kind of take stock of where we're at. We have a brain-body connection. There are many of them, but one of the main ones is the vagus nerve. The vagus collects information about a lot of things - breathing heart rate, stuff that's happening in the gut, etc. And gut by the way, includes the stomach and the intestines - sends that information up to the brain. The brain is using that information to decide one of two things: move towards something or move away. It can also pause, but essentially pausing is not moving toward. So, that's the dopamine pathway. And foods rich in L-tyrosine generally give us an elevated mood and make us want to do more of whatever it is that we happen to be doing - as well as other things. Motivation generalizes to other things. It's not unique to just ingesting foods, but foods that give us a big pulse of dopamine will make us crave more of that food. It will make us crave more of the activity that led to the ingestion of that food. And as I mentioned earlier, a lot of that is happening at a subconscious level that you're not even aware of. And this is why I think the concern about hidden sugars and overingestion of sugars is serious because it's not just that the sugars are impacting our blood glucose in negative ways - although, often it is. It's not just the obesity crisis that's happening. It's also the fact that it's disrupting our dopamine systems. Now that doesn't mean all sugar is bad. Some people have a quite healthy relationship to sugar, but I think most people are just not aware that sugar isn't just operating at the level of taste. It's operating at the level of neurochemicals and it's doing it subconsciously.

### **Serotonin**

So, I'd like to talk about some of the other pathways between brain and body that regulate our moods and emotions, but also are actionable. So, the other neuromodulator that's really interesting in the context of the vagus is serotonin. Serotonin - just to remind you - is a neuromodulator. Therefore, it creates a bias in which neural circuits - which neurons in the brain and body - are going to be active. And it makes it less likely that other ones are going to be active. I think it's fair to say without ever having measured it, that my bulldog Costello, it must - just his brain and body must be swimming in serotonin because he's very calm. And he eats a lot, but he generally feels pretty sated. He's - kind of - an animal that's obsessed with comforts. He's a bit of a hedonist. And serotonin, when it's elevated, tends to make us feel really comfortable and - kind of - blissed out wherever we are. And that contrasts with dopamine and epinephrine - which mainly put us in pursuit of things. Motivation is pursuit. Serotonin is more about feeling really comfy where we are. The conversation around the brain-body relationship, and mood, and serotonin - for many years was, "Well, you eat a big meal. The gut is distended. You've got all the nutrients you need. You rest and digest. And serotonin is released." That's sort of true, but there's a lot more going on. And a lot more that's interesting and actionable that's going on. First of all, some of you - but perhaps not all -

have heard that more than 90% of the serotonin that we make is in our gut. And indeed, we have a lot of serotonin in our gut. We have neurons in our gut that make serotonin. We have neurons in our brain that make serotonin. But here's the deal. Most of the serotonin that impacts our mood and our mental state is not in our gut. Most of it is in the neurons of the brain in an area called the raphe nucleus of the brain. There are a few other locations too. And those are the neurons that control whether or not we feel satiated or not - whether or not we feel happy and calm.

You can't have a discussion about serotonin without having a discussion about antidepressants because during the late '80s and early '90s, there was this explosion in the number of prescription drugs that were released - things like - first one and most famous one is Prozac - Zoloft and a Paxil - a number of other ones that are so-called SSRIs - selective serotonin reuptake inhibitors. That's a long acronym, but basically those drugs work by preventing the gobbling up of serotonin or reuptake of serotonin into neurons after it's been released - which leads to more serotonin overall - which leads to elevated serotonin. And indeed, those drugs were and can be very useful for certain people to feel better in cases of depression and some other clinical disorders as well. So, I really don't want to dismiss them as useless or dangerous for everybody. They can be quite useful for many people. Not everyone responds well to them - as I'm sure you've all heard - and their side effect profile has effects like blunting affect. It can make people feel kind of flat - kind of "meh". It can reduce appetite for food. It can reduce appetite for sex. It can do all sorts of things. Or it can work really well. Sometimes, it's a dose-related issue - etc. Serotonin is fascinating, however, because how well those neurons in the raphe work is impacted by some events within the gut - although, you might be surprised to find out what those events are.

### **Increasing Serotonin - Carbohydrates**

So, let's go a little bit deeper into the gut. And again, the gut includes the stomach and then the small intestine, and the large intestine. And ask: What is going on with serotonin in the gut? How is it impacting serotonin in the brain? And let's think about this in the context of how some of us might want to increase or decrease our serotonin levels. So, as far as I know, there aren't any really good at-home blood tests for things like serotonin and dopamine. There are some commercial products out there. But to me - just to me - I'm not particularly impressed. It's not the same as getting your hormones levels measured or your metabolic factors measured. That's - can be done. It can be done rigorously. There are tests out there. There are even some - believe it or not - there are some questionnaires - you know - that - and I think actually last year, it made some of the bigger newspapers. "Are you more of a dopamine or a serotonin? Are you of this or that?" I find that stuff to be a little silly - although, I do appreciate and like the fact that people are thinking about and talking about neuromodulators. There aren't really great ways to measure these things outside the clinic. There are some great clinical tools that you can get inside of a hospital, or from a proper endocrinologist, or neurologist - but no great at-home tool. So, maybe that's a call to arms - for some of you entrepreneurial folks out there - to create these tests - accurate tests, please - that could be done at home. But you know, some people feel like they're too anxious or they're always in a motivated state and they're trying to adjust their serotonin.

Many people adjust their serotonin by just eating more food and carbohydrate-rich foods will increase serotonin. I've talked about this on a previous podcast, but I personally am a big fan - at least for me - as I usually fast and exercise in the early part of the day - I eat a relatively high-protein and moderate-fat - zero-carb or low-carb meal at lunch and in the afternoon to stay alert because those foods tend to favor dopamine production, acetylcholine production, epinephrine production, and alertness. And my mood is generally pretty good most of the time. And then, as evening comes around and I'm concerned about sleep and a good night's sleep - not concerned in an anxious way - but I want to get a good night's sleep - I will ingest foods that promote serotonin release because they contain a lot of tryptophan. So if I do eat meat, it would be like a white meat turkey meat. I don't tend to - I've never liked turkey. I don't mind the animal, but I don't like ingesting the meat. But starchy carbohydrates will increase serotonin.

### **Increasing Serotonin - 5-HTP**

Some people also will take serotonin. They - you can now buy 5-HTP supplements. This is a little bit tricky. 5-HTP supplements can, of course, increase 5-HTP. It is 5-HTP - or serotonin. But that sometimes can create problems in endogenous - or self-made production of serotonin. So, I'm never a fan of taking things very close to the chemical you're trying to increase for very long periods of time - maybe for occasional use. I have the problem that if I take serotonin supplements - 5-HTP - I fall asleep. The sleep I have is very intense and I wake up three or four hours later. And we know, based on sleep studies with good measurements in the lab, that serotonin release tends to be in the later part of the night. And so, by taking it early in the night, it really can disrupt the pattern of sleep and the depth of sleep. Nonetheless, some people are interested in taking serotonin to get some of the more blissed out effects. You can achieve that with foods, as I mentioned, that are carbohydrate rich.

