

Huberman Lab #16 - How Our Hormones Control Our Hunger, Eating & Satiety

Published - April 19, 2021

Transcribed by - thepodtranscripts.com

Introduction

Welcome to the Huberman Lab podcast where we discuss science and science-based tools for everyday life. I'm Andrew Huberman and I'm a professor of neurobiology and ophthalmology at Stanford School of Medicine. 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 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. I've long been a fan of getting blood work done. And the simple reason for that is that most of the things that you want to know about your health - such as hormones, metabolic factors, blood sugar levels, etc. - can only be analyzed from blood. And nowadays, there are also excellent DNA tests that can also give you valuable information about what's going on at the cellular, molecular - even the neural circuit level - within your brain and body. InsideTracker makes getting blood and DNA tests easy. You can go to a testing site where they draw your blood. They take your DNA sample. Or they can come to your home if you prefer that. As well, they have a really amazing dashboard. The dashboard lets you understand what your levels of various hormones, and metabolic factors, etc. mean and what you should do about them. And I think that's one of the main things that really separates InsideTracker apart from other blood and DNA tests. Most tests you get the results back, but there are no directives about what to do specifically in order to bring the numbers into the ranges that you would like for your goals. InsideTracker makes all of that extremely simple and extremely clear. If you'd like to try InsideTracker, you can go to insidetracker.com/huberman. And if you do that, you'll get 25% off any of InsideTracker's plans. Use the code "huberman" at checkout. That's insidetracker.com/huberman to get 25% off any of InsideTracker's plans.

Today's episode is also brought to us by Athletic Greens. Athletic Greens is an all-in-one vitamin mineral probiotic drink. I started taking Athletic Greens back in 2012 and I've taken it ever since, so I'm delighted that they're sponsoring the podcast. The reason I started taking Athletic Greens - and the reason I still take it now - is that Athletic Greens really lets me cover all my nutritional bases in terms of vitamins, minerals, and probiotics. There's so much data now pointing to the fact that the gut microbiome and the gut-brain axis is important for metabolism and for endocrine health. The vitamins, minerals, and probiotics in Athletic Greens make me feel confident that I'm covering all my bases. I do take other supplements, but with Athletic Greens, I know that I've got all the foundational stuff handled. It also tastes really good. It tastes fine on its own. You can mix it with water, which is what I do. I add a little bit of lemon juice or lime juice, because I like a little tartness flavor in there as well. But most people just mix it with water. It mixes up super easily. I drink it once or twice a day - usually once mid-morning and once again in the afternoon. If you'd like to try Athletic Greens, you can go to athleticgreens.com/huberman. And if you do that, you can claim their special offer - which is a year's supply of vitamin D3K2. There is now a ton of evidence that vitamin D3 is involved in countless metabolic processes - hormonal processes - that are important

for overall health and well-being. Vitamin D3 - you can get from the sun, of course - but most people are deficient in vitamin D3. So if you go to athleticgreens.com/huberman, you'll get the Athletic Greens, you'll get the year's supply of vitamin D3 and K2, and you'll get five free travel packs. So once again, it's athleticgreens.com/huberman to get Athletic Greens, the vitamin D3K2 - that's a year's supply, plus the five free travel packs.

Today's episode is also brought to us by Munk Pack. Munk Pack is a company that makes keto-friendly snacks that taste incredible, but have just one gram of sugar or less. And indeed, they taste incredible. In fact, my production team here at the Huberman Lab podcast teases me because I actually have to keep the boxes of Munk Pack bars in my basement because otherwise I'll tear through all of them. I remember the first time I tasted it. I was like, "Alright, here we go - a keto bar." I'm not a big fan of bars in general. Most of them don't taste good to me. And I tasted the Munk Pack bars and they are absolutely awesome. They come in a lot of different flavors. I'm partial to the caramel sea salt one, but they also have sea salt dark chocolate - peanut butter dark chocolate. They have a bunch of flavors. They're all incredible. I've tried them all, which is why I keep them in my basement. As I've mentioned previously on this podcast, I'm neither keto nor carb-o. I don't really follow a particular diet in that sense. I eat in a way that maximizes my alertness and my levels of focus during the day when I want to work and that maximize my transition to sleep at night. So, I basically eat low-carb keto-ish during the day - and I know that keto-nistas will say that I'm not in ketosis. And I can manage to get into ketosis, but the main idea is I keep my carbohydrates low during the day. At then at night, I do eat carbohydrates. So for me, the Munk Pack bars are a really good snack - usually in the afternoon - maybe with a cup of coffee, especially if I'm going to train soon after that - or if I just want a snack and I'm going to continue working. As I mentioned before, they are absolutely delicious. They also don't have any of the stuff that's bad for you. No soy, trans fat, sugar alcohol, artificial colors - all that stuff that we know we should avoid. If you want to try Munk Pack bars, you can go to Munk Pack - that's M-U-N-K - munkpack.com - and enter the code "huberman" at checkout and you'll get 20% off your first purchase of any Munk Pack product. That's Munk Pack - M-U-N-K-P-A-C-K.com - and enter the code "huberman" at checkout to get 20% off your purchase.

This month, we're talking all about hormones. Hormones are incredible and they control so many processes in the brain and body. Last episode, we talked about the role of estrogen and testosterone. Today, we're going to talk about how hormones impact feeding and hunger - as well as satiety - the feeling that you don't want to eat or that you've eaten enough. Now, it's important to understand that hormones don't work alone in this context. Today, I'm going to describe some hormones that have powerful effects on whether or not you want to eat more, or less, or stop eating altogether. But they don't do that on their own. They do that in cooperation with the nervous system. So today, I would say as much - or perhaps even more than any other episodes - we're going to hear a lot of biology. But there are multiple - what I'm going to call "entry points" - for tools that you can apply in order to regulate your levels of hunger, your meal timing, your levels of satiety - of not wanting to eat more. And many of this is actionable with behaviors. But of course, we're also going to talk about supplements and we're actually going to talk about a little bit of brain-machine

interface - devices that can actually be involved in manipulating these incredible things that we think of as hunger, and appetite, and satiety.

Hypothalamus

So, the first thing that you need to know about the nervous system side - the neural control over feeding and hunger - is that there's an area of your brain called the hypothalamus. It's in the forebrain - which tells you it's in the front of your brain. And it's at the base of the forebrain. Now, the hypothalamus contains lots of different kinds of neurons doing lots of different kinds of things. There are neurons in your hypothalamus controlling sexual behavior, controlling body temperature, controlling circadian rhythms - the desire to sleep or be awake - even neurons controlling rage. There are actually neurons that if we were to stimulate them would send you or anyone into a rage. They're just powerful control centers for the brain and body.

Ventromedial Hypothalamus

There's a particular area of the hypothalamus called the ventromedial hypothalamus. And it's one that researchers have been interested for a long time now in terms of its relationship to hunger and feeding. And the reason is, it creates these paradoxical effects. What do I mean by that? What they found was that sometimes lesioning or disrupting the neurons in the ventromedial hypothalamus would make animals or people hyperphagic. They would want to eat like crazy. And other lesions in other individuals or animals would make them anorexic. It would make them not want to eat at all. It would make food aversive. So, that means that the ventromedial hypothalamus is definitely an interesting control station for hunger, and feeding, and satiety. But it doesn't really tell you what's going on at a deeper level. In fact, it's a little bit confusing or paradoxical. It turns out that there are multiple populations of neurons in there. We're going to talk about those. Some are promoting feeding and some are promoting not feeding or not eating.

Insular Cortex

Now, the other neural component of all this that you need to know about actually has to do with your mouth. So, there's an area of your cortex. So, that's a little bit further up in your brain - called the insular cortex. And it processes a lot of different kinds of information - mostly information about what's going on inside you - so-called interoception. The insular cortex has neurons that get input from your mouth - from the touch receptors in your mouth. And insular cortex has powerful control over whether or not you are enjoying what you're eating, whether or not you want to avoid what you're eating, whether or not you've had enough, or whether or not you want to continue eating more. And that has to do - believe it or not - with the touch or sensation of eating. I'm very familiar with this. I'm one of these people. I love eating so much that I just like the mere act of chewing. You know, I like celery sticks enough. I'm not crazy about them. But you know, they taste fine to me and I like chewing on celery sticks. But I actually just like chewing on them. I - I could eat all day long, except that it's not healthy to do that. But the mere act of chewing for me is very pleasurable. People who chew gum feel this way as well. And just as a point about gum or chewing - if you chew something like celery, or cucumber slices, or chew gum - provided it doesn't have any sugar or caloric content - it's not going to drive increased hunger. That generally isn't the case. But

if you eat something with sugar as we'll find out, it has a very specific action in the insular cortex and in other areas of your nervous system that promotes the desire to eat more. But the key point right now is to know you got these two brain areas - the ventromedial hypothalamus - that's involved in hunger and lack of hunger - sort of an accelerator and a break on feeding. And you have this insular cortex that gets input from your mouth and cares about chewing, and the consistency of foods, and all sorts of interesting things that are just very tactile. And I think most people think about the touch receptors on - excuse me, the taste receptors - on the tongue. But we often don't think about the touch or tactile essence of food. The thing that comes to mind just now is - I've gone to sushi several times and some people really like the urchin. I don't like the urchin. There's something about it that kind of creeps me out about the consistency. Other people love it. So, it's highly individual, and it's probably learned, and there's some - probably - cultural background to this - if you were raised eating urchin. Some people love that consistency or that touch. So, touch has a lot to do with whether or not you want to eat or not.

Experiment - Parabiosis in Rats

Now, let's get back to the ventromedial hypothalamus. Sometimes it makes animals or people want to eat more, sometimes less. So, what's going on there? There's a classic experiment that was done in which researchers took two rats and so-called "parabiosed" them to each other. What that meant is that they did a little surgery and they linked their blood supply so that they were forever physically linked to one another and could exchange factors in the blood. But their brains were separate. Their mouths were separate. And they essentially did everything separately except that they were linked to one another. So, they had to walk together and go to the same places in order to do it. This parabiosis experiment revealed something really important. When they lesioned the ventromedial hypothalamus in one of the rats that was connected to the other rat, that rat got very, very fat. It's just really obese - huge rat, super rat, jumbo rat. The other one, however, got very thin. It actually lost weight despite consuming the same amount of food that it had prior to the other one getting the lesion. So, what does this tell us? This tells us that there's something in the blood that's being exchanged between the two animals because it was their blood supply that was linked. And that tells us that there's hormone or endocrine signals that are involved in the desire to eat, and hunger, and appetite.

