

Controlling Sugar Cravings & Metabolism with Science-Based Tools | Huberman Lab Podcast #64

I explain how to blunt sugar cravings through fundamental knowledge of how sugar is sensed, metabolized, and utilized within the body. I explain how sugar is processed through the digestive tract and nervous system and how both the taste and nutritive components of sugar can lead to specific appetite changes and cravings. I discuss the connection between sugar, dopamine, and cravings and outline many tools to curb sugar cravings, specifically craving highly processed refined sugars.

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- Welcome to the Huberman Lab Podcast, where we discuss science and science based tools for everyday life. I'm Andrew Huberman, and I'm a professor of neurobiology and ophthalmology at Stanford School of Medicine. Today, we are going to discuss sugar, in particular, how our nervous system regulates our sugar intake and our are seeking of sugar. We're also going to discuss how sugar regulates our nervous system. And as you'll soon learn, sugar really impacts our brain and body by two main mechanisms. One of those mechanisms is based on the sweet taste of sugar, which itself is rewarding. Even if you're not much of a sweet tooth, I confess I'm not, most people enjoy sweet tastes more than bitter tastes. And the sweet taste of sugar and its various forms, is strongly reinforcing, meaning it triggers the activation of neurons, nerve cells in the brain and body, that make us want to consume more of that sweet substance. Incidentally, sweet tastes also make us want to eat more of other substances as well. You may be familiar with that phenomenon. Now sugar also triggers mechanisms in the brain and body based on its nutritive content, independent of its sweetness. What that means is

that the actual caloric content and the way that sugar interacts with your nervous system at a subconscious level, without your awareness, also impacts your craving and seeking of sugar and other foods. Today, we are going to discuss what happens when you ingest sugar in terms of your body's reaction and your brain's reaction. We are also going to talk about what happens when you don't ingest enough sugar. 'Cause it turns out sugar is such a powerful fuel for the brain that under conditions where people don't ingest enough sugar, or where their so-called blood glucose, which is basically blood sugar of a particular form gets too low, their neurons don't function as well. That said, there are conditions of very low blood sugar in which neurons can function even better. So today we are going to talk about the ins and outs, the ups and downs of sugar as it relates to your nervous system. And by the end of this episode, I'm confident that you have a much clearer picture as to how much sugar you should be ingesting, whether or not you should avoid sugars that you're currently eating, and you will certainly understand much, much more about the energy and fuel sources that your brain relies on, which I'm certain will allow you to make

00:02:25 The Brain-Body Contract

better informed choices about the foods you eat and avoid toward mental health, physical health, and performance. I'm pleased to announce that I'm hosting two live events this May. The first live event will be hosted in Seattle, Washington on May 17th. The second live event will be hosted in Portland, Oregon on May 18th. Both are part of a lecture series entitled The Brain-Body Contract, during which I will discuss science and science based tools for mental health, physical health and performance. And I should point out that while some of the material I'll cover will overlap with information covered here on the Huberman Lab Podcast, and on various social media posts. Most of the information I will cover is going to be distinct from information covered on the podcast or elsewhere. So once again, it's Seattle on May 17th, Portland on May 18th, you can access tickets by going to [Hubermanlab.com/tour](https://hubermanlab.com/tour). And I hope to see you there.

00:03:13 Thesis, AG1 (Athletic Greens), InsideTracker

Before we begin, I'd like to emphasize that this podcast is separate from my teaching and research roles at Stanford. It is however part of my desire and effort to bring zero

cost 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 Thesis. Thesis makes what are called nootropics, which means smart drugs. Now, to be honest, I am not a fan of the term nootropics, I don't believe in smart drugs in the sense that I don't believe that there's any one substance or collection of substances that can make us smarter. I do believe, based on science, however, that there are particular neural circuits and brain functions that allow us to be more focused, more alert, access creativity, be more motivated, et cetera. That's just the way that the brain works, different neural circuits for different brain states. And so the idea of a nootropic that's to make us smarter all around, fails to acknowledge that smarter is many things. If you're an artist, you're a musician, you're doing math, you're doing accounting, at different parts of the day, you need to be creative. These are all different brain processes. Thesis understands this. And as far as I know they're the first nootropics company to create targeted nootropics for specific outcomes. They only use the highest quality ingredients, which of course is essential. Some of those I've talked about on the podcast, things like DHA, Ginkgo biloba, phosphatidylserine. They give you the ability to try several different blends over the course of a month, discover which nootropics work best for your unique brain chemistry and genetics and goals. And with that personalization, design a kit of nootropics that's ideal for the different brain and body states you want to access. I've been using Thesis for more than six months now, and I can confidently say that their nootropics have been a total game changer. My go-to formula is the Clarity Formula, or sometimes I'll use their Energy Formula, before training. To get your own personalized nootropic starter kit, go online to take thesis.com/huberman. Take a three minute quiz and Thesis will send you four different formulas to try in your first month. That's takethesis.com/huberman and use the code Huberman checkout for 10% off your first order. Today's episode is also brought to us by Athletic Greens, now called AG1. Athletic Greens is an all in one vitamin, mineral and probiotic drink. I've been taking Athletic Greens since 2012, so I'm delighted that they're sponsoring the podcast. The reason I started taking Athletic Greens and the reason I still take Athletic Greens once or twice a day is that it helps me cover all of my basic nutritional needs. It makes up for any deficiencies that I might have. In addition, it has probiotics, which are vital for microbiome health. I've done a couple of episodes now on the so-called gut microbiome and in the ways in which the microbiome interacts with your immune system, with your brain to regulate mood, and essentially with every

biological system relevant to health throughout your brain and body. With Athletic Greens, I get the vitamins I need, the minerals I need, and the probiotics to support my microbiome. If you'd like to try Athletic Greens, you can go to athleticgreens.com/huberman and claim a special offer. They'll give you five free travel packs, which make it easy to mix up Athletic Greens while you're on the road. Plus a year's supply of Vitamin D3+K2. There are tons of data now showing that vitamin D3 is essential for various aspects of our brain and body health. Even if we're getting a lot of sunshine, many of us are still deficient in vitamin D3. And K2 is also important because it regulates things like cardiovascular function, calcium in the body, and so on. Again, go to athleticgreens.com/huberman to claim the special offer of the five free travel packs and the year's supply of Vitamin D3+K2. Today's episode is also brought to us by 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 believer in getting regular blood work done for the simple reason that many of the factors that impact your immediate and long term health can only be assessed with a quality blood test. What's unique about InsideTracker is that while there are a lot of different tests out there for hormones and metabolic factors, et cetera, with InsideTracker, you get the numbers back in terms of your levels, but they also give you very clear directives in terms of lifestyle, nutrition, and supplementation, that can help you bring those values into the ranges that are best for you and your health goals. And that's very different than a lot of the other programs where you get a lot of information, but you don't really know what to do with that information. InsideTracker makes that all very easy to understand and very actionable based on the very easy to use dashboard at InsideTracker. If you'd like to try InsideTracker, you can visit insidetracker.com/huberman, to get 20% off any of InsideTracker's plans.