So as you're seeing, this isn't really a discussion about nutrition per se. This is a discussion about food - which contains amino acids. Amino acids being the precursors to neuromodulators. And neuromodulators - having a profound effect on your overall state of alertness or calmness, happiness, sadness, and well-being. So, there are a number of things that one can take, as I mentioned, one of them being 5-HTP itself. Now, I'm not recommending people take anything, but if you're interested in what this does and you want to explore this - of course, you'd want permission from your doctor - you can go to this free website. I love this resource. They don't pay me to say that. I just love this resource. I've followed it for a long time - called [examine.com](http://examine.com). Thank you folks at [examine.com](http://examine.com) for putting this free resource out on the web that has links - through what they call the human effect matrix. So, it's links to all the PubMed studies for particular effects of particular compounds that one can buy in ingest - incredible - as well as important health warnings. So, I'm not going to read through everything, but if you were to go to [examine.com](http://examine.com), as I have now, and you put in "5-HTP" - they're only looking at things that have strong evidence - PubMed articles - articles that are - are - are in the PubMed archive.

So, for instance, I didn't know this. But 5-HTP produces a notable decrease in appetite - three studies. And this appetite suppression makes sense, of course, because we ingest foods to get

serotonin and if we have enough serotonin, then there's no reason to ingest more foods. It tends to have a blunting of appetite. It probably does that also through other mechanisms. So, I'm not saying you should do this. But if someone's trying to blunter appetite, it could be an interesting route - although, I don't recommend chronic use. Not surprisingly, there's a decrease in body weight, as a consequence. An increasing cortisol - so, that's kind of important to note that when you - typically in biology, if you pull on one string really hard, another one moves. It's a little bit like a puppet and there's more than one string on the puppet. So, it does seem to increase cortisol - though they report as a minor effect. Again, links to all those studies are there - which is why I'm not listing them out in our caption notes. You can go and get them at [examine.com](http://examine.com). Put in "serotonin" and you'll find that.

So, I find it fascinating that - nowadays - there are things that are somewhere between doing nothing - getting serotonin from tryptophan in foods - and prescription drugs. There's this other category of supplements that are really interesting for modulating these chemicals in the body.

### **Mucuna Pruriens**

And I should mention before I move on - because I mentioned L-tyrosine. I neglected to mention earlier in our discussion about dopamine. If you're interested in the dopamine pathway, go to [examine.com](http://examine.com). Put in "mucuna pruriens", it's M-U-C-U-N-A - P - separate word - P-R-U-R-I-E-N-S. It is a velvet bean that grows from vines and is very itchy to touch due to serotonin on its surface - amazing. This bean has serotonin on its surface. And indeed, serotonin - if you were to put it on your skin, would cause some irritation of the skin - amazing. Inside the bean is L-dopa. Mucuna pruriens is not just something that promotes dopamine release because of some weird mystical ancient thing or whatever - or sorcery. It is chemically L-dopa - the precursor to dopamine. It contains some other molecules as well - and low levels of other psychoactives. This stuff is available over-the-counter - incredible. I personally find it incredible. Its effects are really interesting. I'm not going to read them all off, but I mention these effects not because I'm encouraging you to take it, but because you get a window into what dopamine - acute dopamine increase - does in the non-Parkinsonian context.

And you can start to think about foods that are rich in L-tyrosine as biasing certain effects or not others. So, when you hear, "food is medicine" - food isn't really medicine. Food is food, but food has these chemical effects as well. First one listed is three studies with a very high rigor that overall have a minor effect on - of all things - sperm quality. It appears that sperm motility itself - I'm assuming when they say sperm quality - I don't know what features of sperm - of quality they looked at with sperm. That's not a discussion I want to have, but I'm assuming its motility because I know enough about reproductive biology to know that sperm's ability to swim depends on some proteins that are present in the front of the sperm - etc. - things like pentraxins. And sperm motility is generally associated with sperm quality. Sperm that don't move are generally not very useful sperm. Symptoms of Parkinson's disease are notably degraded with mucuna pruriens - fascinating. That's not surprising. There are a lot of other effects here - feelings of subjective well-being, testosterone, reductions in prolactin. Not surprising - prolactin is a hormone that's involved in milk

let-down. It's in - in lactating mothers. It's involved in feelings of peace and generally is antagonistic to sexual desire in both men and female. So, it's really interesting that things like mucuna pruriens - which are L-dopa - reduced prolactin, increased motility, increased testosterone, subjective well-being. So, you're starting to see a theme. Dopamine really makes us motivated, feel in pursuit, makes us feel good. Serotonin makes us feel more relaxed and calm.

Now, this whole month is about emotion. So, you might be thinking, "Wait, where are we going with all this as it relates to emotions?" But in the last episode, I said something. I'm going to repeat it now briefly - which is that much of what we talk about is good emotions or bad emotions, there's a context to that. There's a social context. You can't really say an emotion is good or bad. Grieving at a funeral is healthy. Being happy at a funeral - assuming you loved the person that died - is - most people probably wouldn't think that was healthy. So, we can't really say that certain - you know - emotions like sadness, or happiness, or healthy. Its context is important - cultural context is important. Many of you have asked for book recommendations. This is an opportunity to raise - mention another book. Again, I don't have any financial affiliation or anything, but if you want to read more about emotions and how the context and cultural things impact our emotions, I'm a huge fan of Lisa Feldman Barrett. I learned about her from the Lex Fridman Podcast. I've had discussions with her on my Instagram Live. She's at Northeastern University - a world expert in emotions. Her first book is "How Emotions Are Made". This is not a book she sent me. I paid for this with my own money. Years ago, bought it - read it - loved it - long before I met Lisa. I'm just delighted that we've got to know each other a little bit. It's a really interesting read into the psychology of emotions and some of the subjectivity of emotions. Whereas I'm talking about mainly the biology of emotions, this gets a little bit more into the psychology - although, the biology as well. And Lisa's just terrific. She's also putting a lot of information out into the world about emotions. So, if you want to learn more about that, check out her work. Again, it's Lisa Feldman Barrett. That book is "How Emotions Are Made". Hopefully she'll continue to write many more books.