Endocrine Factors Regulating Feeding, Hunger, and Satiety

And so, next we're going to talk about what those endocrine signals are. And then, I'm going to immediately point to some entry points that you can use - and you can use these even if you're not parabiosed to anything - and that can allow you to time your meal frequency and predict when you're going to be hungry or not - as well as drive up appetite. Believe it or not, there are people out there who are trying to eat more - although, I think far many more people are trying to eat less. Because, nowadays - you know - the data just point to the fact that there is essentially an epidemic of diabetes - type 2 diabetes - and obesity. And most everyone agrees now that maintaining a healthy body weight and body weight composition is one of the best paths to longevity and to just feeling very good and actually being able to think. Cognitive functioning is actually linked to levels of adipose tissue and so forth.

Arcuate Nucleus

So, let's talk about the endocrine factors that regulate feeding, hunger, and satiety. One of the really exciting things to emerge in the science of feeding and appetite in the last 20 years is the discovery of another brain area - not just the ventromedial hypothalamus, but it's an area of the brain called the arcuate nucleus. And the arcuate nucleus has some really fascinating sets of neurons that release even more incredible molecules and chemicals into the blood. And these chemicals act as accelerators on feeding and appetite - or breaks. And the really cool thing is that you can actually control these molecules through simple behaviors. And once you understand what these molecules are, you'll start to understand why that's the case and the control points that you have right now in order to control your appetite in either direction - increase or decrease.

Pro-opiomelanocortin (POMC) Neurons

So first of all, there are a set of neurons in this arcuate nucleus called the POMC neurons, okay? I don't want to get into what the acronym stands for - but I'll do it anyway. It's the pro-opiomelanocortin system, okay? So, these are POMC neurons - pro-opiomelanocortin. And if you heard "melano", that should tell you it has something to do with pigmentation in skin cells or in hair cells - pigmentation of some sort - because of melanin. Last episode, I talked a little bit about the relationship between light, dopamine, and melanin. So, you should already be thinking, "Wait, 'melano' means - it probably has something to do with that system." And indeed, it does. Now, the POMC neurons make something called α -MSH - melanocyte-stimulating hormone - alpha-melanocyte-stimulating hormone. If you don't want to remember any of the other acronyms and terms I've talked about this episode so far, do try and remember MSH, okay? Mouse-Sam-Hamster - MSH, okay? MSH reduces appetite. And it's a powerful molecule, alright? So, just put that on the shelf. MSH reduces appetite.

AgRP Neurons

Now, there's another population of neurons in the arcuate nucleus called the AgRP neurons. And there, I'm truly not going to read you what that stands for because it's related to the mouse strain it was first identified in. But humans make these - have these cells as well. But AgRP neurons. The AgRP neurons stimulate eating. And anytime you are approaching food - or you feel some excitement about food - or anxiety, because some people actually experience a kind of heightened anxiety - some people actually get a little bit of a resting tremor before they eat - even if they don't have any sort of eating disorder. There's kind of a ramping up of autonomic activity. That's largely due to the activity of these AgRP neurons. So, the activity in these AgRP neurons goes way up when animals or people are starved. And I don't mean starved for long periods of time, but I mean when they haven't eaten for a while. And the activity of MSH - the release of MSH - goes up when we've eaten. However, there are other things that will stimulate the release of things like MSH. So just briefly, the experimental evidence. If you kill AgRP neurons, animals and people stop eating. There are people who have lesions. They just stop eating. They become anorexic. That's actually - I know you're familiar with anorexia as a clinical term, but that's actually a term that's used in the scientific literature about a pattern of behavior, okay? As well as a clinical term, of course. If you were to stimulate the AgRP neurons, animals or people eat like crazy. They will eat to the point

where they burst - which just sounds horrible. But it just tells you this is the accelerator on eating. And yes, it has a relationship to the ventromedial hypothalamus I talked about earlier, but I don't want to go back there just yet. We will circle back.

α -MSH

So, melanocyte-stimulating hormone - such an interesting hormone. This thing can shut down the desire to eat. The melanocyte-stimulating hormone is released from the medial pituitary. We talked about the pituitary last time. This is a - a gland that is very closely positioned to the hypothalamus. Actually, some of the hypothalamus neurons actually project their neural connections directly into the pituitary to release things like gonadotropins and luteinizing hormone - stuff we talked about last time in reference to testosterone and estrogen. But MSH is released from the medial portion of the pituitary and it stimulates the desire to not eat - to cease eating.

Tool - Ultraviolet Light

What's really interesting is that melanocyte-stimulating hormone is activated by ultraviolet light. And it's not activated by ultraviolet light to the skin or directly to the pituitary. It's activated by ultraviolet light to the eyes. Now, if you've been watching this podcast, or listening to this podcast for any period of time, or you've heard me on other podcasts, or you follow my Instagram - I am a big fan of this whole thing of getting morning light in order to synchronize circadian rhythms, etc. - avoiding light in the middle of the night. This is yet another reason why getting ample light - ideally sunlight - but it could be other sources of UV light to the eyes - stimulates MSH. This has been shown over and over again - and keeps the desire to eat or appetite - in check - in healthy ranges. This is also why in the spring and summer months, animals and people eat less. Now for hibernating animals, it's different because the bear hibernating - actually, bears don't truly hibernate, technically, by scientific criteria - they don't hibernate, but they go into a kind of torpor. The hibernating animals, they don't eat much because they're in burrows, or dens, or they're just wrapped up in a little ball, or whatever it is that hibernating animals do. So they're, of course, going to eat far less in the winter, but that's a unique scenario. We are not hibernating animals. But humans, generally, have greater appetite in the cold winter months. It's not just because of the holidays and the abundance of food that we're presenting ourselves with. But when we get a lot of sun, our appetite is reduced - or at least it's easier to control. And that is due, in part, because if you're getting ample sunlight to the eyes, it's converted into a signal for the MSH neurons - the neurons that release MSH, excuse me - these POMC neurons release MSH. And then, MSH can bind its receptors and can keep the break on appetite in check.

So, the takeaway tool from this is make sure you're getting enough light - not just in the morning, but throughout the day. And yes, it has to be light to your eyes. And blasting your eyes with sunlight or artificial light to the point where it's damaging or painful won't accelerate or improve this process. It's about getting photons - ultraviolet light - to the eyes consistently throughout the day. That's best accomplished by not wearing sunglasses - provided you can do that safely. And if you don't have access to enough sunlight, then you can do this with artificial light. This also points again to our old friends - the blue blockers. Many people know I'm not a huge fan of blue blockers -

especially not during the daytime because they block a lot of the UV and shorter wavelength light that you want and need to create alertness, but also to create release of MSH from the medial pituitary.

Injecting MSH

Now, there are people out there - subcultures - that actually inject MSH - that are taking MSH or things similar to it. I am not suggesting people do that, but there are three main consequences of doing that. First of all, it reduces appetite - no surprise there. They're actually using it as a dieting drug. This is - kind of - in the underground. I don't know what the legal status is. And again, I'm not promoting that people do it. Two, it makes them very, very tan - which makes sense, right? Melanocyte-stimulating hormone. And the third, is it purportedly - never tried it - purportedly sends libido through the roof to the point where it's actually distracting for other activities. It actually can create priapism - which is a - kind of - chronic erection in males to the point where it actually can be physically damaging to the genitalia. So, this is a drug of - or a - I - I don't know whether or not to call it a drug. It's a - it's a substance that one can regulate with healthy levels - with sunlight and perhaps artificial UV light. I have not heard much about treatments for obesity involving getting ample sunlight or getting ample UV light. But to me, the logic is just very clear. And so, if you're pursuing those avenues, you might want to - you certainly should talk to your physician, but you might want to think about how some of those logic hangs together. Absolutely fascinating hormone. I think most people aren't aware of it. And the subcultures that are aware of it are using it for - to - very particular endpoints and they're using it at supraphysiological levels. That's enough about that, because I really don't know. I've talked to a few people in research - believe it or not - for this podcast. I've reached out to a few people and asked whether or not the - these "side effects" in air quotes I've heard about are true. And indeed, they're true. But again, that's supraphysiological. Controlling MSH - it's actually α -MSH - levels through viewing ultraviolet light seems like an interesting and mechanistically logical thing to do if your goal is to keep appetite in check.

Ghrelin

So, MSH inhibits hunger. Next, let's talk about a hormone peptide that activates hunger. And this is a really interesting one because it relates to when you get hungry - in addition to the fact that you get hungry at all. And it's called ghrelin. It's spelled G-H-R-E-L-I-N. Ghrelin is released, actually, from the GI tract. And its main role is to increase your desire to eat. And it does that through a variety of mechanisms. Part of that is to stimulate some of the brain areas - the actual neurons - that make you want to eat. In addition, it creates food anticipatory signals within your nervous systems. So, you start thinking about the things that you happen to like to eat at that particular time of day. And this is fascinating. Ghrelin is sort of like a clock - a hormonal clock - that makes you want to eat at particular times. Now, the signal for ghrelin is reduced glucose levels in the blood. We're going to talk a lot today about glucose and insulin - ways to manage glucose and insulin. But for now, the simple version of this is you normally want your glucose to be in a - kind of - modest range. And I'll explain what that range is in a little bit. But if it drops too low, ghrelin is - is secreted from your gut. It activates neurons in your brain at various locations - including the POMC neurons and the other neurons of the arcuate. It also activates the VMH in particular ways. And it

might even activate some of these neurons that are in the periphery - in your mouth - that actually makes you - kind of - salivate and want to eat. Now, we all know about the famous Pavlovian experiments of Pavlog's dogs. You know, they start salivating to the bell. After the bell, was presented with food. You remove the food and then just the bell can stimulate the - the salivation. We become "Pavlovian" at times. But rarely has it ever discussed what the neural pathways for that are. And it turns out that these hormones that are secreted from the gut can stimulate the neurons to create a sensation and a desire for certain foods at certain times of day.