00:07:40 Sugar & the Brain

Just use the code Huberman at checkout. Okay, let's talk about sugar, let's talk about how sugar impacts your brain, and how your brain impacts your pursuit or your avoidance of sugar. Let's get a few things out of the way first. The first thing is that there's nothing inherently bad about sugar. I know the word sugar gets a bad rap nowadays, and indeed, you're going to hear over and over again, during this podcast, that consuming a lot of refined sugars, in particular high fructose corn syrup, is known to

have a very large number of bad effects on the brain and body. I don't know that there's anyone that really debates that anymore. Even if we just agree, and I think we should all agree, on the so-called calories in, calories out principle, right? It's a principle thermodynamics that if we ingest more energy than we burn, we are going to gain weight. If we ingest less energy than we burn, we are generally going to lose weight. And if the two things are in balance, ingestion and burning of energy, well, then we're going to maintain weight. So everyone agrees on that, I agree on that. But beyond, there are a number of ways in which particular nutrients, in the case of today's episode, sugar, impact the way that the brain works, such that we tend to seek out more of particular nutrients. For instance, if we eat sugar, there are two, or at least two mechanisms, by which we will crave more sugar. I think most people are aware of that experience, but today I'm going to explain exactly how that works. But also that when we ingest sugar it has a bunch of different effects on the way that our neural circuits work that can allow us to be more or less focused, more or less agitated, a more or less happy, more or less depressed in some cases. So today, as we explore this thing we're calling sugar, we are going to explore that mainly in the context of the nervous system, but also in the context of how the nervous system regulates many, many functions and behaviors that are important to all of you, your ability to think, your ability to extra size, your ability to gain weight, lose weight, whatever your goals might happen to be, sugar plays a critical role in achieving those goals. And in some cases, if you're ingesting too much at the wrong times or the wrong forms, sugar can actually impede those goals. In fact, sugar can prevent all the right behaviors from allowing you to achieve the goals that you want. So today we are going to place sugar into its proper context. The way I want to start off by doing that

00:10:06 Appetite & Hormones: Ghrelin & Insulin

is to tell you a little bit of what happens when we eat and a little bit of what the brain does to respond to those events. So what happens when we eat? Well, I've done an entire episode on metabolism. So if you're interested in the full cascade of hormonal and neural events that occurs when we eat, please check out that episode. But for the sake of today's discussion, let's just take a, what I call top contour view of the hormonal response to ingesting food. Now, anytime we eat, that is the consequence of a number of things that happened before we ate. There's a own in our brain body called Ghrelin,

spelled G-H-R-E-L-I-N. Ghrelin is a hormone that increases depending on how long it's been since we ate last. So the longer it's been since we had a meal, Ghrelin levels are going to be higher and higher and higher, and it essentially makes us hungry by interacting with particular neurons in an area of the brain called the arcuate nucleus of the hypothalamus and some other areas as well, like the lateral hypothalamus. You don't need to know the names of those brain areas, but if you'd like to know them, there they are. Ghrelin increases, it tends to make us hungry. And then when we eat, typically what happens is Ghrelin levels go down. So it's a very logical system. Now, when we eat, assuming that we eat carbohydrates, but even if we just eat some protein and some fats, we will experience a slight, or in some cases, a large rise in blood glucose, blood glucose is simply blood sugar. And the body and brain, we should say in particular, the nervous system doesn't function well if blood sugar is too high or too low. So as a consequence, we have another hormone, which is released from the pancreas, which is called insulin, which helps regulate the amount of glucose in the bloodstream. So even if you were to ingest an entire cup, an eight ounce cup of pure table sugar, which would send your blood glucose very, very high, assuming that you have a normal insulin response, that you're not diabetic, that insulin response would help clamp that blood glucose level so that it did not cause damage to your brain and body. Because if blood sugar goes too high, it's actually toxic to neurons and other cells of your body, it can kill them off. And neurons of the central nervous system, meaning the brain and spinal cord, once they are dead, they do not come back. So your biological systems understand this at a biological level that is, and prevent that death of cells due to high blood sugar, by keeping insulin around, in order to clamp blood glucose. Diabetics, we call them type one diabetics, who don't make insulin, have to take insulin when they eat in particular, when they eat foods that raise their blood sugar, specifically to avoid that neurotoxicity and the other deleterious effects of high blood sugar. So Ghrelin is a hormone that goes up the longer it's been since we've eaten, it tends to stimulate hunger. When we eat, Ghrelin is suppressed. Blood glucose typically goes up, especially when we eat a carbohydrate containing meal. When blood glucose goes up, it's regulated in the body, meaning its peaks and its valleys are more or less smoothed out, and that glucose is sequestered, it's taken away where it needs to be taken away. And in certain locations, it's delivered to cells so that those cells can use the glucose. Now, one of the chief organs for glucose utilization is the brain, neurons are tremendously metabolically active. And their preferred mode of metabolism is glucose metabolism. In other words, neurons

basically run on sugar, which is not to say that you should eat a lot of sugar. As you'll see today, there are states of mind and body, for instance, fasted states, in which people report having immense amounts of mental clarity and their blood glucose is actually quite low. So it is simply not the case that the more sugar that you ingest, the better that your brain will function. But it is the case that for most people, meaning people who are not on a ketogenic or very low carbohydrate diet, they're not adapted to low carbohydrate diets, that neurons in their brain and body are using glucose in order to function. That's what allows those neurons to fire electrical potentials, that's how we refer to it, firing, meaning sending electrical signals down their length to communicate with other neurons.

00:14:17 Glucose & Brain Function

To illustrate just how important glucose is for brain function, I'd like to describe a study that just recently came out, that sits on a long history of similar studies. But the one that just came out is particularly interesting. Now I want to point out that, unless I say otherwise, I'm going to refer to typical diets, meaning I have to believe that most people out there are ingesting some starch or carbohydrate. I do realize there are people following very low carbohydrate diets or moderately carbohydrate diets. I even know that there's some folks out there who are on the so-called carnivore diet, they only eat meat and organs, maybe a little fruit. But I'm going to assume that the vast majority of people listening ingest proteins and carbohydrates. So unless I say ketogenic, or I emphasize ketosis itself, which I will, I'm referring to a kind of typical diet where people are consuming fats, proteins and carbohydrates. I count myself as one such individual. At some point I might try the carnivore diet, who knows, I might I a pure vegan diet, who knows. But for my entire life up until now, I'm 46 years old, I've been a proud omnivore, meaning I've tried to eat high quality as much as I can, unprocessed foods, I try and really avoid highly processed foods. But I do eat from those three macronutrient groups, proteins, carbohydrates, and fats, and I'm going to assume that most of you do as well. The study I'd like to emphasize, recorded from neurons, nerve cells, in the brain, in particular in the part of the brain that responds to visual images, the so called visual cortex. And neurons in the visual cortex are beautifully tuned, as we say, to particular features of what we see. The primary example of this, the kind of classic example, is if you put a little electrode next to a neuron in your visual cortex, or if