So, now you understand the relationship - I hope - between foods and dopamine - foods and serotonin - and that they're both being communicated to the brain via the vagus, right? We ingest these foods. These supplements are things people take. They don't put them directly into the brain. They put them in our gut. So yes, there's a gut-brain connection, but it's not about the serotonin in the gut that makes you feel calm and placid. It's not about the dopamine in the gut. It's just been oversold that way because I think there's something really attractive - and I understand - about the idea that because certain things about our experience of life and our emotions is happening in our body, that maybe we have a little more control, right? Because this thing is a hard container. We can't just stuff some dopamine in there. I can't just - you know - I could probably take a mucuna pruriens bean and stuff it in my ear. Please don't do that. It'd make my ear itchy because of the serotonin on the outside. But you can't get stuff in there. What you have to do is ingest things that are metabolized in certain ways that communicate to the brain - or - so, maybe they pass into the brain themselves across what's called the blood-brain barrier. I'll talk about the blood-brain barrier in a minute. It's actually called the BBB. So, it ends up sounding like "baby" - BBB. I guess that's like "BB" - anyway, BBB. But there are also nerves in the gut that are sensing the nutrient contents of



food and then saying, "Oh, you should feel better and want more. Oh, that's got a lot of bitterness and acid taste to it. You should want less of that." Okay?

So, as I transition out of the discussion about dopamine, and serotonin, and the gut - hopefully, you've got some actionable items there under your belt - pun intended - where you can understand how certain foods and certain nutrients - and you can look these up - might impact your mood. If you're somebody who's really anxious and really wired - well then, the dopamine/adrenaline pathway - epinephrine pathway - is probably not one that you want to lean on any harder. If you tend to be someone who's pretty passive and you're having trouble with motivation - well then, think about ramping up the dopamine pathway through - I always think behaviors and proper food choices is the best way to start - and behaviors include things like exercise, etc. But one of the problems with the discussion around mood and exercise - or mood and meditation - is that it's so subjective. It's like, "I love certain forms of exercise and not others. Certain ones are aversive to me. Certain ones are attractive to me." And it's never really clear. No one's ever told me, "Okay, you have to do 10 minutes on the bike at X number of RPM at so-and-so or on the skier in order to get your dopamine up." But we can actually say: If you ingest more L-tyrosine, there's a high probability that you're going to make more dopamine. And I'm talking about ingesting it through food - or through supplementation, if you'd like.

Mucuna pruriens I've tried - I should just mention. It was too dopaminergic for me. I really, really jazzed up and then, severe crash for me the next day. But that's - I think because I tend to ride pretty high on the - kind of - alertness and motivation scale. I'm always being told by Costello and other people in the podcast studio to slow my speech down. This is me uncaffeinated and I could probably afford a little more serotonin in my life. So - whereas Costello, you can afford to - you can afford to wake up every - every couple days and just say hello to us. This dog sleeps more than any other creature. It's remarkable.

So, there are things that we can do and they're actionable and they are - in some ways, they're quantitative - because you can regulate dosages, and you can regulate amounts, and you can regulate timing. And everyone has to play with these things and figure out what's right for them in terms of feeding. And everyone has to explore and understand what's safe and right for them. But - and of course, exercise is still very important. I talked about social connection in the last episode - super important for activation of serotonin. But when it comes to this gut-brain - body-brain relationship - what we eat really matters in terms of the neurochemicals that we make.

### **Tool - 1000 milligrams of EPA**

So, let's talk a little bit more about things that we ingest in our body and then allow our body to inform our brain to shift our mood. And this is something I've - I've been doing for years and I just want to say I've found to be a complete game changer. There's excellent science to support it. And I think most people are familiar with it in a different context, but I don't think most people know this simple fact - which is that the omega-3 to a omega-6 fatty acid ratio has a profound effect on depression. It has a profound effect on mood. So much so that in a double-blind placebo-controlled

study - that I will provide the link to - this was a study first published in 2008, but there have been many others as well - first of all, in an experiment done in animals, they found there's a model of learned helplessness in animals. It's not very kind to the animals, but they put rats or mice in a jar. They let them swim. And they'll swim, swim, swim to try and save their life. And eventually they give up - so learned helplessness. They don't let them drown. They take them out. Adjusting the omega-3 / omega-6 ratio so that the omega-3s are higher led to less learned helplessness - meaning these animals would swim longer, okay? Now that's an animal - that's a rat - not a particularly kind study. But that same study was essentially done in humans - although, they didn't have them swim to the point of near-drowning. What they did is they took people who were clinically depressed - major depression, okay? Major depression is severe maladaptive state - meaning it inhibits job, relationships, appetite - all sorts of negative health effects. And they did a comparison of a 1,000 milligrams a day of EPA - so, EPA is one of the elements with - that contains high levels of omega-3s - that's in things like fish oil. I'll talk about other sources in a little bit. But it wasn't a 1,000 milligrams of fish oil. It was a 1,000 milligrams of EPA - compared that to 20 milligrams of fluoxetine - which is Prozac, okay - really increases serotonin. And in this study of 60 individuals - again, I'll provide the links to the study - they found that they were equally effective in reducing depressive symptoms. So, imagine that. A food-based compound that you can't make without, right? This is not a situation where you can make your own omega-3s. You have to get them from food sources or from supplementation. It was as effective as 20 milligrams of fluoxetine over the course of eight weeks.

And what was really interesting - in addition to that - is that the combination of 1,000 milligrams of EPA and fluoxetine had a synergistic effect in lowering depressive symptoms. I find this remarkable. I heard about this when it first came out. And I wasn't sure what to make of it because there are a lot of studies that come out. And I generally like to focus my changes in behavior around things where there's a large center of mass. There's a lot of information. A couple years later, I did - in fact - start taking 1,000 milligrams per day of EPA - in fish oil. Now, there are a few side effects of fish oil.

People who have blood - who are bleeders - who have factor V Leiden mutations - or in women who are taking birth control, which can make you - which can affect blood clotting and things of that sort - really should talk to your doctor. Make sure it's okay for you. Fish oil also can give people fishy breath - which is pretty gross, frankly. But there are now fish oils that either because of the encapsulations or because of the - they put some lemon flavoring in there - it doesn't have that effect. In any event, 1,000 milligrams per day of EPA - I started ingesting that regularly. I just felt better. I wasn't clinically depressed, but I generally - I did feel, at least for me, an increase in mood, and affect, and a number of other things. It's supposed to reduce inflammation. The cardiovascular effects are controversial. For a long time, everyone thought the effects on platelets were really terrific. Then there were articles that came out in major newspapers saying maybe not so much, but the effects on mood are really profound.