Tool - Intermittent Fasting / Random Meal Skipping

You've done this experiment. If you are somebody who eats breakfast at more or less the same time each day. Let's say 8am \pm 20 minutes. And then, you eat lunch - 12:30 \pm 20 minutes. Or let's say you're somebody like me who typically skips breakfast and just eats lunch - usually around 11:30, or 12, or something like that. Your ghrelin secretion will start to match when you typically eat. And it does that and it's able to override the low levels of glucose in your bloodstream because the ghrelin system also gets input from a clock in your liver that is linked to the clock in your hypothalamus in your brain. And what this means is if you eat at regular meal times, you will start to get hungry a few minutes before those meal times. If you've ever wondered why your stomach - kind of - starts to growl because it's a particular time of day. And you're like, "Oh, I must want to eat." Well, that's ghrelin. And for those of you that don't know why your stomach growls, I'll also tell you that today. It's actually really interesting. It's not at all what you expect and it's not just the gurgling of liquids in your stomach. That's not what it is. It's actually a muscular phenomenon. So, ghrelin is secreted as a - kind of - food anticipatory signal to get you motivated to go eat at regular times.

So nowadays, there's a lot of interest in intermittent fasting. There's also a lot of interest in just what meal plans, and schedules, and what to eat in general in order to maximize one's health and well-being. And people have all sorts of cosmetic reasons, and brain reasons, and metabolic reasons for wanting to control this kind of stuff. So, let's make it really simple by first looking at the extremes. Some people need to eat every 2 or 3 hours. They feel this, "I need to eat every two or three hours" or else their blood sugar drops. In general, blood sugar doesn't drop so low that they truly need to eat in order to alleviate a blood sugar issue - although, sometimes that can happen. Some people are truly hypoglycemic - low blood sugar. But most people - as the blood sugar starts to head down towards the low-ish ranges, ghrelin is secreted. And so, for those people not eating on the clock is very disruptive to them because it activates these neurons in the brain. For people who eat once a day, or twice a day, or tend to shift their meals - they might eat a lot, but during a limited so-called feeding window. It's kind of interesting. Humans now eat and talk about foods in ways that for years I used to hear about in classes, and courses, and research lectures about feeding animals - you know - restricted feeding windows.

And we owe a - a great deal of gratitude to Satchin Panda - who was a colleague of mine when my lab was in San Diego at the Salk Institute - who really is one of the pioneers of this restricted feeding window work and has done beautiful work. He has a book that's excellent called "The Circadian Code" that I highly recommend. And he's done a lot of important work on neurons in the

retina that control circadian timing, but also the relationship between feeding windows and health. And he's sort of the major proponent out there - among the major proponents - I should say of circadian eating - that means eating during the daytime, not at night - or intermittent fasting, restricting feeding windows to anywhere from 4, to 6, to 8 hours. I'll use myself as an example of the transition from regular feeding schedule to more intermittent-ish fasting - although, I don't really fall into true intermittent fasting. So, I was one of these people that just got so accustomed to waking up and eating about an hour after I woke up - that to go from eating every 3 or 4 hours to eating twice a day - lunch and dinner - maybe a couple snacks in the afternoon or something - at first was excruciating. I remember thinking like, "This is really brutal - pushing out feeding." I didn't think I could exercise unless I had eaten first. We now know that during most all forms of exercise - unless you're really focused on optimal performance - like you've got to hit key lifts or you have to - you know - sprint at your maximum speed - and maybe even then, that you can exercise fast at just fine because you're mainly relying on sources like glycogen from the liver - some undigested food sometimes - as gross as that might seem, it's true - as well as body fat if the exercise bout is extremely long. But what that means is that if you suddenly go from eating on a very regular schedule to skipping a meal, or pushing your meal timing out, or shifting it all - you're going to have ghrelin in your system and that ghrelin is going to stimulate the desire to eat by acting at the level of your brain. And it is indeed, at that point, just mental. When we hear about "just mental" - "just physical" - it's really kind of the same thing because it's all chemicals - brain and body. But it's the stimulation of neurons that anticipate feeding. You're stimulating the arcuate nucleus neurons that make you want to eat those AgRP neurons. So, ghrelin stimulates the AgRP neurons - which makes you want to eat.

So, what can you do with this? What this means is if you want to start shifting your feeding schedule to one where you're not eating quite as frequently - and there are some advantages to that that aren't just in the biochemistry and health related - you know - cellular health things. Some of them include not having to think about or buy food, right? You actually don't have to think about food all day if you're not eating so often. The other is it gives you far more social flexibility, right? You can go to a noon meeting if you have to or you can go out to dinner at a particular time. And - you know - I guess it makes it kind of tough if you want to meet somebody for breakfast. Because then, you're the - you're the dork who's just like sipping black coffee and like refusing everything. Anyway, I've been that dork. So, it's - you know - one of those things you just - kind of - work with. But the fact of the matter is ghrelin secretion - because of its relationship to the nervous system - can be shifted by about 45 minutes per day. Now, it's going to vary. Some of you have more so-called willpower - you know - but if you really want to just start pushing that first meal out or shifting it in any direction - some people might want to eat in the early part of the day and not in the evening - trying to shift the meal times out - the spacing - by about 45 minutes is what the - the - the neural circuits that link the ghrelin system to the neural circuits that control feeding really can handle. Because it's a form of neural plasticity. And so, what this would look like is if you normally, you eat breakfast at 8 o'clock \pm 20 minutes and you want to start eating your first meal at noon, you would take maybe 4 or 5 days and just start pushing the meal out by about 45 minutes to an hour each day so it's not quite as painful. Or you can just take the plunge and just do it all at once.

I have a colleague who was a neurosurgeon at Stanford - came up through my lab. He's now at Neuralink. And he has a great practice. He keeps his ghrelin system at random. What he does is he skips one meal per day and he makes his external schedule dictate that. So, sometimes he skips breakfast. Sometimes he skips lunch. Sometimes he skips dinner. He just skips one of the three major meals per day. And in doing that, the ghrelin system is always kind of kept off-kilter and it probably also allows him to have a lot of neural flexibility - what we call top-down control - just the knowledge, "Oh, you know - the hunger I'm feeling isn't necessarily hypoglycemia." And in his case, it's almost certainly not. And therefore, what I'm feeling here is an activation of these AgRP neurons and therefore, I can push my meal schedule around however I want.

Now, I should mention that top-down mechanisms are powerful - belief - motivation. These things can really shift neural circuits. We're going to talk more about that a little bit later. But there are also people who are genuinely hypoglycemic and that need to take really good control of their blood sugar levels and try and keep them stable. And so, of course, you want to do what's medically safe for you. I'm not at all recommending that people that suffer from hypoglycemia suddenly - you know - disrupt their blood sugar patterns in any direction. That wouldn't be healthy. But for most people out there who have reasonable blood glucose levels, it's kind of interesting and kind of fun to play with these parameters in order to optimize what you want to do. And sometimes that might change across the year or with schedules. Many people find great benefit in having flexibility over when they eat. Regularity of eating equals regularity of ghrelin secretion - equals regularity of activity of these AgRP neurons - meaning you will be hungry at very regular intervals. So, that's something that you can work with. It's grounded in deep mechanism of hormone and neural systems. And there's a lot of modern research to support what I just said.

Cholecystokinin (CCK)

So, if MSH inhibits feeding - makes us want to eat less. And ghrelin makes us want to eat more. There's another hormone called CCK - cholecystokinin - that is potent in reducing our levels of hunger. Now, I learned about CCK back when I was an undergraduate. So, well over 20 years ago - when it was first discovered. And there was a lot of excitement about CCK at that point as a diet drug. You know, anytime there's a molecule or a chemical discovered in the brain or body that can suppress feeding, the diet industry just goes wild and they think, "This is going to be the thing that's going to allow people to move from being obese to losing all sorts of unhealthy weight" - etc. A similar phenomenon was observed with leptin. Leptin is a hormone that's made by body fat that signals to the brain when there's a lot of body fat. And in animals, injections of leptin can make fat animals thin. They lose a lot of adipose or fat. In humans, it didn't work out that way. It just - the studies were done and leptin was successful in treating a certain rare form of diabetes, but it really wasn't very potent as an anti-obesity drug. Similarly, CCK has been looked at as an obesity drug - something to reduce obesity - but it had some pretty unhappy side effects - actually caused some pretty serious side effects. Now, that's as a drug. However, CCK - when released at normal levels by your gut - has a powerful effect in suppressing appetite for a period of time. And there are healthy and direct ways to activate CCK.

CCK is in the GI tract. It's released from the GI tract. And its release is governed by two things. One is a subset of very specialized neurons that detect what's in the gut - the specific contents of the gut. And by certain elements of the mucosa - of the mucus lining - of the gut and the gut microbiome. So, what's really interesting is that CCK is stimulated by fatty acids - and particular fatty acids that we'll talk about, amino acids - and particular amino acids that we'll talk about, as well as by sugar. Now, let's put sugar on the shelf for a moment. We're going to talk a lot about sugar, because if CCK inhibits appetite and reduces feeding - and it can be triggered by fatty acids, amino acids, or sugars - then you might say, "Well, then eating a lot of sugar should make us not want to eat more." But we all know that eating sugar makes us want to eat far more. That's the role of a lot of sugars. And that has to do with a separate mechanism we'll talk about today.

Stimulating CCK - Omega-3 / CLA / Amino Acids

So, which fatty acids in the gut stimulate the release of CCK? It turns out it's the omega-3 fatty acids - the ones that come from algae, or krill, or fish oil. I talked about this in the episode on nutrition and some of the things related to the gut microbiome, but I'm going to revisit that now. Omega-3 fatty acids and conjugated linoleic acid (CLA) - either from food or from supplements - stimulate the release of CCK - which then reduces or at least blunts appetite. And I'm not talking about blunting appetite to anorexic levels where you don't want to eat at all. I'm talking about regulating appetite to the point where animals and people don't overconsume. So, it's keeping appetite at a healthy level.