we put you into an fMRI scanner machine, which can detect neural activity, and I were to show you a bunch of just little lines, bars of light, they could be dark bars of light, they could be light bars of light, on a screen in front of you. So some would be vertical, some would be horizontal, some would be at 45 degrees, what we would see is that some neurons respond best, meaning they fire a lot of electrical activity to vertical lines, other ones respond to horizontal lines, and others respond to 45 degree lines. And this so called orientation tuning, meaning because of the orientation of the line, is a cardinal classic feature of the way that your visual system is built. And everything that you see, whether it's a face or a dog or a cat or a landscape, is built up from these very simple neuron responses. In other words, when you look at a face, there are neurons deep in the brain that respond to faces. But the only reason that those neurons can respond to those faces is because they receive signals from neurons in your visual cortex. Some of which respond to vertical lines, some of which respond to horizontal lines, and some which respond to 45 degree lines. And all of those are built up in what we call a hierarchical representation, which just fancy language for those are the building blocks by which you see a face and you recognize a face. And it's really an amazing phenomenon, it happens very, very fast. You never notice that you're doing this, but everything is built up from these fundamental orientation-tuned neurons. Now orientation-tuned neurons are so fundamental that they are the building blocks by which you make up all other things that you see, it's the way you read, it's the way that you recognize faces, as I mentioned, and everything else. Experimentally, it's quite straightforward to measure how sharply tuned one of these neurons is. In other words, if I were to show you a vertical line and find a neuron in your brain that responds to vertical lines, I could also ask whether or not that neuron fires any electrical activity in response to a line that's not quite vertical, maybe just 10 degrees off vertical or 20 degrees or 30 degrees. And what I eventually would find is that that neuron was orientation-tuned over a particular range of angles. It's not only going to respond to vertical lines, it's also going to respond to lines that are about 10 degrees off vertical on either side, but probably not much more, maybe 20, but usually it's going to be anywhere from vertical to just tilted slightly. In the recent experiment that was published in the journal, "Neuron," Cell Press journal, excellent journal, the authors asked a really interesting question, they asked whether or not the sharpness of tuning, the precision of orientation tuning of these neurons is dependent on blood glucose level. So just to cut to the chase, to give you the answer, what they found is that when subjects are well fed, neurons that responded to

vertical, responded very strongly to vertical, but not very much at all to other angles, of what we call stimuli, so lines that are 10 degrees or 20 degrees off. If they looked at neurons that were primarily tuned, right, that preferred horizontal lines, they found the same thing. So it wasn't something unique to vertical lines. What they basically found was the sharpness, the precision of tuning of neurons in the brain, was best when subjects were fed. And conversely, when subjects were fasted, the orientation tuning of these neurons became much broader. What it meant was that a neuron that normally would only respond to vertical now responded to other angles of lines as well. You might say, well, that's great, right, these neurons that at one point could only do one thing are now tuned to other things. But it's not so great because what that means is that in the fasted state, your perception of the outside world is actually distorted, it's blurred, it's not as precise as it is when you're fed. And when I say fed, what I really mean is when glucose is available to neurons. Now, for some of you, maybe many of you, and including myself, intermittent fasting, or some variant thereof, is actually a state that I like. It allows me to focus. For instance, as I mentioned before, and even earlier in this podcast, I tend to eat my first meal sometime around 11:00 AM. And then I generally eat my last meal sometime around 8:00 PM, plus or minus an hour on either side, I'm not super strict about it. And occasionally I'll wake up really hungry and I'll eat something before 11:00 AM. I'm not super strict about this intermittent fasting thing. It just seems to be how my appetite works best, given my schedule, et cetera. In the morning, I tend to be most focused. And I always associated that with the fact that I was fasted. I ingest water and some caffeine about 90 minutes after waking up, I drink my caffeine, but I hydrate from the time I get up, et cetera, et cetera. And I know a lot of other people have had the experience of being fasted and feeling like they have a lot of mental clarity. When you are in a fasted state, typically you are going to use fuels that are available to the neurons, based on your intake of food the day before, maybe you're using some glycogen, maybe you're using some fat, maybe you're using some blood sugar, that's derived from other storage sites in the body. You don't actually use fat as a fuel source for neurons under typical conditions. But there are ways in which proteins and fats and glycogen, et cetera, are converted into fuel that neurons can use. What's interesting about this study is that the study says that when well fed, meaning when blood glucose, sugar, is at a properly elevated level in the bloodstream, it can be delivered to the brain in a way that allows neurons to work best, which is really all just to underscore the point that I made earlier, which is that your nervous system is extremely metabolically

demanding, and it loves glucose, neurons love glucose. So the takeaway from this study is not that you should avoid fasting, the takeaway from this study is that there are elements of the fasted state in particular the elevations in things like epinephrine and norepinephrine, also called adrenaline and noradrenaline, that can give us this kind of clarity of mind that many people are pursuing when they fast. That's kind of one of the reasons a lot of people fast, they like the way that they feel, mentally and physically. But I think it's only fair to point out that glucose is the preferred source of fuel for the brain. And this study that I mentioned is one of many studies that have explored how nutritional status or blood glucose status in the brain and body influence neuronal tuning and neuronal function. And it really points to the fact that ultimately, your brain as an organ, is a glucose consuming machine. Now, when you eat a food, that food is broken down and if it contains carbohydrates, it's going to be converted into glucose. And that glucose can't get directly into the brain as a fuel source. It actually has to be carried across the so-called blood brain barrier, the BBB, and the actual metabolism of glucose and the delivery of the glucose to the neurons is carried out by a different cell type. And it's a cell type that you should all know about because it's the most abundant cell type in your brain, and maybe even in your entire nervous system, and that's the so-called astrocyte. Astrocytes are one of several types of glia, the word glia means glue. But many people have taken that name, glia, glue, to think that, oh, the only thing that the astrocytes are doing is just kind of holding things together. Actually, the astrocytes are involved in delivering glucose to the neurons, they are critically involved in shaping your neuronal function and brain plasticity, the brain's ability to change in response to experience. So these astrocytes are like the little waiters and waitresses bringing glucose to the neurons and the neurons are going to do the heavy lifting that's involved in perception and behavior and action. So if prior to this episode, you didn't already realize that glucose, blood sugar, is vital to the function of your brain and other neurons of your nervous system, now you know. And for those of you that have experienced the increase in mental clarity that comes after a properly timed, properly composed, meaning it has the right macronutrients in the right ratios, and a properly sized meal, well then now you have justification for eating something as a way to improve the way that your brain works. It turns out that your brain is going to work best when it's got glucose available, whether you like to fast or not, that's just the reality of things.