And now, there are lots of studies. If you go into PubMed and you were to put "EPA" or "fish oil and depression", you would find that there were a number of really impressive results showing that it's at least as effective as certain SSRIs - antidepressants - at these dosages. And it can amplify or improve the effect of low dosages of some of these SSRI. So, I feel like more people should know about this. This is nutrition, but it's profoundly affecting mood. And depression is terrible, right? Depression can have a component of anxiety in some cases - where people are - they feel lousy and very uncertain. That's kind of how I talk about depression with anxiety is - you know - you talk to someone who's anxious and you can tell them, "Everything's going to be okay, okay?" And they're always concerned about what they might - they might not know. You don't really know the plane isn't going to crash. You don't really know that life is going to go okay. And in some sense, they're right. No one has a crystal ball or can predict the future. But they tend to perseverate or fixate on the uncertainty. And then of course, there are the versions of depression that involve certainty. People are lethargic and they're certain. They say, "Yeah, I'm certain I'm never going to get another job. I'm certain I'm never going to meet anyone new. I'm certain I'm going to fail." So, there's this kind of divide in the sphere of depression around certainty and uncertainty. But what's interesting is this 1,000 milligrams per day or more of EPA has been shown to relieve both forms of depression. Now, does that mean it's going to work for everybody? No. I'm not here to try and play psychiatrist. I want to point you in the direction of these manuscripts so that you can make informed choices for yourself. You can discuss it with your doctor and family and make the choices that are right for you. But here's what's especially interesting about the heart effects because we've heard that these omega-3s - which, of course, you can get from other sources too. You can get from fatty fish. There are flax seeds - hemp seeds. There are a number of - chia seeds - these kinds of things. But the levels of EPA that are required are quite high. So, this 1,000 milligrams per day. That's - that's pretty hard to get from food - although, it can be done depending on what you're eating.

### **Heart Rate Variability**

What's interesting is that the heart effects that are solid - that really stand up in the literature - have a lot more to do with something we talked about in a previous episode and I'll mention again - which is heart rate variability. So, we know that having a heart rate that's really high or a heart rate that's really low - neither of those are good. A lot of people think, "Oh, you just want a low heart rate - big stroke volume. You know, if you're running a lot, you may have 30 or 40 beats per minute." That's great - to be in shape - but you still want heart rate variability. It has a lot to do with the tone of the autonomic nervous system. I talked about last time - how when you inhale, it speeds up heart rate - when you exhale, it decreases heart rate. That's called respiratory sinus arrhythmia. It's the basis of heart rate variability. We'll maybe do a short post about this so you don't have, you can get all the mechanism and the behaviors that spill out of that - that might be useful for you. But the point is heart rate variability (HRV) is good.

And what's interesting is that there was a study in 2009 that showed that people who eat a diet where they're - and fail to supplement in a way that there's a high omega-6 to 3 ratio - so, not enough omega-3s. Not only are there markers of inflammatory cytokines elevated - things like IL6 and TNF- $\alpha$  - but they tend to be non-responders to antidepressants. Shifting that omega-3 /

omega-6 ratio did a couple things. First of all, increasing the amount of EPA shifted the ratio - so, it was higher omega-3 to omega-6 ratio - which was good - lowered the inflammation markers and then allowed antidepressants to have their effect even at low doses. And here's the really interesting thing. It worked by increasing heart rate variability. And I thought - you think, "Well, how in the world would this happen?" But, you know - how - I mean - that's a ton of effects. But the way it works is because of the way that these things are impacting the gut and the autonomic nervous system. Remember, earlier I said the vagus includes connections from the heart - signaling about sensory information about how fast the heart is beating to the brain - not just stuff in the lungs, but information from the heart - and the brain then adjusts heart rate by heart rate variability. So, it's incredible that there's a way that one can use the gut - the ingestion of more of these EPAs - either through food or supplementation - to increase heart rate variability and thereby to improve symptoms - meaning reduced symptoms of depression - and to even make low levels of antidepressants that wouldn't otherwise work, work. And I think I like this study so much because (a) it's super cool. It bridges the brain-body axis. It incorporates nutrition and micronutrients in the brain, but also because it really points to something that we hear all the time - which is that, "Our body is a whole system. It's working as a whole system." The brain isn't working in isolation up there in the - in the skull. It's reacting to things that are happening in the body, in the gut, and in the heart rate and heart rate variability - and that the things we ingest can have a profound effect on them. Now, of course, I really want to emphasize something which is that no one compound, or nutrient, or supplement, or drug, or behavior for that matter is going to be the be-all end-all of shifting out of depression, or improving one's mood, or improving sleep. It's a constellation of things. And this is especially true when people start to get excited about supplements and drugs of all kinds and their potential for various things. Right now, there's a lot of excitement about psychedelics and their therapeutic uses. And I think, "Great." But as a good friend of mine - who's a physician/clinician - says, "Better living through chemistry still requires better living." You cannot expect to take a compound - regardless of source or potency - and have it completely shift your experience of life without having to continue to engage in the proper behaviors - all the things we know: proper sleep, exercise, social connection, food, etc. There are many others as well. So, I still find that this collection of studies about omega-3 to omega-6 ratios to be profoundly important - so much so that it's completely changed the way that I think about food - the foods I eat. I do supplement. I don't necessarily think that's for everybody, but I really think it's incredible that there are these compounds that have these robust effects on our feelings of well-being - and there are others too.

### **Alternative Sources of Omega-3**

So, that 1,000 milligram per day threshold of fish oil that's beneficial requires that one take a - you know - reasonable amount of these things - either through food or through supplementation. I acknowledge that not everyone wants to take fish oil. There are a couple reasons why one might want to avoid that. One would be for ethical reasons. You have a - an emotional relationship or a relationship to the environment that makes you not want to ingest fish-related products. There's krill oil. Krill is still an organism. It's a little tiny thing that whales eat a lot of and people generally eat very little of. So, krill is out there. I personally - just me - I don't know why - I didn't react well to - to krill. It didn't make me feel very good. I had some like - kind of - skin itches and things like that - and

they stopped when I stopped taking it, but I don't want to bias you against it, if that's your preference. Some people really like krill oil as a source of omega-3s. I did mention some of the other sources like chia seeds and flax seeds. But as you'll notice, these are not things that we tend to ingest a lot of on a regular basis. It is possible to get omega-3s from meats if the animals have grazed on grasses that contain a lot of omega-3s. So, for those of you that ingest meat - you know - the source of those meats is going to be very important as it relates to omega-3s. Even within the category of fish oil, there's a concern sometimes about mercury and other contaminants. You want to go with a brand that emphasizes that they've gone to really good sources and that they decontaminate regardless - and so you have to search out those brands.