The other thing that stimulates CCK that I mentioned are amino acids. So, when we eat, we have the ability to break down different macronutrients - you know - carbohydrates, fats, or proteins - into sugars and glucose that then we can convert to ATP and all that stuff from - remember Krebs cycle from high school. We're not going to go into that today. That's for a future episode. But amino acids are one of the things that we are eating for. Amino acids both can be used as energy through a process called gluconeogenesis - of converting proteins into energy - or those amino acids can be broken down and then rebuilt into things like preparing - excuse me - repairing muscle tissue - as well as other forms of cellular repair. They're involved in all sorts of things related to protein synthesis.

What does this mean? If we eat the proper amino acids at the proper levels - if we ingest omega-3s and CLA - conjugated linoleic acids - at the proper levels - or get them from supplements - there's a blunting of appetite. Appetite is kept clamped and we don't become hyperphagic. We don't overeat. We tend to eat within healthy or normal ranges. So, this is very important because most people don't understand that when we're eating, we are basically fat-foraging and amino-acid-foraging. And there are several studies now - have shown that people and animals will essentially eat until they feel they've consumed enough omega-3s, omega-6s, CLAs, and certain amino acids. In other words, even if it's not conscious, we are eating until we trigger the activation of CCK. Now, there are other reasons why we shut down eating too. Our - literally the volume of food in our gut can be large and we can feel very distended. That's the physical reason, obviously. There are other reasons - maybe we just have top-down control. We - we have knowledge that this is the end of the meal and

we stop because we have to go back to work, or to a meeting, or we tell ourselves that we've had enough. But at a subconscious level, the gut is informing the brain - via CCK and other mechanisms - when we've ingested enough of what we need. And these omega-3s, and CLAs, and certain amino acids are vital for sending out that signal that we've had enough.

Now, which amino acids is actually really interesting. We have essential amino acids and we have non-essential amino acids. Among the essential amino acids, there's one in particular that can trigger the release of CCK very potently and that's glutamine. Glutamine is a very interesting amino acid. First of all, it's been shown in a few studies to play a role in bolstering the immune system. It can increase the number of killer cells in the immune system. It is consumed by - in supplement form. You know, people can take it - you know - a teaspoon of glutamine - or some people take glutamine throughout the day, if they're really into it - or for whatever reason. They think they're battling off an infection or something of that sort. Glutamine can also of course be derived from foods. And you can just - you know - put into the internet - do an internet search and find out what foods are rich with glutamine. Some of the ones that I'm aware of off the top of my head are cottage cheese and things of that sort. But other foods have glutamine as well.

Once a threshold level of glutamine and other essential amino acids are reached - once a threshold level of these alpha-3 - excuse me, omega-3 - fatty acids and CLAs are reached, CCK is released and it helps reduce the activity of those AgRP neurons that promote feeding. So, as you can see, feeding is an interplay between brain and body. And it's some of the micronutrients and even the breakdown of particular nutrients that's putting the accelerator or the break on the feeding process. It's not just one thing. So, from an actionable standpoint, you - we - should probably all be trying to get our omega-3/omega-6 ratios correct anyway because they are antidepressant. I talked about the peer-reviewed studies on that. They are healthy for the gut microbiome and we should be seeking sufficient glutamine. Now, whether or not you decide to supplement with glutamine or not is up to you.

One of the reasons why one might want to do that - and again, you should always check with a doctor - especially if you have any predisposition to cancers or you have cancer. Many cancers and tumors like glutamine. So, that's something to note. But one reason why you might want to supplement with glutamine or consider eating foods that are rich in glutamine isn't just to keep your appetite in healthy ranges. But as well, glutamine can actually reduce sugar cravings. So, this is very interesting. I have a friend. He's an absolute chocolate/sweets addict. He's a grown adult but he eats candy and chocolate as if it was - you know - as if he was like a 14-year-old kid hanging out at the local convenience store. It's really incredible. And he has probably a - a sugar addiction. But he's very aware of this and he's managed to kick all other addictions. So, for whatever reason, it stimulates his brain and body in the ways that make him want more. But he hates this. It's actually quite frustrating for him. He's somebody who cares a lot about his health. He took the approach - that I know many other people have who know about this role of glutamine - of taking a teaspoon or a couple teaspoons of glutamine several times throughout the day or anytime he craves sugar. And indeed, glutamine will reduce sugar cravings.

Some people who are really on the - kind of - ketogenic front will mix it with a little bit of half and half and down that because I guess it makes it taste better. It's a little bit chalky. So, glutamine has some very interesting properties. But I think for most people that aren't suffering from adverse levels of craving, making sure you're getting the right omega-3s. That can come from a variety of sources. Check out the episode we did on nutrition if you want to learn more about that. And CLAs. And making sure that you're getting enough glutamine is going to be important for making sure that the CCK signal gets through.

Tool - Glutamine

The one thing I do want to mention about glutamine. It's a minor effect. But it - it alone can have a small increase - excuse me - it alone can increase blood sugar. It's not a huge increase in blood glucose, but because the gut takes proteins and breaks them down into these amino acids and essentially looking for glutamine and things like it - other essential amino acids as well. When you ingest glutamine or branched-chain amino acids, there is a small but real increase in blood glucose. And that's because they are essentially food. And there, I'm talking about the supplemental version. So just know, glutamine can increase blood sugar slightly - especially diabetics should know that. It can reduce sugar cravings. And just know that what your gut is doing at a core level is it's foraging, it's waiting, and it's trying to assess levels of omega-3 fatty acids, conjugated linoleic acid, and glutamine, and other essential amino acids. You are essentially trying to eat to get these nutrients. And then, a signal can be deployed up to your brain that you're not really interested in eating that much more.

Tool - Avoiding Highly Processed Foods / Emulsifiers

Whenever preparing an episode for this podcast, I'm always faced with a particular challenge - which is: How many tools should I offer that involve doing something new? A new behavior, a new exercise, supplement, something - things of that sort. And how many should be related to not doing things - avoiding things? It's never really fun to talk about all the things that we're supposed to avoid. But some of them are so powerful - in light of the mechanisms of a given topic - that I'd be remiss if I didn't mention them. So, now you understand how hormones and peptides like CCK and ghrelin impact appetite. There's one particular aspect of food that can powerfully impact CCK. And I think most people - I'm guessing 99.9% of people out there - are not aware of this. And it has to do with highly processed foods. There's a lot of reasons why one would want to avoid highly processed foods.

In fact, if you're interested in that topic and the history of whole foods transitioning to highly processed foods in this country, I highly recommend you listen to a YouTube video by Dr. Robert Lustig. He's at University of California, San Francisco. It's very easy to find. Put "Stanford Robert Lustig". It was a talk hosted by Stanford. It gives a - a beautiful description of the history of this and why the food industry started packing in additional sugars and salts - and turning foods into commodities. It's really fascinating. It has no conspiracy theory. It's just all scientific facts. It's really a wonderful lecture. It has millions of views. It should be very easy to find. We can provide a link to that and we will.

There's another reason to avoid highly processed foods, however. And that has to do with what's called emulsifiers. Now, many of you are familiar with emulsifiers - even though you don't know it. When you put detergent in the laundry, that is an - contains emulsifiers. The - the goal of that detergent is to bring together fatty molecules with water molecules and be able to dissociate them and break them up - to get the stains out of clothes and things of that sort. There are a lot of emulsifiers put into processed foods. And those emulsifiers allow certain chemical reactions to occur that extends the shelf life for those foods. So, it's like candy bars, and cereals, and all sorts of things that are in processed foods. The worst of which are the typical - kind of - pastries that you see at the convenience store. But this extends into chips of various kinds and even some meats of various kinds. They pack this stuff into meats. They have names like soy lecithin and other things. Why are emulsifiers bad? Okay, there are a lot of reasons why they're bad. But the reason why they're bad for the mechanisms that we've been talking about today is that when you ingest those foods, you're bringing those emulsifiers into your gut. And those emulsifiers strip away the mucosal lining of the gut and they actually cause the neurons that innervate the gut - that extend those little processes we call axons - into the gut - to retract deeper into the gut. And as a consequence, you're ingesting a bunch of food and the signals like CCK never get deployed. The signals that actually shut down hunger are never actually triggered. And so, as a consequence, you want to eat far more of these highly processed foods. In addition, if you then go from eating a highly processed food to - to non-highly processed foods, you're not able to measure the amounts of amino acid sugars and fatty acids in those foods as accurately. You've actually done structural damage at a micro-level - but structural-level damage - excuse me - to the mucosal lining of the gut. Now, this can all be repaired if you stay away from highly processed foods for some period of time, but the negative effects of these emulsifiers are quite real.

So, to make it really clean and simple: emulsifiers from highly processed foods are limiting your gut's ability to detect what's in the foods you eat and therefore, to deploy the satiety signals - the signals that shut down hunger. In addition to that, there's a parallel mechanism at play - that I talked about in a previous episode, but I'll remind you again - that you have neurons in your gut that are sensing sugar and are sending a subconscious signal up to the brain via the vagus nerve. And those neurons trigger the release of dopamine - which makes you crave more of that food. So, now you've got parallel signals making you want to eat more sugar, making you unaware of how much sugar you've eaten, and that are disrupting the inputs to the nervous system that signal to the rest of your brain and body that you've obtained enough fatty acids and you've obtained - obtained enough amino acids. So, these highly processed foods are really terrible. And, you know - I'm not out here to say - you know - never enjoy a processed food of any kind. I'd be a hypocrite because I do eat processed foods from time to time. Although, the ones that I tend to eat - I try and make of the healthier variety. But eating whole foods has tremendous value and eating highly processed food has tremendous negative impact on the gut and on the gut-brain axis.