The same thing is also true for the neurons in your body. The way that you are able to move the limbs of your body, the way you are able to perform exercise or movement of any kind for that matter, is because as neurons, called motor neurons, send electrical potentials to the muscle fibers, they release a neurotransmitter called acetylcholine, which causes contraction in the muscle fibers, and allows you to move your limbs. Those neurons are also very metabolically demanding, especially when you're doing demanding types of physical work, and that could be cycling or running or weightlifting or yoga or whatever it may be. Those neurons require a ton of glucose. If you've ever had the experience of having to think very hard about how you're generating a movement or force yourself to continue to endure in a given exercise, you might have thought, oh, you know, I'm running out of fuel, that's why I'm getting tired, it's hard to do. That's actually the case sometimes, but that's not always the case. One of the reasons that it feels like work is because your so called upper motor neurons, the ones that control the lower motor neurons in your spinal cord, which control your muscles, they have to be very metabolically active. It's one thing to engage in a reflexive movement where you're just walking around or if you're running continuously. But when you suddenly have to focus on what you're doing, and you have to generate specific patterns of motor movement, well, that feels demanding because one, it increases the release of adrenaline in your brain and body, which makes you feel a little bit agitated and more alert, but also deliberate thought, deliberately controlling the way that your brain and body is moving, requires more glucose uptake, more energy in those very neurons. And this is also why after doing a long about of exercise, you might be tired, but also if you do a about of skill learning of any kind, or if you've been reading and thinking about what you're reading, or if you had a intense conversation with somebody where you're really forcing yourself to listen, and hopefully they're listening to you too, and you're really trying to parse what they're saying, and maybe you're doing that right now, and you're trying to really track something, that's work,

00:26:16 Fructose vs. Glucose

and that work requires glucose uptake by neurons, both in the brain and in your body. Now that we've established that glucose is the preferred source of fuel for the nervous system, I'd like to concentrate on a few of the other types of sugars that we ingest on a

common basis, and the impact that those have on brain function and body function. I'd particularly like to focus on fructose. Fructose, of course, is found in fruit, it's also found in the infamous high fructose corn syrup, which we will talk about today. It's worth pointing out that the concentrations of fructose in fruit is quite low compared to the concentrations of fructose in high fructose corn syrup. High fructose corn syrup is approximately 50% fructose, which turns out to be an enormously high percentage of anything, really, especially when we cut contrast that to the concentrations of fructose in fruit. Fruits have other types of sugars in them as well. You know, the sucrose content of most fruit and fruit juices is low. Although there are some fruits like melons, peaches, pineapples, and so forth, that contain a little less than 10% or so of sucrose. Things like mangoES can have a lot of sucrose. But typically the amount of fructose, fructose, I think is the proper pronunciation, people are always correcting me. Fructose is anywhere from 1% to about 10%, right? It's really going to vary quite a bit. And many of you have probably heard of the so-called glycemic index, which is basically a measure of how fast blood sugar rises after eating particular foods, et cetera. We're going to set aside the glycemic index for now, we will come back to it. It has some relationship to the concentrations of fructose in fruit. But the point that I'd like to make is that fructose as a sugar, is handled very differently in the body than is glucose. But I also want to emphasize that because the percentage of fructose in fruit is rather low, especially compared to high fructose corn syrup, many people have demonized fructose saying that fructose makes you fat, or that fruit makes you fat. If you look at the data, that's not really the case. The fact of the matter is that the concentrations of fructose in fruit are so low that unless someone is consuming a lot of fruit, or they're consuming a lot of fruit on the backdrop of a highly processed diet or a diet that has a lot of other stuff that they might not want to be ingesting, you can't really say that fructose is fattening. I don't really think that there's any basis for saying that fructose itself is bad. Now high fructose corn syrup is a different issue, and too much consumption of anything, fructose included, whether or not it comes fruit or otherwise, can be a problem for the ways that it impacts the neural circuits that process sugar, not just glucose, but fructose. And so we'll illustrate those neural circuits in a bit, and it'll become very clear to all of you, regardless of whether or not you have a background in biology or metabolism, nutrition, or otherwise, why ingesting very high concentrations of fructose is not going to be a good thing for the way that your brain functions. One of the key distinctions between glucose and fructose is that fructose most likely cannot directly access the brain. It actually

needs to be converted into glucose in the liver. And the way that conversion occurs feeds back to a set of hormones and neural pathways that we talked about earlier, which have a lot to do with appetite. And to just summarize what is now a lot of very solid data, fructose and specifically fructose, has the ability to reduce certain hormones and peptides in our body whose main job is to suppress Ghrelin. As you recall, Ghrelin is a hormone that increases the longer it's been since we've eaten, and Ghrelin makes us hungry by stimulating particular neurons in our hypothalamus, it actually makes us really want to eat. And in particular, really makes us want to eat sugary and fatty foods. Fructose reduces the activity of the hormones that reduce Ghrelin. And so the net consequence of that is that fructose increases Ghrelin. So, although I and I think pretty much everyone out there, say for a few individuals, agrees that calories in and calories out is the fundamental principle of weight loss, weight maintenance or weight gain. Ingesting fructose shifts our hormone system, and as a consequence, our neural pathways within our brain, the hypothalamus, to be hungrier regardless of how many calories we've eaten. Now I also want to be absolutely clear, this does not mean that eating an apple or eating a melon or eating a couple of apricots or something is going to make you hyperphagic, meaning it's going to make you just want to eat, eat, and eat, that's simply not the case. But if you compare fructose and you compare glucose, not only are they metabolized differently in the brain and body, but in addition to that, fructose has this impact of reducing the hormones that reduce hunger hormones in neural circuits. And so fructose does have this kind of twist in its phenotype, right? Or I guess if fructose had a dating profile, this would be a kind of a red flag in that profile, because fructose itself, while it's actually a pretty good fuel source in many ways, and it's often packaged in things like fruits, which bring along fiber and vitamins and minerals, that I think for many of us are things that we should be eating more of and ingesting more of, it can suppress the pathways that suppress hunger. And as a consequence, it can increase hunger. So current recommendations for most people are to eat more fruits and vegetables. But for those of you that are trying to control your hunger, ingesting a lot of fruit to is probably not going to be a good idea. Certainly, ingesting it from high fructose corn syrup is not going to be a good idea because of the enormous percentages of fructose in high fructose corn syrup, 50%, or sometimes even more. But even from fruit, some people will find that fruit really quenches their appetite. Other people will find that fruit stimulates their appetite. And I suppose if you're trying to stimulate your appetite, then ingesting more fruit might actually be advantageous to you. So fructose

provides a bridge for us between a particular kind of sugar, hormone function,

00:32:41 When to Eat High-Sugar Foods?

in this case Ghrelin and the hypothalamus. which leads us to the next question, which is what is it about sugar that makes it such an attractive thing for us? Why do we like it so much? And the obvious answer that most people arrive at is, well, it just tastes really, really good. But that's actually not the way it works. The rewarding property is as we say of sugar, whether or not they come in the form of sucrose or fructose or foods that increase glucose to a very high level, actually is not just related to the taste of the foods that produce that elevation in glucose, sucrose, or fructose. It is in part, but that's only part of the story, and the rest of the story, once you understand it, can actually place you in a position to much better control your sugar intake of all kinds, but also your food intake in ways that can allow you to make much better choices about the foods you ingest. And actually at this point, I should probably give a confession, I've said today, and I'll say it again, and I've said it I'm pretty podcast. I don't have much of a sweet tooth and indeed that's true. And I can kind of pass on chocolate or ice cream or things like that, it seems like with each successive year, sweet things are less and less appealing to me. Of course, savory foods, anything that is really fatty, salty, savory, those don't last long in my presence, but I always say, I don't really like sweet things so much, and I like sweet people, but I don't tend to like sweet foods, which is true. But there's probably one exception and that's mangoes. And it turns out that mangoes have the highest percentage of sugar in them, in particular fructose, as well as other forms of sugars. So what I do, because I love mango so much, is I will have mangoes probably twice a week, but I'll have them after some sort of resistance training or hard run or something like that. Because it is the case that after you exercise hard, in particular exercise that is of the high intensity variety, that your body is more efficient at using circulating sugar. It's able to store that or use that for fuel. And so what I'll typically do is just take the mango, I actually eat the peels too. I know there probably some people are going to cringe when they hear that, I find them delicious. So I'll just bite into those things like apples, I don't eat the pits, however. So now I want to take us on a journey