There is a test that you can do as to whether or not the fish oil is rancid or not. Some people take it in liquid form. Some people take it in capsule form. The liquid form is going to be more affordable. The capsule form is more - is a little easier and a little more portable. You can actually just chew one of the gel tablets and if it tastes really fishy and kind of rancid, you'll know. It's disgusting. You'll want to spit it out. And if it doesn't and it's tolerable, then you'll know that - that it's okay. Unfortunately, you have to buy it first in order to do that - although, I don't know - maybe you can get them to open up the bottle for you in the store and tell them that - you know - want to try it. Someday, perhaps, fish oil and omega-3s - it'll be like tasting wine at a restaurant - where you can send it back. For now, I think you have to purchase it first, but find - find a brand you trust and like and then work with then - if you decide to go that route, of course.

## **L-Carnitine**

There are other compounds that are also interesting for mood elevation that are essentially like foods or are supplement-based. That now, fortunately, there are really good data from peer-reviewed studies. And the next one I want to mention because I think it's really interesting is L-carnitine. Now, L-carnitine has been around a long time and it's been discussed in the context of heart health and a number of other things. It was actually being touted as a bit of a weight-loss agent in the early '90s. But L-carnitine actually has some really impressive effects on depression. And again, we will look to PubMed - because looking at examine.com is essentially - for me, anyway - looking at PubMed. What is L-carnitine? L-carnitine is most prevalent in meat and in beef in particular. Now, for the vegans, please know that L-carnitine is available through non-meat sources as well - although, it's not as enriched in non-meat sources. It's a really interesting molecule because acetyl-L-carnitine is essentially what's made from L-carnitine, but it's acetylated. If you're interested in the biochemistry, you can look that up. It's acetylated into a form that can cross the blood-brain barrier. The blood-brain barrier - or BBB - is a barrier. It's a wall around the brain and you have this barrier because the brain is so important and it has this feature that the neurons there don't recreate themselves after injury - like other organs of the body. There's not a lot of turnover of cells - despite what you might have heard. And so, nature has created this BBB - this blood-brain barrier - to make sure that certain molecules - in particular, large molecules, don't get across the blood-brain barrier because it can be damaging to those tissues. Incidentally, you also have a very rigid or stringent barrier around other organs - which are the gonads. So, the ovaries, and the testes, and the brain are the organs of the body that the - that nature has gone out of its

way to protect - give this additional layer of the blood-brain barrier or - as you might imagine - for the testes and the ovaries, it's going to be the blood-gonadal barrier. These barriers exist and make it such that just because you eat something - just because you ingest it - doesn't mean it's going to cross the blood-brain barrier. But L-carnitine, when taken, is acetylated and converted into this form that gets across the blood-brain barrier and it has a lot of effects. It's involved in mitochondrial activation of long-chain fatty acids - which - that's a big mouthful that we can get into sometime when we're talking about metabolics. But it has some interesting effects on the neuro-side. So, if you decide to check it out on examine.com, you'll see some really interesting things - lots of effects on ammonia - c-reactive proteins - things of that sort - blood glucose is lowered, etc. That's all stuff that's at the level of blood and periphery - slight effects in lowering cholesterol. Here's some interesting ones. Rates of pregnancy go way up when people are taking L-carnitine - both the father and the mother - both the source of sperm and the source of egg are affected in ways that favor pregnancy. It does increase - here we go again with sperm quality - sperm motility - in males. And it seems to have positive effects on females that have polycystic ovary syndrome. So, check that out. You know, the effects are very strong. There are three studies listed there. Again, I'm not promoting this, but - that - that people take L-carnitine - especially if you're trying to get pregnant. But check it out, because the - the effects there and the studies that are mentioned are published in peer-reviewed rigorous journals. In terms of the - the neural effects, those are quite interesting. The effects on depression are still emerging, but they do seem to exist - that people feel a notable decrease in depressive symptoms. There are seven studies listed on examine.com that has a notable benefit in a variety of circumstances where participants have heightened depression already. They start taking L-carnitine and they start feeling better and they talk about dosages in those various studies. It also has been shown to have a notable decrease in the symptoms of autism - which I find fascinating also. Again, the things we ingest impact the chemicals in our brain and how they impact the rest of our body. There's other things. It's been used to treat certain forms of alcohol dependence. I think this is going to be a very exciting and emerging area.

We're going to do a whole month about addiction. I've got a great guest lined up for that month. But there's now an emerging field about what people can take and supplement to help ease the cravings and the withdrawal when trying to quit drugs of abuse - like cocaine, alcohol, heroin, and smoking - and things of that sort. So, really interesting area. This is - I like to think is the early days and we're going to discover a lot more. There's a huge list of things here. Since we talked about pain in a previous episode - and I know a lot of people have written to me about fibromyalgia - it does - L-carnitine has been shown to reduce symptoms of fibromyalgia. Again, all the links to studies are on examine.com - totally - totally free site.

And that was my bulldog being a battering ram. There's nothing graceful about this bulldog. He's decided he wanted to leave to go get drink of water and so, please forgive the noise. Okay, so now let's turn to another aspect of the gut-brain relationship that will surprise you - in some cases, might shock you - and that has some really cool and actionable biology. And that's the gut microbiome, probiotics, and prebiotics.

## **L-Carnitine & Migraines**

I know today we're talking about emotions and not pain, but I'd be remiss if I didn't mention another effect of acetyl-L-carnitine that's been reported - and that you can find listed with link to study on examine.com - which is its effect in reducing the symptoms of migraine. This was a randomized control trial with 133 participants who had frequent migraines. They were taking 500 milligrams of L-carnitine - or nothing - for 12 weeks. So, the control is a little bit - the control experiment there is a little bit tricky, but it had a significant effect on reducing the number of migraine attacks per month. So, I find that really interesting. And there's a lot more listed there about the study and I think these compounds are powerful. They carry risks for certain people - not for others. So again, you have to find out what's right for you, but I do think they are super interesting as potential therapeutics for various people.