And so, recently there was a paper that came out in Cell - Cell Press journal - it's kind of the apex of Cell journals - which is phenomenal. This paper showed that ingesting highly processed food leads to more intake of not just highly processed foods, but other types of food in general. There was -

kind of - an overeating compensation, generally, across foods for people that consume these highly processed foods. And there are a lot of other reasons to avoid highly processed foods. So again, I don't like to focus too much on the "do not's". I like to arm you with tools "to do". But I think this visual of certain foods and these emulsifiers actually stripping away some of the critical lining of your gut and disrupting the hormone signaling to the brain controlling feeding is important enough and cryptic enough - meaning it hasn't been talked about. It works at a subconscious level. And that it's important that people are aware of it so they can make decisions about what they do want to eat or not want to eat for themselves.

Research - Chris Gardner

Before moving on, I just want to say one more thing about highly processed foods. There was an absolutely beautiful study done by my colleague Chris Gardner at Stanford exploring whether or not certain diets were better than others. They looked at vegan, vegetarian, omnivore - I don't know if they looked at all-meat or not - but they looked at the different forms of diets - intermittent fasting, etc. And they essentially found that whichever diet people adhered to - whichever one they followed - was equivalent to the others - provided that they followed it. They lost the equivalent amount of weight. There really wasn't a strong effect of the food-type or the pattern of eating, etc. However, in a study like that, adherence is very high because people are part of a study. And for many people, the ability to adhere to a certain eating plan is one of the most - if not the most - powerful determinants of whether or not a given diet - meaning nutritional plan - works.

Research - Calorie is Not a Calorie

Now, this thing about highly processed foods, however, is really diabolical because it truly says - and I think the recent data in Cell Metabolism and other journals - really proves that a calorie is not a calorie. That's absolutely absurd because of these emulsifiers and the content of these highly processed foods. In fact, the data - in humans - points to this. So, what they did is they took inpatient adults - so, they had total control over their food intake - and they received either ultra-processed or unprocessed diets for 14 days. It's a short study. The diets were matched for calories, sugar, fat, fiber, and macronutrients. So, everything else was matched - just processed or non-processed is the major variable. And basically what they found is that the people who were eating the processed food diet happened to eat much more, right? This was after this period of putting them on either diet and clamping for all other variables. Then they would eat much more, and the body weight changes were much more, and those body weight changes were such that they couldn't be accounted for by just increased calories. So, the bottom line is that highly processed foods are just bad for you. They increase weight gain. They disrupt the lining of your gut in a way that disrupts things like CCK, and proper satiety signals, and they contain a bunch of things - in particular, sugars - but other things as well - that disrupt not just the hormonal systems, but also the neural systems that control the desire to eat after the diet is done. So, there's just so many reasons why these highly processed foods are terrible and they can explain a lot of the ill health effects that we've seen in the last 50 years - not just in the United States, but all over the world - the enormous increase in diabetes - juvenile diabetes. It's just remarkable how far down the path of bad we've gone. And it's clear - it's almost a smoking gun what the cause of this is. If you'd like to learn

more about that, please refer to the Lustig lecture. He also spells out why non-processed foods is far more economical in terms of - just at the level of the household or individual - as well as at the societal level. Really interesting stuff - I highly recommend you check it out.

Insulin & Glucose

So, now let's move on to some other hormones that regulate hunger and satiety. In particular, insulin. Now, you've probably heard of insulin before. Insulin is the thing that's lacking in type 1 diabetics. That's why they have to inject insulin whenever they eat. The reason they have to do that is because when they eat, their foods are broken down into glucose. And in order to shuttle glucose to the appropriate tissues in the body - and also to keep glucose levels in check - you need insulin. So, the simplest way to think about insulin and glucose is that when you eat, that food is broken down into sugars. That's true whether or not it's fats or it's sugars - or eventually, if it's proteins. They are oxidized into fuels, as we say. And those fuels can be used - as the name "fuel" implies - into energy. They're eventually made into ATP. There's a bunch of biochemical steps that we're not going to go into today, but that's essentially how it works. You break down food into glucose.

Now, if you're ketogenic, we'll talk about that in a little bit. But in general, you eat, food is turned into glucose. Your blood sugar needs to be kept in a particular range. Hypoglycemic means too low. Hyperglycemic means too high. And what they called euglycemic - E-U - glycemic - is the healthy range. Now, what those healthy ranges are - in general, the healthy range - the euglycemic range - is about 70 to 100 nanograms per deciliter, but most of you aren't walking around with a glucose monitor. Some of you are, but most of you are not. The more important question for us to address right now is: Why is it important that glucose be kept at a particular level? Once you understand that, keeping glucose in check starts to have a rationale behind it and the ways to do that start to make a lot more sense. So the reason is, if glucose levels get too high, because of the way that our cells - in particular, neurons - interact with glucose - high levels of glucose can damage neurons. It can actually kill them. You can start getting what are called peripheral - excuse me - peripheral neuropathies. One of the symptoms of some forms of diabetes is that people start losing the sensation of touch in their fingers, or their hands, or their feet - and they can start going blind. There's diabetic retinopathies. So, it's very important that insulin manage your glucose levels. Now, there's also type 2 diabetes where there's insulin secreted from the pancreas, but people are insulin-insensitive. There's a disruption in the receptors and insulin-insensitivity isn't quite the same as having no insulin at all, but it parallels some of the same mechanisms. Now, type 1 diabetes is often picked up because someone has a sudden weight loss - because they're not processing blood sugar the same way they were before. Type 2 diabetes is often - although, not always - associated with being overweight and with obesity. Both of them are - are challenging conditions. Type 2 diabetes almost always can be managed by managing one's weight. And of course, there are prescription drugs and supplements that can help manage those. We're going to talk about all of that. But for most people that don't have diabetes, the important thing is to manage glucose, to keep it in that euglycemic range.

And there are a number of different ways to do that. Some of them are behavioral. Some of them are diet-based. And some of them are based on supplements or prescription drugs. So, let's talk about those now. So, if you eat - and in particular, if you eat carbohydrates - blood glucose goes up. If you eat fats, blood glucose goes up to a far less degree. And if you eat proteins - depending on the protein - it'll eventually be broken down for fuel or assembled into amino acid chains for protein synthesis and repair of other tissues and bodily functions. But glucose goes up and then is kept in range.

Glucagon

When you are hungry, you secrete a different hormone - and that's called glucagon. And glucagon's main role is to pull stores of energy out of the liver and the muscles. And once those are depleted, you'll eventually tap into body fat, okay? And this is for people that have a typical blood glucose range - so, that 70-100 euglycemic range. So, the two - kind of - push-and-pull systems that we're going to think about now - to keep this simple - is that you have the insulin system managing glucose and you've got the glucagon system pulling energy out of your liver and muscles for immediate fuel. And eventually, you'll pull fuel out of body fat, if you've been active for a very long time and all your glycogen stores are depleted or close to depleted.

Tool - Order of Foods

So, what does this all mean? There's a lot of important biochemistry and a lot of important cellular processes involved in whether or not you're anabolic or catabolic - whether or not you're breaking things down or building things up. Let's talk about feeding in a simpler way, however. And let's weave the tools to manage blood glucose - to keep it in check - as we do that. So, let's say you had a meal and that meal consisted of rice - a carbohydrate, some meat or fish - let's say a piece of salmon, and some vegetable - some fibrous vegetable - like asparagus, or cabbage, or something like that. If you were to eat all of that at once - you know - you take a bite of one - a bite of the other - you mix it up - you know - one of these "it all ends up in the same place" - kind of people - mix it all up. Then you will experience an increase in insulin and increase in blood glucose that's moderately fast. It's going to increase pretty quickly. What's remarkable is that the order that you consume each macronutrient has a pretty profound influence on the rate of insulin and glucose secretion into the blood - and how quickly those levels rise. So, if you - we'll make it really simple: if you were to eat the rice first, your glucose would rise in a sharp spike - especially if it doesn't contain any fats to slow the absorption. Now, that might be good if you're very hungry and you want to get an increase in glucose. In fact, this is the reason why you're often served bread before meals because it is - and sometimes it's bread and butter - but - or chips before meals - or appetizer - are designed to get your blood glucose going up high because big steep increases in blood glucose tend to promote the desire to consume more glucose. And this also relates to the dopamine system and the way that something tasty in the mouth - and sugar in the gut - and fats and sugars in the mouth - trigger the activation of a lot of systems in the brain and body to consume more of whatever you have - or whatever is available to you.

So, the basic idea is that eating carbohydrates and/or fats early in a meal will give a steep rise in blood glucose. However, if you were to eat the fibrous thing first - so, a lot of chewing, but not a big rise in blood glucose - because, in general, there's - unless it's laden with sugar or something, we're just talking about a - you know - some - some vegetable - fibrous vegetable - that will actually blunt the release of glucose until you eat the fish and the rice. But believe it or not, it will actually blunt the glucose increase that the rice would cause. Now, I'm not talking about neurotically eating each macronutrient separately in sequence. I'm just trying to give you a picture of what's happening ordinarily.

So, what this means is if you feel a lot of food-related anxiety or you feel you're one of these people that - you can - kind of sense - like your blood sugar increasing very quickly. A lot of people can sense this. Some people can't. It has a lot to do with how well they manage their blood sugar as well as some of the psychological factors. And yes, there are family and historical reasons where - you know - I've got friends who had a lot of siblings and when they sit down to eat, they have to really suppress the desire to not - you know - beat up everyone else at the table and take all the food. It's sort of like not - it's hard for them to understand that there's plenty to go around because of their upbringing. So, there are psychological top-down effects. A lot of the psychology around food is geared towards getting people to be relaxed when they eat and these sorts of things. But these blood sugar effects are real - just cellular and basic biochemistry of how the body manages sugars ingested into the blood.

So, what does this all mean? It means that if you want a steep increase in glucose - you are very, very hungry - then you should eat the carbohydrate-laden food first or you should eat a bunch of macronutrients combined. So, that would be like the hamburger or the sandwich - the - the bread - whatever is in that sandwich altogether - usually that's protein and - and - you know - vegetables as well. If you want to have a - kind of - more modest increase in glucose or you want to blunt the increase in glucose, then have - at least some of - the fibrous thing first. And then, the protein. And then, the carbohydrate. You will notice that your blood glucose will rise more steadily and that you'll achieve satiety earlier in the meal - or at least, you won't get this huge peak. It's sort of the Thanksgiving meal effect. Some of you are international. So, if you are - don't celebrate Thanksgiving, it's a time of year where it - used to be the one time of year or two times a year - where Americans would give themselves permission to eat enormous meals. Now, that seems to happen a lot more often. But there is this effect of you're full and yet, you're hungry for more. That's because your blood glucose has gone through the roof and it's triggered a number of other mechanisms. There's also usually a lot of alcohol consumption and alcohol itself - because it's a sugar - will increase blood glucose very, very sharply. It - it depends on the alcohol. Some alcohols have more sugar than others. But basically what you're trying to avoid are steep increases in blood sugar. And the order that you eat foods has an enormous impact on that.