00:35:01 Sugar's Taste vs. Nutritive Pathways, Sugar Cravings

into the nervous system to explain, the pathways in the brain and body that regulate our appetite for sugar. Now, keep in mind what I already told you before, which is that when we ingest foods, they're broken down into various components and glucose is going to be shuttled to the brain, and of course, to other neurons in our spinal cord and elsewhere, and to our muscles, cetera, in order for all of those cells and organs and tissues is to be able to function. The fact that so many cells and organs and tissues require glucose in order to function has led to a situation where you have dedicated neural machinery, pieces of your brain, that are almost entirely, if not entirely devoted, to seeking out of sugar or foods that contain sugars. And to make sure that you not only seek those out, but you know where those foods are and that you ingest more and more and more of them. And there are two main ways that these neural circuits work. In fact, we can see that there are two neural circuits entirely that work in parallel. And this is a common theme throughout the nervous system, and that's parallel pathways. Parallel pathways are the ways that you can distinguish light from dark, parallel pathways are the ways that you can distinguish high pitched sounds from low pitched sounds, parallel pathways are the ways that you can flex your muscles versus extend your muscles. For instance, if you move your wrist closer to your shoulder, you're flexing your bicep and you're actually inhibiting, you're actually preventing the action of your tricep. If you move your wrist away from your shoulder, you are essentially using your extensor, your tricep, and you're inhibiting the activity of your bicep. So for every function in your body that you might think is controlled by one brain area or one neural circuit, almost always there are two or more so called parallel pathways that ensure that that particular behavior happens. Now, in the case of sugar consumption, the two parallel pathways involve one pathway related to the actual taste and the perception of taste that lead, not just you, but every animal that we're aware of, to seek more sweet containing foods. The other parallel pathway is related to the nutritive component of sweet foods. Meaning the degree to which a given food will raise blood glucose. I want to repeat that. One pathway in your brain and body is devoted to getting you to seek out sweet tasting things that you perceive as sweet, and another parallel pathway is devoted to getting you to seek out foods that lead to increases in blood glucose. It just so happens that the foods that lead to big increases in blood glucose typically are associated with that sweet taste. Now, this is distinctly different than the neural pathways that control seeking of savory foods or salty foods or spicy foods, for that matter, or bitter foods. The sweet pathway is what we would call hardwired. It exists, as far as we know, in every mammal, it even exists in fruit

flies, hence fruit fly. Basically getting sweet stuff into the body might seem like it has a lot to do with the taste, but it has just as much to do with the nutritive components that sweet tasting foods carry, and the fact that your nervous system and so many cells in your brain and body run on glucose. If you recall earlier, I said, even if you ingest fructose, fructose can be converted into glucose in the liver. And I mentioned, of course, that fructose may actually work directly on the brain, that's still unclear for humans, the jury's still out on that, we will see. But the fundamental thing to understand here is that when you think you want a piece of chocolate or you think you want a piece of cake or you're craving something sweet, you are both craving the taste and your neurons are literally craving the nutritive components that arrive with that taste. And simply by understanding that can allow you to circumvent some of the sugar cravings that you might otherwise be a complete hopeless victim to. Also in this episode, I will talk about ways that you can sort of undermine or short circuit these circuits, if you will, in order to reduce sugar cravings on a regular basis, if that's your goal. Two parallel pathways, one of the parallel pathways has to do with conscious perception. So animals of all kinds of mice, rats and humans, will prefer sugary taste to non-sugary taste. When we eat something that tastes sweet, we register that sweet taste by way of sweet receptors, literally little ports or portals of neurons on our tongue and on our pallet, a lot of people don't realize this, but there are a lot of taste receptors on the soft pallet and around the mouth, on the sides of the mouth. So you're actually tasting things, not just with your tongue, but with your entire mouth and your pallet. So when you ingest something sweet, very quickly there are signals sent from those neurons in your mouth to brain areas that cause you to seek out or at least pay attention to, the source and the abundance of those sweet things. They literally change your perception. In fact, there are beautiful neuroimaging studies that show that when people ingest a sugary drink, their perception of images of foods change very much to make those foods appear more appetizing, and not just foods that contain sugar. Results of those studies do show that there's an increase for instance, in the perception of detail and images of ice cream, after you ingest a sweet drink or even if you put like a hard candy into your mouth, it will make you seek out sugary things more, it will make sugary things look more appetizing, but also other foods, more appetizing. So I think it's important that people recognize that fact, that when you have a sweet taste in your mouth or when you've tasted something sweet within your mouth, I should say, your perception of has immediately shifted. These are fast neural pathways. We'll get into some of the brain structures in a moment, but

these are fast neural pathways that shift your entire self toward seeking more sugary stuff and more food generally. Now, does that mean that you should never ingest anything sweet? No, certainly I'm not saying that, everyone has to decide for themselves what the appropriate amount of sugar intake is, but I find it remarkable when people say, oh, you know, I need to get my sugar fix, or I need to have my chocolate, or I need to have a little bit of something to just kind of take care of that sugar appetite. Because in taking care of that sugar appetite, maybe for the very disciplined of you, you can just have that one piece of chocolate and it's great, and you can relish in it,

00:41:46 Tool: Sugar & the Dopamine, Pleasure – Pain Dichotomy

but it does shift the way that you perceive other foods as well. And the way it does that is through our, probably if you're listener this podcast, now old friend, but incredible neuro modulator, dopamine. Dopamine is a molecule that is released from several places in the brain. There's a so-called mesolimbic reward pathway, which is a whole set of places in the brain or circuits, designed to get us motivated and craving and in pursuit of things. And then of course there are areas of the brain that are involved in movement that are linked up with those areas involved in motivation. That makes perfect sense. Why would you have a brain area involved in motivation if you couldn't actually do something with that motivation? So the way that your brain is designed is when there's an increase in dopamine, in the mesolimbic reward pathway, there are signals sent to an area of the brain called the striatum, we're going to spend a little bit of time today in the striatum. It's got a dorsal part, meaning in an upper part and a ventral part, which means a lower part. And the dopamine sent to those area, places us, excuse me, into modes of action, to pursue particular things. Sugar or sweet tastes, I should say, to be more specific, have an incredibly potent ability to activate dopamine release within the mesolimbic reward pathway. This has been shown over and over and over again in animal models and in humans. This is especially true, I should mention, through the ingestion of sweet liquids. Now this becomes a very important point to us a little later on when we talk about the proliferation of sodas and sweet drinks, and dare I even say, non-sugar or diet sodas, we're going to get into that a little bit later. They are perhaps one of the most third rail topics in nutrition. But when we ingest something sweet, the perception of that sweet taste increases dopamine in the mesolimbic reward pathways, which then are conveyed to pathways for motor behavior, and in general, place us into modes of focused action