## **Gut Microbiome / Gut-Brain Axis**

So, what's the deal with the gut microbiome and the gut-brain axis? Today, we've actually been talking a lot already about the gut-brain axis. That has nothing to do with microbiomes. We've been talking about this vagus nerve that connects - providing sensory information from the body to the brain and then, the brain also sends - in the same nerve - motor information to control the motility, the gut, the heart rate, how fast we breathe, and deployment of immune stuff - killer cells - and things of that sort. But oftentimes, when we hear about the gut-brain axis these days, it's a discussion about the gut microbiome. And once again, we're in a situation where there's incredible biology. I'm very happy there's so much discussion about the gut microbiome. I am somewhat dismayed and concerned that most of what I hear out there is either false or partially false. So, we're going to clear up some of the misconceptions - first, by understand the biology - and then, we're going to talk about some of the actionable items. It is true that we have a lot of these little micro - microorganisms living in our gut. They're not there because they want to help us. They don't have brains. They are adaptive, however. They try and find and create environments that make it easier for them to proliferate. So, they don't care about you and me, but they are perfectly willing to exploit you and me in order to make more of themselves - the same way viruses are. Viruses don't have a mind. They infect cells. They hijack the genome and they use that genome to make more of themselves. The microbiota that live in us vary along the length of our digestive tract. But let's just take a step back and think about how our body plan is made. We are actually a series of tubes. Our brain is actually a tube. You see it's all squishy on the outside and then, it's got that long thing - the spinal cord - that goes down to the base of the spine. That's the central nervous system. That all started out as a tube. It just looks like a cauliflower on the other end - up in the brain - because the tube is so big and it has to be crammed into the skull so it gets all wrinkled up. But if we were to splay it out, you'd find that it's just one big tube. Similarly, our digestive tract and our airways are essentially one big tube. It starts with our mouth - also our nose - and then, we have all these other tubes that go down through our throat - and then, into our stomach - and then, into our various intestines - and then, the tube ends out the other end. So, we are one long tube for digestion. And inside of that tube is a mucosal lining. It's these little microvilli - tiny, tiny, tiny, little - like velvety ends of cells - that are able to move and move things along and mucus - mucosa. And the conditions of that mucosal lining set a number of different things. It sets the rate of our digestion

and the quality of our digestion. It sets, for instance, our immune system. I - most people probably don't realize this, but most infections in the environment - well, they have to get into our body somehow. Some of them are inhaled. A lot of them go into our mouth and lodge in the mucosal lining of the mouth and then, infections start there. You've probably had the experience, unfortunately, of - you know - of feeling like you have a tick in your throat - like something's irritating your throat - and then, it kind of migrates up into a head cold - or a runny nose. Sometimes it'll start as a headache. Sometimes it won't. But things that are in our - can migrate down into the gut. So, we're ingesting things all the time. Think about it - air - you know, bacteria - viruses - they're making their way into our gut. And some of those bacteria live in the gut. And some of those bacteria bias the mucosal lining in the gut - stomach and intestines - to be more acidic or more basic so that they can make more of themselves - so they can replicate. They like a particular comfort. It's like they like a particular kind of bedding to lie down in and create more of themselves. Now, some of those mucosal linings that they promote make us feel better. They make us feel more alert. They bolster our immune system and others make us feel worse. So, first rule: the microbiome isn't good or bad. Some of these little bugs that live in us do bad things to us. They make us feel worse. They lower our immunity. They affect us in negative ways. Some of them make us feel better. And they do that mainly by changing the conditions of our gut environment. In addition to that, they do impact the neurotransmitters and the neurons that live in the gut and that signal up to the brain to impact things like dopamine and serotonin that we've been talking about previously. So, there's a vast world now devoted to trying to understand what sources of food - what kinds of foods - are good or not good for the gut microbiome.

### **Tool - Probiotics / Fermented Foods**

So, let's just talk about some general rules of thumb related to the research - quality research that's peer reviewed. And then in a future episode, we will go far deeper into the gut microbiome and gut-brain axis. But here's a few things that I think you might find surprising. First of all, supporting a healthy gut microbiome is good for mood, great for digestion, and great for immune system function. However, that does not mean maxing out or taking the most probiotic and prebiotic that you can possibly manage. As I mentioned many times before, I do believe in probiotics. I take probiotics. But there are studies that show that if you take lots and lots of certain probiotics - like lactobacillus - and you really ramp up the levels more, it is not a case of more is better. There are things like brain fog that can come from that. Brain fog is just this inability to focus. People feel really not well, generally. Some of those studies are a little bit controversial, but I think it's fair to say that if people really increase the amount of probiotic that they're taking beyond a certain amount, then they start feeling foggy in the mind. Now, what's too much? Well, I get probiotics from - I've mentioned before - from Athletic Greens. You can get them from fermented foods like sauerkraut, pickles, kimchi, natto. These are different sources from around the world. I - actually, I'd love to hear some of the other sources that people know - other foods from around the world. I'm fascinated by the way in which different cultures have all arrived at these foods that provide and support healthy microbiomes - because they're fermented. I have a colleague at Stanford, Justin Sonnenburg. He and I have talked about this. I don't want to quote him inappropriately, but - you know - we've had discussions about it. And they've published that the ingestion of fermented foods



is one of the best ways to support healthy levels of gut microbiota without exceeding the threshold that would cause things like brain fog. So, foods and fermented foods are going to be the best source. And there are a number of different ways that one could do that. Some people don't like fermented foods, however. Some people supplement it. So, it isn't a case of more is better. So, we know that.

### **Probiotics & Psychiatric Illness**

The other is that it is true that healthy gut microbiota have been shown to improve symptoms of certain psychiatric illnesses as well as certain conditions like particular features along the autism spectrum - which is interesting. And those effects are probably due to not just improvement of immune system function, but to the - the conditions in which the neurons that sense nutrients convey information to the brain and increase levels of serotonin and/or dopamine. So, gut microbiome provides - kind of - a foundation for healthy gut and healthy gut-brain axis. So much so that some people report that when they start eating small bits - because it doesn't require a lot - of fermented foods - that their overall mood is better - not unlike the effects of EPA - although, I don't think it's been looked at directly in the context of clinical depression yet. And if someone knows of a study, please mention it in the comments. That would be terrific.

### **Damaging Gut Microbiome**

There are some things that you can do to really damage your gut microbiome. And this is where there's a huge misconception that I want to clear up.

There was a study published in Nature - which is among the three top journals that we have in science. You know - Nature, Science, and Cell are considered the top-tops - but excellent journal - that showed that artificial sweeteners - but a particular artificial sweetener - which was saccharin - can disrupt the gut microbiome in ways that is detrimental to a number of different health markers - increasing inflammatory cytokines and all the other bad things that happen when the gut microbiome is thrown off-kilter. That study was widely discussed, but there were a few things that were not mentioned there that are really important. That study was about saccharin, in particular. Saccharin is not the most typical artificial sweetener that's used. The most typical sweetener - artificial sweetener - that are used are things like aspartame - so-called NutraSweet - sucralose - or these days, Stevia. There's monkfruit. To my knowledge - and please correct me if anyone knows of any studies - to my knowledge, the negative effects of these artificial sweeteners on the gut microbiome were restricted to saccharin. Now, there is enough chemical similarity between saccharin and some of the other ones that I mentioned - but not all of them. For instance, Stevia/monkfruit are distinct in their chemical makeup so that they probably don't have - if they have any - have lower effects - negative effects on the gut microbiome. But it should still be tested. So, saccharin is really - it was shown in this study and several other studies - can really negatively impact - impact - excuse me - the quality of the gut microbiome. Interestingly, the narrative around artificial sweeteners in gut microbiome is incorrect. Most people thought, "Oh, saccharin is bad for the microbiome. It must kill the microbiome." And so you hear people saying, "Oh, you know, artificial sweeteners kill the microbiome." That's not true at all. In fact, in that very same study published in Nature, they showed that the negative effects of saccharin on the microbiome could

be blocked or eliminated by giving antibiotics. So, what happens is certain artificial sweeteners - in particular, saccharin - disrupt the microbiome and make the environment within the gut - that mucosal lining - more favorable to - to bacteria - microbiota - that are not good for the organism, okay? This is an important distinction. It's not just that - a language thing - where people say, "Oh, you know - it kills the microbiome." It doesn't kill the microbiome. It shifts the microbiome. And shifts in the microbiome can be good or they can be bad.