Tool - Exercise Around Mealtime / GLUT4

The other thing that has an enormous impact on how long and shallow - or how steep - that curve of glucose is depends on whether or not you recently were moving, or moving, or start moving after

you eat. So, it turns out that your blood glucose levels can be modulated very, very powerfully by movement. If you did any kind of intense exercise - or even just walking, or jogging, or cycling - anything before you eat - your blood glucose levels will be dampened somewhat. And that has to do with the release of something called - some people call it GLUT4 - which sounds like "glutton". Other people call it GLUT4. These are things that are involved in shuttling glucose to particular cells in the body - namely toward muscle and glycogen stores and away from body fat stores. It has to do a sequestering of glucose from the blood. The point is that if you're somebody who struggles with blood sugar regulation - in addition to getting your body weight in a healthy range - doing all the other sorts of things that you should be doing - the key thing is to try and get some movement - some time circa meal. Now, very few people can actually eat and walk at the same time - although, I do it all the time. Not because I'm trying to regulate my blood sugar, but just because I tend to be busy. I eat and drive. I eat while I'm busy. Basically, if I'm not giving this podcast or sleeping, I'm eating - except the early part of the day when I fast. But the bottom line here is that if you, for instance, take a 30-minute walk after a meal, your blood glucose will be blunted in ways that are beneficial. If you have exercised in the recent hours before a meal, that can be beneficial. The order that you consume foods is beneficial. And there are a few things that you can consume that can also adjust blood glucose levels. So, let's talk about those. But I thought it was important to really tamp down that it's not just what you eat - we talked about that before - but also the order that you eat those things, believe it or not - whether or not you combine macronutrients, carbohydrates, proteins and fats, and fiber vegetables - and whether or not you've moved recently - the higher intensity of the movement, the - the greater the GLUT4 for increase, and the more that the blood glucose will be blunted, and you'll shuttle more of that to glycogen and muscle stores. And even just moving after a meal - even just a - a calm, easy walk - can really adjust the ways in which blood sugar is regulated for the better.

Hidden Sugars

I don't want to perseverate on this processed foods / hidden sugars thing too much. But understanding now a little bit about how insulin and glucose work, you can probably imagine why hidden sugars are such an attractive thing from the standpoint of processed food manufacturers. Because if they can put sugar in that you can't even taste, that sugar is going to amplify the amount of glucose. It's going to increase the rate of glucose increase into your bloodstream and it's going to promote more feeding. So in that case, you're really being tricked. It's not that you're actually reaching for the additional appetizer and your blood glucose is going up. The food that you ate is actually increasing your appetite as you eat it. It's a positive feedback loop. So, don't want to demonize those any more than I already have, but you should be aware that these things are happening at the level of your bloodstream and brain.

Stable vs Labile Blood Sugar

The other thing I'd like to address for a moment is this notion of stable blood sugar versus labile blood sugar - or unstable blood sugar. Some people just have stable blood sugar. They can go long periods of time without eating and feel fine. Other people get really shaky, really jittery, and/or when they do eat, they feel really keyed up. Sometimes they'll even sweat. Sometimes their vision

will go blurry. And some of that can actually be because they become hyperglycemic. And those effects that you experience when you are hyperglycemic are the early warning signs of the kinds of things that damage neurons and lead to the really terrible stuff that we talked about before - like peripheral neuropathies. Now, it takes some time for those things to occur - those neuropathy to occur. But whether or not your blood sugar is all over the place or whether or not it's stable can be impacted by a number of things.

Tool - Zone 2 Cardio

One of those things is exercise. So, these days there's a lot of interest in what they call "zone 2 cardio" - which is that kind of steady state cardio where you can just nasal breathe - even at pretty high output - where you could maybe have a conversation - although, I'm such a huge proponent of nasal breathing during exercise - most forms of exercise - especially zone 2 cardio - that you probably shouldn't be talking while you're doing that cardio unless it's absolutely essential. But periods of zone 2 cardio that last anywhere from 30 minutes to an hour - or sometimes more for you endurance athletes - can create positive effects on blood sugar regulation such that you - people can sit down and enjoy whatever it is - the hot fudge sundae - or whatever the high sugar content is. And blood glucose management is so good - your insulin-sensitivity is so high - which is a good thing - that you can manage that blood glucose to the point where it doesn't really make you shaky. It doesn't disrupt you. And it - to say nothing of the weight-related issues or the adipose fat gain, etc - that's a separate issue because people vary there. But basically, doing zone 2 cardio for 30 to 60 minutes - 3 to 4 times a week - makes your blood sugar really stable. And that's an attractive thing for a variety of reasons.

Tool - High-Intensity Interval Training (HIIT) / Resistance Training

On the flip side, high-intensity interval training or resistance training - a.k.a. weight training - are very good at stimulating the various molecules that promote repackaging of glycogen. So sprints, heavy weightlifting, circuit-type weightlifting - provided there's some reasonable degree of resistance - those are going to trigger all sorts of mechanisms that are going to encourage the body to shuttle glucose back into glycogen - converted into glycogen, into muscle tissue, restock the liver, etc. Depleting one's glycogen actually takes some time. You know, if you do - you know - a couple sets of tricep extensions and some crunches - you're not depleting your glycogen. Glycogen-depleting workouts are very high intensity. Generally, they're less than an hour or so, but those are the sort that are going to lead to big increases in the kinds of enzymes and metabolic pathways that are going to repack glycogen and shuttle most things towards restorage of foods - not into adipose tissue - not into fat - but taking glucose and making it into fuels that you can access later for more of that high-intensity activity.

And I should mention that one of the advantages of high-intensity interval training or weight lifting of various kinds is that it also - it causes long-standing increases in basal metabolic rate. I don't want to go too far down this path because we're going to do an entire month on - on human performance and athletic performance. But it's not just the increases in muscle that increase metabolism - because muscle burns more energy than other types of tissues - except your brain,

which truly burns the most energy - and is the main reason why your basal metabolic rate is what it is. Well, high-intensity training - so, it could be sprints, it could be high-intensity interval training of different kinds, it could be weight training - also has an effect of increasing thermogenesis even long after you've completed the exercise. So, there's a long tail - there's a - kind of - post-exercise metabolic effect that's also beneficial. So, it's not an either/or. It's really that high-intensity interval training, and resistance training, and things of that sort are very good for one reason. And the zone 2 cardio is very good for other reasons. And now, you can see why. It's just a healthy thing and why most people should probably be doing exercise most days of the week - if not every day of the week - if your goal is to manage blood glucose and your goal is to manage some of the metabolic factors that control repackaging of glycogen and encouraging excess glucose to not get diverted into body fat stores.

Cholesterol / HDL / LDL

We haven't talked a lot about lipids today. That's because most of today's discussion is about hormones - and insulin is the dominant hormone in terms of mobilizing and managing glucose in the body - at least for most people. But fats are very important and there's just a little anecdote about fats that I think will be useful in thinking about why you want to manage what they call the LDL or HDL ratios. And this is deserving of an entire episode - many - perhaps even several episodes. But some of you may be familiar with LDLs and HDLs. Some of you may not. The LDL is low-density lipoprotein. This is the one that you don't want it to be too high. Costello is dreaming. He is barking. He doesn't - he loves all forms of cholesterol. But that's just Costello dreaming. So, LDLs are the ones that you want to keep low. You don't want those to go excessively high. HDLs - the high-density lipoproteins - are the ones that - are the so-called healthy lipoproteins. That's all fine and good. But you might ask yourself, "What are they doing? What is the actual role of these things? And why would you want healthy levels of HDL and not too much LDL?"

Well, one of the reasons is that fats don't like water, right? They are hydrophobic. And yet, you need to move fats in your bloodstream. All tissues in your body need fats. They need cholesterols. They're - last episode, we talked about how cholesterol is a precursor to the sex steroid hormones - estrogen, and testosterone, and other hormones as well. Well, HDL and LDL actually coat fats to allow them to be transported through the bloodstream. They do a number of other things as well. But HDL is a key component of the delivery system that brings those fats to the liver, ovaries, testes, and adrenals. In other words, having adequate levels of HDL is good because it allows fats to be delivered to the tissues that manufacture testosterone, estrogen, cortisol in healthy levels - and the liver. So, this is why when LDLs are too high, what's happening is you're not getting fats to the correct tissues and you can get buildup of fats - so, like fatty liver disease and some of these things can happen. High sugar content can even lead to some of these fatty liver conditions. That's starting to happen. It's actually the first time in human history perhaps - that we're aware of, anyway - that we're starting to see liver conditions that normally were associated only with severe alcoholism starting to come from sugar content.

So, what does this mean? This means keep your LDL and HDL ratios proper. You want those HDLs in order to deliver fatty molecules to the very tissues that use cholesterol in order to manufacture hormones. So, how do you keep LDLs and HDLs in their proper ratios? Well, a lot of people don't realize this, but the debate about dietary cholesterol and its relationship to LDL and HDL ratios is a - it is a barbed wire debate. I don't want to get into it right now. There are still a lot of open questions as to how much dietary cholesterol impacts LDL and HDL ratios. I don't want to get into that now. I'm not taking a stance either way. But what is very clear is that having highly elevated glucose - consuming too much sugar or not managing glucose in your body through some of the mechanisms that we've been talking about up until now, can also negatively impact LDL and HDL ratios. So, managing glucose goes way beyond just managing blood sugar, and making sure that you don't lay down too much body fat, making sure your metabolism stays high, making sure you're not getting jittery at meals. It also has to do with making sure that you're creating enough of the molecules HDL and not too many of the molecules LDL that are going to disrupt the delivery of things to the organs of your body that allow you to make healthy levels of testosterone, estrogen, and so forth.