toward getting more of whatever was sweet. Again, for those of you that are very disciplined, you can probably eat that one piece of chocolate and be just fine. But if you understand the way that dopamine works, what you'll realize is that when this dopamine pathway is triggered, it tends to create not the sensation or the perception of satiety, of feeling like something is enough, but rather to produce the sensation of wanting more. As described in the episode that I hosted with my phenomenal colleague from Stanford School of Medicine, Dr. Anna Lembke, she's an expert on addiction and dopamine pathways, the dopamine circuits of the brain have what we call a pleasure pain balance. And there I'm paraphrasing what Dr. Anna Lembke has said, and has written about in her beautiful book, "Dopamine Nation." If you haven't read that book, I highly recommend it. Whether or not you have issues with addiction or you know people that do, or you don't, it's an incredibly important read, especially if you're interested in understanding motivated behaviors and ways to channel your behaviors in life toward healthy, motivated behaviors, and make sure that you avoid some of the common pitfalls that people fall into, not just addiction, but things like overuse of social media or wasting time in general, it's a phenomenal book. In that book, and of course, within research articles, you will find evidence of this so-called pleasure pain balance that exists within our dopamine circuits. Nobody has dopamine circuits that allow them to escape this pleasure pain balance. And the way this works is that anytime that we engage in a behavior or we ingest something that increases our levels of dopamine, there is a subsequent increase in the neural circuits that control our sense of frustration, pain, and lack. You can actually notice this phenomenon if, for instance, you're somebody who really likes chocolate, or you really like something else, pay attention to the way that you experience indulging in that thing. If you eat that piece of chocolate and you really focus on savoring its amazing taste, you'll notice that it provides some quenching of your desire for let's say sweet stuff or chocolate or both, but right as you stop experiencing that, right as that chocolate intake tapers off, as you swallow it down your throat, or you just pause for a second afterwards, what you'll notice is that your brain and body actually orient toward wanting more. And that wanting of more is really the action of the neural circuits that underlie pain and are pushing your dopamine levels back down. And when these circuits go awry or I should say, when people fail to who control themselves within the context of that pleasure pain balance, the typical behavior is to reach for yet another chocolate or to then look for something that will quench that desire and get dopamine levels back up. Now the way these pleasure pain circuits work is very diabolical.

Because it turns out that were you to take another piece of chocolate, yes, your dopamine levels would go back up, but not to the same extent that they did the first bite of chocolate that you had. In fact, we can say that the longer it's been since you've indulged in something that you really enjoy or would like, the greater the dopamine you will experience when you finally engage in that behavior or indulge to that thing, ingest that thing, and the greater the dopamine increase, the greater the subsequent action of those pain circuits. So this puts you on a very complicated seesaw. It's a very wobbly precarious state to be in. Which is not to say you shouldn't have a piece of chocolate, it's just to say that the sweet taste of sweet things in particular, things that we crave very much and we wait and wait and wait, and then we allow ourselves to indulge. Those trigger changes in our neurochemistry, in our neuro circuits, that place us in a very vulnerable place, to either want more and more of that thing or to seek out other ways to fill that kind of emptiness that we feel or that gap, like, oh, I would love more, but I'm not going to allow myself more. Now again, I'm not saying that you shouldn't pursue pleasurable things. I mean this molecule dopamine exists for a reason. Frankly, because of its involvement in sex and reproduction, it's the reason we're all here in the first place. Because last time I checked, the only way any of us got here was one way or another, sperm met egg and there was conception. I still believe there are no exceptions to that, that I'm aware of anyways, that is a process, or I should say, the events leading up to that process typically involve dopamine in one way or another. There are exceptions to that too, but you get the idea. These dopamine pathways are not evil, they're not bad, but once you understand the way they work,

00:48:43 Subconscious Sugar Circuits, Hidden Sugars in Food

you can leverage them to your advantage as opposed to them leveraging you to their advantage. So when you ingest something sweet, you perceive that sweet taste and a cascade ensues within your brain that makes you want more of the sweet thing. That's the conscious pathway for sugar perception, for sweet perception. Now there's the second pathway, the second pathway is what's called the post-ingestive reinforcing properties of sugar, which is really just a fancy nerd speak way of saying there are events that happen within your stomach and below your conscious detection, that are also driving you to seek out sweet tasting things, independent of their taste, and foods that increase blood glucose, independent of their taste. In order to illustrate the immense

power of these subconscious circuits for sugar seeking, I'd like to describe an experiment. And this is just one experiment of many, of dozens or more experiments done in animal models and humans, which essentially illustrate the same thing. And as I describe this experiment, I think you will come to understand the power of these circuits. I'll provide a link to this study in the caption. The first author is Freeman. The paper was published in *Frontiers in Bioscience*, but there have been others, papers in *Nature Neuroscience*, papers in *Neuron*, *Cell Press* journals, et cetera, many, many journals, many, many papers. If subjects are given the choice of drinking plain water or a sweet tasting fluid, their preference for the sweet tasting fluid is much, much higher, right? Sweet tastes better than plain water, at least for most people and certainly for animals. Now, if, for instance, you take an animal which completely lacks sweet receptors, and you can do this through some molecular genetic tools and gymnastics in the laboratory, we call these knockout mice, where you can knock out a particular receptor for sweet taste, you can confirm that there's no perception of sweet things or at least no preference for sweet things in those animals. In humans, you can numb the mouth, there are other pharmacologic ways that you can eliminate sweet receptors in the mouth. And by doing that, you people will tell you, no, I can't taste anything sweet. You could give them an ice cream, you could give them pure sucrose, you could give them table sugar, and they wouldn't be able to perceive it as sweet. If you eliminate the perception of sweet taste in the mouth and you offer people or laboratory animals, water versus some sugar containing solution, you eliminate the preference for the sugary solution. Which tells us that the perception of sweet is important for the preference for sweet tasting drink. This is also true for sweet tasting foods, I should mention. However, in both animal models and in humans, after about 15 minutes, subjects start preferring the sugary water, even though they can't taste that it is sweeter. So to repeat that, if you eliminate the ability to sense sweet, to perceive sweetness in foods, then you eliminate the preference for sweet beverages or sweet foods. So that's not surprising. But if you wait about 15 minutes, the preference for the sweet beverage or the sweet food comes back. Now that doesn't mean that they can perceive the sweetness. In fact, the way these experiments are done is very clever. You offer people various cups of different things or different food items. And then you just look at what they eat more of or what they prefer to eat more of. So this experiment is so crucial because what it says is that the preference for sugar containing foods is in part due to the sweetness of those foods, but in part due to something else. And this something else is what we call the post-ingestive