### **How Changes in Diet Affect the Microbiome**

And that takes us to another topic - that's a bit of a hot-button topic. But I'm willing to go there because I think it deserves conversation - which is - nowadays, there are many examples out there where people have switched from a kind of standard diet - or even a vegetarian diet - to a - or vegan diet - to a keto diet.

Now, keto doesn't necessarily have to mean the ingestion of meats, but it can. And they experience positive effects for themselves - not everybody. And I've talked previously about some of the - kind of - the incorrect - what I believe is incorrect marketing of keto as it relates to the cosmetic effects and some of the challenges with sleep that some people have. But some people love keto and it works great for them. But the ketogenic diet is interesting because when one shifts to the ketogenic diet, there's a lot of people who are going to be able to get a keto diet. But the ketogenic diet is interesting because when one shifts to the ketogenic diet, there is a shift in the gut microbiome and some people end up feeling better. Some people end up feeling worse. Likewise, some people go from ingesting animal products - including meat - or they're vegetarian and they go to vegan - and they experience positive shifts in mood and affect. And we know that the - that the transition to a more plant-based diet - and especially the enrichment of fiber that's present in those diets - also creates dramatic shifts in the gut microbiome. Some people feel better doing that. Some people feel worse. And of course, it's going to depend on whether or not you're ingesting a lot of processed foods or not. There was a paper published in *Cell* - a *Cell Press Journal*, obviously - excellent journal - showing that ingestion of processed foods - regardless of whether or not they come from animal sources or non-animal sources - the processed foods themselves tend to create activity within the body and this surely has roots in the nervous system that lead to overconsumption of calories and weight gain - even some weight gain that couldn't be explained by increased calories. In other words, processed foods are bad regardless of whether or not you're talking about animal products or non-animal products - probably not surprising now given what you know about these sugar sensing and other amino acid sensing cells in the gut that we talked about earlier. So, the point of all this is that when I say, "You have to find what's right for you" - that's not a throwaway statement. Some people's microbiome and the lining of their - of their mucosa - excuse me - their mucosal lining of their throat, of their gut, of their nose - everything - is improved by diets that are heavily meat-based and don't have many plants. Other people do much better on a plant-based diet without many meat products or animal products. It's highly individual. And this probably has roots in genetic makeup. This probably has roots in what people were raised on - because remember the nervous system, of course, is set up by your genetic - your genes - your genetic program - but your nervous system adapts early in life to your conditions. That's what it's

for. The reason you have a nervous system is to move your - your body appropriately towards things that are good for you and away from things that are not. But also, the - it was designed to adapt. The early life period has this incredible thing about plasticity - that we spent a whole month on - so that it can change - so that - yes indeed, some people may like certain foods and react to certain foods better than others because of the way that their nervous system was wired. This enteric - as it's called - nervous system - that lines the gut and that communicates with the brain.

So, most of what I've talked about today is black and white. These are things that are present in all of us - the sugar-sensing neurons of the gut - the way the vagus is wired - the fact that omega-3/omega-6 tend to improve - the ratios tend to impact mood - with high omega-3/omega-6 ratios improving mood. We talked about all sorts of things in the gut-brain and body-brain access. But when it comes to the microbiome, the key thing is that we all have a microbiome. You want a microbiome, but you want to promote the microbiome that is right for you. And that can be shifted and steered by ingesting certain categories of foods and not others. One thing that really frustrates me is when the people show up with an agenda - like you know - all-meat agenda, or a vegan agenda, or a keto agenda - and they talk about these positive effects on the gut microbiome. And it's all true, frankly. And so, it's highly individual.

Now, this doesn't get to any of the ethical issues around animals, or the planet, or - and you hear rabid debates about that - you know - on both sides. And I am not qualified or equipped to talk about whether or not - you know - regenerative agriculture, animal products, or farming, or any of these things - how those actually impact the environment. That is not my expertise. But when it comes to your health and your microbiome, you want to support the microbiome. It's very clear that these fermented foods support the microbiome - that we should be ingesting at least two servings per day - which is quite a lot - that supplementation at low levels can be good. Supplementation at high levels can create this brain fog - even though some people say that result is controversial, I've experienced this myself and the data looked to me pretty darn solid. So, that's one thing to think about as well. And the other thing about the gut microbiome is that it's highly contextual based on other things that you're doing. So, even things like exercise, and social well-being, and connection - those things are also impacting the gut microbiome. So, find the diet that's right for you and that works for you in the context of the other ethical and lifestyle choices that are important to you. That's my advice.

## **Fasting**

A note about fasting. I have a colleague at Yale who's an expert in the gut microbiome and he told me something really interesting - which is when we fast, we actually digest certain components within our dietary tract. It actually depletes a good amount of the gut microbiome. And this is interesting. I've - I've had good results from - I guess you would call it "intermittent" - or kind of - "circadian-type" fasting - where - I've never done long fast, but - where I push out my first meal by a few hours. My first meal is generally around lunch time or so. But the longer periods of fasting - that go for a day, or two, or three days - are known to deplete the gut microbiome in major ways. And - but that's not always necessarily a bad thing because when it's replenished, it often is replenished at levels that exceeded its previous level. But I think that some of the GI tract - and even some of the mental effects of returning to eating after feeding - sometimes people don't feel so good when

they start eating. They really want food, but then they start eating again. They don't feel as good as they did on the fast. Some of that may be related to the depletion of the microbiome that occurs during long fast. So again, this is something to think about and talk about with your doctor, but the idea that fasting across the board is good. There may be some merits to that - and certainly, in some cases - but it does deplete the microbiome. And that depletion of the microbiome is significant because it means when you return to eating, you're actually not in the same position to digest and assimilate those foods. And those foods are not in the same position to impact your brain and body the same way they were prior to the fast. And this is, I think, why people suggest a kind of gradual transition back to consuming nutrients after a fast.