If that wasn't clear, let me make this ultra-simple. You want healthy levels of HDL and you want low levels of LDL because if you have ovaries, it will allow the fats that need to get to the ovary to produce estrogen to get there. And if you have testes, it will allow the fats and the cholesterol molecules that you need in order to manufacture testosterone to get to the testes. As well, in order to have proper adrenal function and proper liver function, you want HDL and LDL in the healthy correct levels.

Tool - Metformin

So, now we've talked a lot about behavioral tools and the underlying biological mechanisms that justify those tools in particular circumstances. Now, I'd like to turn to supplements and prescription drugs that regulate the hormone systems controlling feeding and satiety. There are a huge number of these. Some have more powerful effects than others. There are two that I want to describe because they've been getting a lot of attention recently. First of all, there's a prescription drug metformin - which was developed as a treatment for diabetes. And it works potently to reduce blood glucose. It has dramatic effects in lowering blood glucose. Metformin involves changes to mitochondrial action in the liver. That's its main way of depleting or reducing blood glucose. And it does so through the so-called AMPK pathway. And it increases insulin-sensitivity overall. Metformin is a powerful drug. In fact, I'm surprised that so many people have sought it out - given that most of the people that I'm aware of that sought it out are not diabetic. I think, for diabetics, it seems to be a useful drug. For non-diabetics, it can also, of course, lower blood glucose. It also has the potential to make people hypoglycemic - genuinely hypoglycemic. So, you really need to approach metformin with caution. I get a little concerned when I hear about people blasting metformin simply because fasted states or low blood sugar states are healthy. Doing that pharmacologically can have long-standing effects. You really want to approach that with caution.

Tool - Berberine

Now, there's a comparable drug. It really should be called a drug. But it's nonprescription. That's also in fairly prominent use out there - called berberine - B-E-R-B-E-R-I-N-E - berberine, correct. So, berberine is a really interesting compound. Its actions very much mimic metformin. So, let's talk about berberine for a second. Berberine actually comes from various plants and tree bark. It is sold in supplement stores. It's sold online. It is, as far as I know, unregulated. It is powerful. If you're going to experiment with berberine, you definitely want to talk to your doctor and you want to approach it with caution. It also works to activate the so-called AMPK pathway. AMPK, by the way, stands for adenosine monophosphate-activated protein kinase - AMPK. And it inhibits a protein tyrosine phosphatase 1B pathway. I think that's enough nomenclature. It inactivates a certain pathway that's associated with fasting and low - low blood glucose. The effects of berberine are, as far as I can tell - when looking at the literature - are very similar, if not identical, to metformin. Now, the number of studies out there on this are many. So, I'm just going to review a few of them and their major effects. As always, I invite you to check out examine.com. It's a wonderful website where you can put in any supplement, or compound, or biological goal for that matter. And it will list out the various effects in the human effect matrix - so, studies on humans - if they're available. And it will tell you whether or not they're strong effects, or weak effects, or modest effects. And it will point to the specific subject population. It's a wonderful resource. So, berberine, not surprisingly, has very strong effects in lowering blood glucose. There are four studies on this. In fact, they say that berberine is one of the more - if not the most - effective supplements for lowering blood glucose. It talks about dosages there. Although, I'll just mention that I've tried berberine and the dosages that are typical on the bottle of most supplements is much higher than I needed. So, when I took berberine, two things happened. First of all, I got a pretty splitting headache. It gave me pretty vicious headache. So for me, it was a "no" almost immediately. The other thing is I became so hypoglycemic that in order to get my blood sugar back up, I think I ate something like 10 donuts. And I didn't feel like I had ingested all that much sugar. It was really kind of weird. I was hyperphagic for sugar. I was craving sugar - craving sugar. And I was very thirsty as well. And so, I don't want to promote any bad behavior. But I know that certain people use this when they've overeat in sugars or they're doing their "cheat days" - something that I'm personally just not a fan of - and they want to keep their blood sugar in check. Or they know they're going to consume a huge meal - they'll take berberine to keep blood glucose clamped. And it does do that.

It has very strong effects - three peer-reviewed studies - on HbA1c levels. HbA1c is something that can be measured in a blood test that is sort of an average readout of your blood sugar levels over the previous two or three months - sometimes shorter period - but that's mostly what HbA1c is about. So, it radically decreases your blood sugar levels. It actually lowers cholesterol. It acts, remember, on the liver. And the liver is involved in cholesterol metabolism. And remember, it's both sugars - blood glucose - and dietary fats - perhaps. It's still heavily debated in terms of how your blood - total cholesterol, HDL, and LDL - are regulated. So, it seems to lower total cholesterol. And it seems like it lowers HDL and LDL in parallel. So, that's interesting. One study showed a minor increase in HDL - the so-called good cholesterol. Insulin levels drop - not surprising. Another study showed a slight decrease in LDL. Those seem to be kind of minor. Here's a kind of interesting one.

Just to help you remember, berberine - as if the fact that it comes from tree bark isn't - you know - trigger enough to remember it - direct contact of berberine on canker sores seems to eliminate canker sores very quickly - which is kind of cool. I've been at canker sores in a few years. But when I did get them, they're extremely painful. I don't like those. So, that's kind of interesting. And there's some study references there.

I find it amazing that these compounds exist. You've got this prescription drug metformin. And then, you've got berberine - this stuff from tree bark. And they have effects that are essentially equivalent to one another. So again, I'm not promoting their use or even their exploration. But those compounds do exist. They're out there. And check out examine.com if you'd like to learn more. Certainly, do your reading - do your homework - before you start just popping this stuff. And if you have hypoglycemia or hyperglycemia, be especially careful. And also, do understand that dosages and dose requirements vary. So, if you do go down this path, really approach things carefully. Always start with the lowest amount that you could get away with. For me, the headache thing just made it a "no-go". I do keep a bottle of it - in full disclosure - in the odd chance that I feel like eating a ton of donuts. It's not so much about not ingesting the calories. It's just that I don't like the feeling of being hyperglycemic - the blurry vision - just feeling lousy. I do love donuts.

Tool - Chromium / L-Carnitine / Panax Ginseng / Caffeine / Magnesium

Other things that impact blood glucose in supplement form - chromium has been shown in 29 studies to have a minor - I want to emphasize a minor effect - on reducing blood glucose. Things like L-carnitine - something we've talked about here on the podcast before - in terms of its relationship to power output in ATP production for both aerobic and anaerobic exercise - as well as sperm quality and egg quality. We talked about that long ago. Things like panax ginseng can have positive effects on - I would - I should say - can have effects of reducing blood glucose slightly. I don't want to give valence to or judgment to whether or not it's positive or negative. Here's something that's interesting that you should know about. Caffeine has very reliably been shown to increase blood glucose just a little bit, okay? So, I always thought that caffeine would drop blood glucose, but it actually can increase blood glucose - just slightly. Things like magnesium. We talked about magnesium for - as a tool for enhancing the passage into sleep. In particular, magnesium threonate and bisglycinate. Magnesium can also have a modest reduction on blood glucose. You're trying to get the impression. Everything reduces blood glucose. But that's certainly not the case.

Tool - Stevia

And then, a couple episodes ago, on the - when we were discussing nutrition, we talked about artificial sweeteners - sucralose, aspartame, NutraSweet - some of those are generic names - some of those might be brand names - and how they have negative effects on the gut microbiome. And that's supported by a number of studies. There's one "artificial sweetener". It's Stevia - S-T-E-V-I-A - which seems to lower blood glucose just slightly. And I still can't find data on whether or not Stevia impacts the gut microbiome in either direction. Many of the things that I consume do have small amounts of Stevia in them, so I'd love to know if anyone out there is aware of quality peer-reviewed research as to whether or not Stevia impacts the gut microbiome - similarly or

differently - from other artificial sweeteners. Please let me know. Please send me the references. I'd really appreciate it. You can put in the comment section on YouTube or elsewhere - comment section on YouTube would be the best place. So, Stevia seems to lower blood glucose a little bit - which makes it kind of an attractive artificial sweetener if one is going to use artificial sweeteners. But remember, sweet taste itself stimulates the desire to eat - which will increase more blood glucose. So, I'm guessing that they probably cancel each other out. So, you have to think logically about these things.

Tool - Vitamin B3 / Zinc / Acidic Juice / Capsaicin

Vitamin B3 - so, some of the B vitamins do indeed stimulate appetite by triggering increases in blood glucose - vitamin B3, in particular. I don't know if B6 does. Things like zinc seem to lower blood glucose. And then, there have been an enormous number of other things that have been tested for their roles in blood glucose. Apple cider vinegar - anything acidic. This is well known now that any kind of acidity - so, it could be lemon juice, or lime juice, or apple cider vinegar - lowers blood glucose slightly. Some of those can also have other effects that we're not talking about today. So, that's kind of interesting because there's a movement now towards creating - sort of - people talk about becoming more alkaline. You know, one of these - I hate to break it to you, but you don't really want your body to be too alkaline. You want to stay in the right pH or else you start - there are conditions that make you more alkaline. You don't want to be too acidic or too alkaline. If you see a beverage or something that purports that ingesting that beverage is going to make you more alkaline, that is absolutely false. There's no evidence for that. It's impossible biochemically. It's just - it's just marketing. But nonetheless, ingesting foods that are acidic can make some slight adjustments to the pH of the gut in ways that can slow or alter the absorption of foods and can blunt blood glucose. You can try this sometime if you want. If ever you're feeling kind of oversugared out - like you ate something with too much sugar - you can drink a small amount of lemon juice mixed with water or lime juice and you'll notice that it will blunt that - kind of - hyperglycemic effect just a little bit. Again, you don't want to use this as a medical tool, but the effect is fairly potent. And then - excuse me - and then, there are a number of other things like capsaicin and hot chili peppers that will lower blood glucose. The list goes on and on. The most powerful one is absolutely berberine and metformin. But those - that's really heavy caliber stuff. And the other ones I mentioned have more minor effects.