effect, and as I mentioned before, it took about 15 minutes. And you've actually experienced this, whether you realize it or not, this phenomenon of post-ingestive rewarding properties of sweet foods, meaning what happens in your body when you ingest something that increases your blood glucose very much, has no doubt controlled you from the inside, below your awareness, this was happening to you and you didn't realize it. And here's how it works. We all have neurons within our gut. These neurons have a name, they're called neuropod cells. Neuropod cells were famously discovered by Professor, Dr. Diego Bohorquez at Duke University. And these cells respond to, among other things, to the presence of sugar within the gut. So when we ingest a sugary food or drink, or we ingest a food or drink that simply contains fructose, sucrose, glucose, or some other form of sugar that later, through metabolism, will be converted into glucose, the neuropod cells are able to register the presence of those sweet or glucose stimulating foods. And in response to that, send electrical signals, because electrical signals are the way neurons communicate, up to the brain, via the so-called vagus nerve. The vagus nerve, of course, being a nerve pathway, famous for its role in relaxation. That's kind of the assumption out there, that it's always involved in relaxation, that's not the case. It's involved in a lot of things besides relaxation. But nonetheless, these neuropod cells send electrical signals through a particular highway within the vagus to the so-called nodose ganglion, and this is a cluster, a ganglion is just a cluster of neurons. And then the nodose ganglion sends on information to the nucleus of the solitary tract. The nucleus of the solitary tract is an area of the brain that we're going to talk about extensively today. It's very important for understanding sugar preference. These neuropod cells also trigger activation of dopamine pathways within the mesolimbic reward pathway. In other words, there are signals conveyed from the gut, meaning stomach and intestines, to the brain anytime we ingest sweet foods, but it has nothing to do with our perception of them being sweet, it has everything to do with the fact that sweetness of food is almost always correlated with an ability to increase blood glucose. And the net effect of this is a parallel pathway by which dopamine is increased further. Now, the experiment that I described before of animals or humans ingesting something that contains sugar, but not being able to perceive its sweetness, and yet, after a period of time, still preferring that food or drink to non-sugar containing food or drinks, even though they can't distinguish their taste, is dependent on these neuropod cells and related pathways. What this may for you is that anytime you eat something sweet, that substance is actually causing your gut, your stomach and your intestine, or to

be more precise, I should say, that substance, food substance, is causing the neuropod cells in your stomach and intestines to send a parallel set of signals up to your brain saying, eat more of that, or simply eat more, eat more, eat more, and preferably eat more sweet foods. So we've all heard of hidden sugars, meaning the sugars that manufacturers have put into foods and disguised them with other flavors. I talked about this in the episode on salt, using salt to mask the taste of sweetness so that people ingest more sugar. That is not an accident that hidden sugars are often hidden with salt or with other flavors. It's done so that people will, meaning you or me, will want to ingest more of a particular food, independent of how sweet that food tastes. And in fact, some crackers, for instance, chips for instance, you might think, oh, well, you know, chips, they're not sweet, they're salty and savory. And again, I'll mention, I love salty and savory foods, including certain foods, I love kettle chips, for instance, I try not to walk by them in the grocery store. I usually have to eat one bag while I'm in the store, and then another later. The savory foods are often laden with these hidden sugars that we can't register as sweetness, but trigger the neuropod cells, which then further trigger dopamine, which make us want more of them. Now we may be able to resist eating more of them, but it makes us crave more food in general. Now we will talk about ways to regulate this pathway, to sort of intervene in this subconscious pathway. But for now I'm hoping that just the understanding that we all have this pathway, this is hardwired into our body, could potentially allow people to better understand why is it that their cravings are so intense, that it's not necessarily just about the taste of that food. And when you consider this in concert with the fact that we have this dopamine pain pleasure balance, excuse me, that I referred to earlier, you start to realize that there are multiple mechanisms hardwired into us, that make it especially hard to not eat the sweet thing or to not eat the food that we're craving. And indeed, that's the case. We have two major accelerators. It's like a car with two accelerators, and we will talk about the brakes, but two ways that really get us into forward motion

00:58:03 Glucose Metabolism in the Brain

toward pursuing the consumption of sweet foods. Now, if it doesn't already seem diabolical enough, that sweet things that we perceive as sweet, make us want to eat more of those because of dopamine and then send us down this pain pleasure pathway that I mentioned earlier, and the fact that we have this subconscious circuit coming from

the neuropod cells in our gut that are registering the presence of sugar or glucose increasing foods in our gut and sending those signals to the brain for yet more dopamine and pain pleasure challenges, there's a third layer to this whole thing. And that has to do with how sugar is metabolized in the brain. Or I should say how glucose is used. Without getting into too much detail, some of the more beautiful studies of neuroimaging and evaluating which brain areas are active when we eat certain foods were done by Dr. Dana Small's lab at Yale University, and in some of her previous work when she was elsewhere, and of course by other laboratories too. And they used an approach called positron emission tomography, and they and others have used PET scanning as it's called, positron mission tomography, along with an tool called 2-Deoxy-D-glucose. 2-Deoxy-D-glucose is actually involved in the procedure of seeing which brain areas are active when people eat foods or engage in other types of behaviors. But the way that 2-Deoxy-D-glucose, sometimes shortened 2DG. The way that it works is to block glucose uptake from neurons. And instead, bring along with it, a marker that one can see through imaging. So in other words, a tool for looking at what parts of the brain are active when eating particular foods, actually prevents foods such as sugar, from allowing glucose to get into particular neurons. Now that might seem like a bad situation, you'd say, well, wait, you're trying to understand how sugar works in the brain, and then you block the ability for sugar, glucose, to bind to, or be used by these neurons, because of the thing that you're using for the experiment. Exactly, it's a huge problem, but it turns out to be a huge problem that led to a great insight. And the great insight is this, the preference for sweet tasting foods and liquids is actually blocked by 2-Deoxy-D-glucose. What that means, experimentally, but also in terms of what it means for you and me in the real world, is that there's yet a third parallel pathway that's related to the use of blood sugar, the use of glucose by neurons, that further reinforces our desire to eat more sweet things. And the preference for sweet foods can actually be eliminated through 2-Deoxy-D-glucose. Now I am definitely don't want people going out and consuming 2-Deoxy-D-glucose. This is a laboratory tool, it is not something that you should be ingesting. So don't go look it up and try and get some, there might be other uses for it, but that's not the point. The point is that it is the sweet taste of sugary foods. It is the signals coming from your gut, from your digestive tract to your brain, and it's the use of the metabolic consequences of sugary foods that are acting as a three pronged push on your desire to consume more sugary foods. So this car analogy that I used before, where it's some weird car that has two accelerators, it actually has three accelerators. And so with three

accelerators, all pushing the system hard, we can say, wow, there must be something really special about this pathway. And indeed there is, this pathway is the quickest source of fuel for the brain and the rest of the nervous system, it's the source of fuel for the brain and nervous system. And I realize, as I say that all the ketonistas are probably going no, actually ketones are the preferred source. Okay, I acknowledge that there are conditions under which you can bring your blood glucose very low, and there are reasons to do that. Actually ketosis has been a terrifically successful treatment for a lot of forms of epilepsy, in particular, pediatric epilepsy. Many people do derive benefit from ketogenic diets, so I'm not knocking ketogenic diets, but if you were to look at what neurons normally prefer, meaning in a typical diet regimen, it would be glucose. And the fact that fructose is eventually converted to glucose, the fact that when we ingest sucrose, it's eventually converted into a fuel that neurons can use, that's very much in the glucose pathway, what you basically arrive at is the fact that your nervous system is a glucose consuming machine. And you've got at least three pathways, of which I've described, that are pushing on your brain consciously and subconsciously to get you to seek and consume more sugar. Now that all sounds like a pretty depressing picture, at least for those of you that are trying to reduce your sugar intake. And of course we can all reduce sugar intake by way of sheer will, we can not have those foods at home,