### **Alia Crum - Milkshake Experiments**

So as we round up, I want to share some results with you that without question will impact the way that you respond to food mentally and even physically. And I know that because that's the central theme of the studies I'm about to tell you about. I have a colleague at Stanford, Alia Crum, who's done some remarkable experiments on mindset. And some people could think about these as placebo effects or belief effects, but they actually go way beyond those terms. And there are a number of different examples of this that Alia's lab and her coworkers have demonstrated, but two that are particularly interesting to me - I want to share with you now - because they really emphasize how our beliefs can really impact the way that our brain and body work together. I think the most famous of these is an experiment they did where they had two groups of individuals. They were each given a milkshake and they had some factors measured from their blood by an IV while they ingested the milkshake and then afterwards as well.

And one of the factors that they were looking at was something called ghrelin - G-H-R-E-L-I-N. Ghrelin is a peptide that increases with hunger. So, the longer you have an eaten, the ghrelin goes up. And I know some of you say, "Well, I fast, I fast, I fast - and I eventually lose my appetite." Well, ghrelin still goes up and then, it drops. So, if you're one of these people that eats every three hours regularly, ghrelin kind of gets a little pulse as you get to that two hour and fifty minute mark - so, it's a little bit of a timer as well. It's a really interesting peptide. In any event, what they did is they gave people milkshakes - two groups. One group got a shake that they were told was a low-calorie, healthy shake. The other group got a milkshake that they were told was the very decadent high-calorie shake. I think it was something like two - or maybe even two and a half - times as many calories as the other - perhaps even more. I don't recall the details, but you had a high-calorie and a low-calorie condition. And then, they drank the shake and then they measured ghrelin in these subjects of blood. And what they found was that the high-calorie shake had a much more robust effect on blunting ghrelin and reducing ghrelin. But the interesting thing - you probably guessed already - is that it was the exact same shake given to both groups. So, people's belief about the content of something impacted their physiology in a very - and this speaks to the so-called top-down mechanisms - or modulation - of our physiology. In the previous episode about pain, we talked about the effects of - you know - obsessive - believe it or not - it was an obsessive infatuation and love on pain responses and pain thresholds. This is yet another example where

beliefs or subjective feelings can impact physiology at the level of the periphery - because ghrelin is released in the periphery in the body. Now, these belief effects extend beyond examples like this.

### **Alia Crum - Hotel Worker Experiments**

Another good example that I'd like to share is Ali - Dr. Crum - and her colleagues - did an experiment where they took housekeepers - hotel - they were essentially hotel workers - divide them into two groups. They had to watch a short film. In one case, the film was about how - you know - their work was important. It helped people feel comfortable in the hotel - etc. - etc. The other group heard that the activity that they were doing - cleaning and taking care of the hotel - was good for them. It was good for their health - etc. - etc. They controlled very nicely in the study for health parameters, for individual differences, and for the behaviors of these people in the period that followed this short tutorial. And what they found was eight weeks later, the group that had been told that the activity was good for them showed lower blood pressure. They had lost a significant amount of body fat and they reported enjoying their work far more than the other group - the same work. Simply biased - mentally - by the information that they were given - but their physiology followed that information. And so, this is not just the placebo effect. This is an incredible set of findings that illustrate the extent to which - whether or not we believe a food is going to be good for us or not good for us - well, we can't escape the reality. You can't tell yourself that a poison is going to be good for you and ingest that poison and expect it to not kill you. Nor can you tell yourself that eating - you know, 12 croissants - I confess I've done it. It was after a very long run - a long time ago. But you can't tell yourself that that's necessarily going to be good for you or that it's going to make you lose weight. These belief effects are not about lying to yourself. In these cases - in these experiments - as you'll notice - the subjects didn't have prior knowledge about ghrelin or about the effects of their daily routine on weight loss and blood pressure. So in order for them to work, you have to be naive to the information, right? You can't simply lie to yourself and tell yourself what you want to believe.

### **Conclusion**

And that's important, but also important is that the mind and the body are in this fascinating interplay. And today, we've talked mainly about how the body and things that we put inside this tube - this - that runs from our mouth to - to the other end - the rectum - basically is impacting all these cells - these neurons, microbiota in there, mucosal lining, heart, lungs, - and how all that information is feeding up to the brain to impact how we feel up here. But also, how we feel up here is impacting how our body reacts at levels of very core physiology that you couldn't just tell yourself that this was going to work. But what you believe about certain substances, certain foods, certain nutrients does have a profound effect on the magnitude of their impact and sometimes, even the quality and direction of that impact.

Well, first of all, I want to thank everybody for their support of this podcast. The response that we've received since releasing at the beginning of the new year has been tremendous and we're so grateful for it. I know some of you and people you know have said, "Well, it's a lot of information. It's like a college lecture." Indeed, there's a lot of information. But I believe very strongly that if you learn mechanism - and maybe even if you hear it several times over - eventually those mechanisms

become embedded into the way that you view an entire topic. As well, I always try and put tools - as I go along - that you can look to immediately. Some of them might be right for you - others might not, you know? Try them if you like. And don't if you don't want to. And if they don't work for you, then discard them. If however you are finding benefits from the information and from the tools and you know others that you think could benefit from it, please pass along information about the podcast. Please subscribe to the YouTube channel if you haven't already. Please subscribe to us on Apple and Spotify if you haven't already. Please leave a review in the comments section here on YouTube. Also, if you feel we deserve it, please give us a five-star review on Apple. All those things really help us. In addition, if you'd like to support the podcast further, we've set up a Patreon account. It's [patreon.com/andrewhuberman](https://patreon.com/andrewhuberman). It allows you to support the podcast at a variety of levels. We have the "5-HTP/serotonin" - for \$5 a month, the "Costello" - \$10 a month - in honor of Costello, etc. You don't have to, but if you'd like to, that would be terrific. In addition, please check out our sponsors that we've mentioned at the beginning of the podcast. That's one of the best ways to help support us. And we do believe in all the products that we support and our sponsors very much. Otherwise, we wouldn't be working with them. So much so that when I mention supplements - and I talk about supplements throughout the course of the episodes - I don't mention specific brands. But I would be remiss if I didn't mention the fact that we have partnered with Thorne - T-H-O-R-N-E. And we've done that because we know that Thorne uses the highest levels of stringency in terms of the products they produce. What they say is in each capsule and tablet actually is. They're used by the Mayo Clinic - by all the major sports teams - because of their level of stringency and rigor. If you want to know which supplements I take, you can go to [thorne.com/u/huberman](https://thorne.com/u/huberman) and you can see the supplements that I take and you can get those as well as any of the other supplements and products that Thorne makes for 20% off. So, it's [thorne.com/u/huberman](https://thorne.com/u/huberman) to get 20% off any supplements that Thorne makes.

So today's episode, we took a full journey into the brain-body relationship and discussed a lot of the mechanisms and the actionable items that you can approach if you want to explore this aspect of your biology and psychology further. Last, but certainly not least, I want to thank everybody for your time and attention today. And as always, thank you for your interest in science.