Ketogenic Diet

I do want to mention - because I'm sure some of you out there are curious about the ketogenic diet - I'm going to do an entire episode about ketosis, and the brain, and the body - but the ketogenic diet has been shown in 22 studies to have a notable decrease on blood glucose. And that is not surprising because your - the - the essence of the ketogenic diet is that you're consuming very little or zero of the foods that promote big spikes in insulin and glucose. If you consume enough protein, some of that protein can be converted into glucose, of course - through gluconeogenesis. But the ketogenic diet has very strong support as - for its role in regulating blood sugar - which is glucose. But the specific effects of the ketogenic diet - and one particular effect that I'll address later, but I'll mention now - which is the ability of the - the ketogenic diet to adjust thyroid hormone levels in

ways that make it such that if you return to eating carbohydrates after being in ketosis for too long, you don't manage thyroid and carbohydrates as well. That has been shown as well. So, we're going to dive deep into ketosis in a future episode. So, for you ketonistas out there, don't worry. I certainly have nothing against a ketogenic diet. I actually don't have anything for or against any particular nutrition plan. I know it works for me - at least at this stage in my life. And I'll update it if I need to. I'm simply trying to get you as much information as I possibly can so that you can navigate through that landscape in a way that's - in keeping with your particular goals. So, now you understand a lot about blood sugar, and how it's managed, and the ways that you can manage it better depending on your particular needs.

History of Measuring Glucose

This is also a good opportunity for us to look back at some of the medical literature because it really points to just how far we've come in terms of understanding these important mechanisms. And it points us in the direction of some actionable protocols. So, diabetes - which is these huge increases in blood glucose because there's no insulin - was known about as early as 1500 BC - which is just incredible. And the way physicians then understood that certain people had high blood glucose - without actually knowing what blood glucose was - is that they would take the urine of particular patients and they'd find that ants preferably move toward and consume the urine of certain patients and not others. And they understood that there was something in that urine that was correlated with the sudden weight loss and some of the other probably very unfortunate health symptoms that these people were experiencing. So, they knew that there was something in blood and urine. But you might now be asking yourself, "Wait, that's urine?" But as I tell every kid that I meet - two things. I tell a kid, "Your brain is here." I make them point to their head. And then, I tell them, "Do you know what? Do you know that your urine is actually filtered blood?" And they usually go, "Hmm." I get parental permission to do this first. But most adults don't realize that your urine is actually just filtered blood. And that's why if you see blood in your urine, that's a problem. You want to filter the blood. But urine is filtered blood. Now, this business of measuring blood sugar from the urine has been something that lasted way beyond these early stages of - you know - 1500 BC. Turns out that as late as 1674, physicians at Oxford University were figuring out who had pathologically high levels of blood glucose by analyzing their urine. And again, they were measuring the sweetness of their urine. But - and this is medical fact - they would do this by taking urine samples from different patients and tasting them. And they developed an intuitive sense of what excessively sweet urine was relative to the other urine that they had tasted. So, for those of you that are in the medical profession or those of you that are seeking out the medical profession, do understand this is not done anymore. And you can also just reflect on how far we've come in terms of the medical profession itself in our ability to measure things from the blood and measure things from urine without having to ask ants, "Which urine is sweeter?" - or ask oneself, "Which urine is sweeter?" So indeed, we are making progress as a species.

Tool - Maté

Before we close out today, I want to talk about one more tool that many of you will probably find useful. I certainly have. I'm a big consumer of caffeine - although, I don't consume a ton of it. I

consume it very consistently. So, I'm big on consuming maté - which is a strong caffeinated tea. And I generally do that early in the day - although, I do delay about two hours after I wake up for reasons I've talked about in previous episode - to maintain that nice arc of alertness and focus. I do drink black coffee as well - mushroom coffee as well. I love that stuff. But maté, also called yerba maté, is an interesting compound because unlike coffee, it has been shown to increase something called glucagon-like peptide (GLP-1) and increase leptin levels. Now, we didn't talk a lot about glucagon today. Glucagon is really elevated in the fasting state. I mentioned that it's sort of the opposite of insulin in - kind of - rough terms. That's one way to think about it. But GLP-1 - or glucagon-like peptide-1 - is increased by ingesting maté. And it acts as a pretty nice appetite suppressant. Now, I'm not trying to suppress my appetite. I like to eat - as I mentioned before - but it works really well to stimulate the brain, and to give you a level of alertness, and to do a lot of the things that coffee does.

It also contains electrolytes. So, we - meaning our neurons and our brain - run on a variety of factors - electrical activity, and chemical transmission, etc. But they require adequate levels of sodium, potassium, and magnesium. Actually, if you were to learn the biology or the physiology of the action potential - the firing of a neuron - something we teach every first-year neuroscience student - and I'd be happy to teach you if you're interested - you'll hear about sodium rushing into cells and potassium entering and leaving cells in order to allow neurons to communicate. Electrolytes are critically important for the function of the nervous system. And many things that act as diuretics - that promote excretion of water, like caffeine - can also take electrolytes out along with them - in particular, sodium. And sometimes the lightheadedness or the brain fog that people experience isn't just because electrolytes are low, but because they're - kind of - out of balance. So, I like maté because it has electrolytes. It has caffeine. It stimulates the release of this glucagon-like peptide (GLP-1) and it's been a big help to me in extending that early morning fasting window out to about noon or so when I eat my first meal. It also just tastes really good. I don't drink it out of the gourd - even though I have Argentine lineage. The gourd to me is - it's just - kind of - an inconvenience. I drink it out of a mug. There's no promotional here. I have no relationship to any yerba maté plantations or - or - or companies. I just happen to really like this stuff. And the fact that glucagon-like peptide-1 is enriched or is released more when you drink maté and the fact that GLP-1 can regulate blood sugar in ways that keep your blood sugar in that - we called euglycemic - not too high, not too low mode - is one reason why ingesting maté is attractive to me.

If you go to South America, what you'll see - especially among Uruguayans, but also Argentines - is people actually carry a thermos of this stuff with them around and bring it to meals in restaurants. And that's just considered cultural convention. It's not unusual to see that. So, we don't see that so much here in the States, but I happen to really love the stuff. I brew my own because that's the most economical way to do it. And I really enjoy it. It can be a little bitter for some people. The real key there - if you want to know the maté trick - is to not use water that's really boiling hot. You go just shy of boil and then it doesn't - it doesn't have that same - kind of - tobacco-like or really acidic flavor to. It's - it's a little bit - just a little bit sweeter - although, not quite sweet. So, yerba maté -

GLP-1 - can manage - in healthy ways - leptin levels, glucose levels, and glucagon levels - in ways that, if it serves you, you might want to try.

Conclusion

So once again, we covered an enormous amount of material focused on how hormones regulate feeding, hunger, and when one feels they don't need to eat - so-called satiety - that you've had enough. As always, we covered a lot. But I could not be exhaustive about all the information related to this topic. It's just so vast. For instance, we did not talk about thyroid hormone - an extremely important hormone and pathway in the body and brain. We are going to do an episode related to thyroid and tools to regulate thyroid. I promise. Having seen this episode, you will be able to digest that material with far more ease. We also didn't talk about the fact that testosterone and estrogen can impact blood glucose in ways that are opposite to one another - that when estrogen levels are high, appetite tends to be reduced. When testosterone levels are high, appetite tends to increase. So, there are all sorts of interesting interplays between the various hormones. But that's much too much of a deep dive for now. Right now, we've just focused today mainly on things like ghrelin - on things like melanocyte-stimulating hormone - incredible, powerful hormone that can suppress appetite - on things like cholecystokinin that comes from the gut and can suppress appetite - on things like food emulsifiers - on the fact that when you're eating, you are amino acid-seeking even though you might not realize it - that you are also seeking out particular fatty acids - in particular, the conjugated linoleic acid and omega-3s. So, I've tried to give you a number of actionable tools. Many of them are behavioral - behavioral. Some of them are based on supplements or even prescription drugs. Again, always do what's best for your health and do that in company with a healthcare professional. I'm not a physician. I don't prescribe anything. I'm a professor. I profess a lot of things. And I try and share with you what I think to be the best high quality peer-reviewed literature. So, that's what I've done today. I really appreciate your time and intention.

Many of you have continued to ask how you can help support the podcast and we really appreciate the question. There are several ways to do that. The first is to like a video that you've seen, if you like it. And please subscribe to the YouTube channel. That's perhaps the most important thing about the YouTube channel. As well, leave us a comment. If you leave us a comment in the comments section, that helps us. And please ask questions. Those questions and your comments do inform content of future episodes. We read them all - except the negative ones we don't read. I'm just kidding. We read them all. In addition, please subscribe on Apple and/or Spotify - or both if you'd like. And on Apple, you have the opportunity to leave us up to a five-star review, if you feel we deserve that. Apple also lets you leave a comment - some feedback for us as well. Please do check out our sponsors that we mentioned at the beginning of the podcast. That's the best way, perhaps, to support the podcast. As well, we have a Patreon account. It's patreon.com/andrewhuberman. And there, you can support the podcast at any level you like.

And today, as well as in previous episodes, I've mentioned various supplements. If you're interested in seeing what supplements I take and you want to explore some other supplements as well, you can go to [Thorne - T-H-O-R-N-E.com/u/huberman](https://Thorne-T-H-O-R-N-E.com/u/huberman). Thorne is a supplement company that we

believe to have the highest stringency in terms of what they put in the various supplements that they make and the amounts that they put are very accurate. They've partnered with the Mayo Clinic. They've partnered with all the major sports teams. And we've partnered with them because we believe in their levels of stringency and accuracy. If you go to thorne.com/u/huberman, you can see what I take and you'll also get 20% off any of those supplements or any of the other supplements that Thorne makes. So, that's where you can find out more about supplements and the ones that I take. And again, you get the 20% discount on any supplements that Thorne makes. And last but not least, thank you for being with us. I hope you learned a lot. I hope you explore some of the tools and that the mechanistic information that you learned today will serve you well. If you know anyone that's interested in this topic or you think that someone could benefit from it, please suggest the podcast to them as well. And most of all, thank you for your interest in science.