01:03:00 Tool: Glycemic Index, Blunting Sugar Cravings

we can restrict ourselves from those. But there are some things that we all can and perhaps should do in order to regulate these pathways such that we don't feel so controlled by them, but rather that we control their output. And of course they are us and we are them, so this gets into all sorts of issues of consciousness and freewill that I certainly don't want to cover in this episode. But nonetheless, I think once you understand that these circuits exist and you understand that there are simple substitutions and modifications that one can make to their food intake that can work within these pathways and even bypass some of these pathways, you start to realize that you have a lot more control over sugar intake and sugar appetite than you previously thought. Now, many of you have heard of the so-called glycemic index. The glycemic index is a measure of how quickly blood sugar rises after ingesting particular foods. And very broadly speaking, we can say that there are low glycemic index foods, of less than 55, typically, is the measurement, or medium glycemic index foods, which

go from about 55 to 69, and then so called high glycemic foods, which are above 70. And of course there's additional nuance related to glycemic load and many more features of the glycemic index. A couple of things to understand about how the glycemic index is measured. And then I'd like to just briefly talk about how the glycemic index can be leveraged to short circuit some of the neural circuits that would otherwise lead us to crave and perhaps even ingest sugar foods. First of all, measurements of glycemic indices of food are typically made by having people ingest those foods in isolation. And in general, we can say that anytime we ingest fiber and/or fat, lipids, along with a particular food, it will reduce the glycemic index of that particular food, either the absolute level of blood glucose that a particular food causes or the rate at which that elevation in blood glucose occurs. And this is why there are some seemingly paradoxical aspects to sweet stuff in terms of the glycemic index. For instance, Ice cream has a lower glycemic index, provided its ice cream that includes fat, which I hope it would, 'cause that's the good tasting ice cream, in my opinion, compared to something like mangoes or table sugar, right? So the glycemic index is not something to hold holy, in most cases, because most people are not ingesting foods in isolation. And there's actually a lot of argument as to whether or not the glycemic index is really as vital as some people claim. There's also the context in which you ingest particular foods. As I mentioned earlier, after I do hard training of any kind, meaning training that ought to deplete glycogen, so hard resistance training, I actually make it a point to ingest some very sweet high glycemic foods like a mango, I'll also ingest some starches 'cause I'm trying to replenish glycogen. I'm also trying to spike my blood sugar a little bit because that can be advantageous in terms of certain strength and hypertrophy protocols, et cetera. But most of the time I'm avoiding these high glycemic foods and high sugar foods, I should point that out. Now, why am I telling you about the glycemic index? Well, if we zoom out and take our perspective on all of this discussion about the glycemic index, through the lens of the nervous system, and we remind ourselves that neurons prefer glucose for energy and that all sweet things, or things that we perceive as sweet, but also sweet things that are ingested and registered by those neuropod cells in our gut trigger the release of dopamine and trigger these neural circuits to make us want to eat more of these foods, what we start to realize is that a sharp rise in blood glucose or a very high degree of elevation in blood glucose, is going to be a much more potent signal than would a more moderate rise in blood glucose or a slower rise in blood glucose. So if we think about the analogy of three accelerators, meaning three parallel neural circuits,

all essentially there to get us to seek out and consume more sweet tasting and sugary foods, well then the glycemic index is sort of our measurement of how hard we are pushing down or how fast we are pushing down on those three accelerators. And so for those of you that are trying to reduce sugar take, and you want to do that through an understanding of how these neural circuits work, and you want to short circuit some of the dopamine release that's caused by ingesting sugary foods. It can be advantageous to ingest sweet foods, either alone or in combination with foods that reduce glycemic index or reduce glycemic load. So that might mean making different food choices. So paying attention to sweet tasting foods that can satisfy sugar cravings, but do not have as steep or I should say, do not cause as steep a rise in blood sugar, or it could mean consuming other foods along with sweet foods in order to reduce the glycemic index and thereby, slow or blunt the release of dopamine. You might think, well, why would I want to do that? I want the maximum dopamine output in response to a given sweet food. I don't just want the you know, level 10. I want the level 100 output of dopamine. But you really don't, because of the pleasure pain balance that dopamine causes. And in fact, if we consider some of the non-food substances that really push hard on these dopamine pathways, we can come up with a somewhat sinister, but nonetheless appropriate analogy. The drug, cocaine, causes very robust, potent increases in dopamine within the brain, and typically causes people to want to ingest more cocaine because of those sharp increases in dopamine. But within the category of the drug cocaine, there are various modes of ingestion. Some people inhale it, some people will inject it intravenously, some people will smoke it, and those different forms of taking cocaine actually impact the dopamine circuits differently. And it turns out that crack cocaine, the smokable form of cocaine rock, increases dopamine to a very high degree, but also very quickly. And it is the sharp rise in dopamine over time, not so much the absolute level of dopamine, that makes crack cocaine so absolutely addictive. So sometimes you'll hear, you know, sugar is like crack, well, and that's getting a little extreme because even though I don't think the measurements have been done in the same experiment, I think it's reasonable to think that the absolute level of dopamine caused by ingesting sugar, at least for most people, is not going to be as high as the absolute level of dopamine caused by smoking crack. Of course it goes without saying, please don't do cocaine in any form, by the way. It is appropriate to say that the rate of dopamine increase over time has a profound effect on how people will, and if people will, go on to want to pursue more of what caused that increase in dopamine. So what I'm basically saying is if you're

going to ingest sweet foods in order to satisfy a sweet craving, ingesting sweet foods for which the glycemic index is lower or in which you've adjusted those glycemic index foods through the co-ingestion of fiber, or maybe fat, might be beneficial. So is this justification for putting peanut butter on that piece of chocolate or for having a bit of ice cream along with the mango that you're craving? In some sense, yes, however, there's also the issue of how sweet and how delicious something tastes. Highly palatable foods, absolutely delicious foods, trigger that one neural circuit, that one accelerator that we were talking about in terms of our analogy of three accelerators, and the more delicious something tastes within our mouth, the further increase in dopamine. So if you really wanted to adjust your sugar cravings and you really still want to ingest some sugary foods, you probably would be better off combining fiber with that sugary or sweet food. Now I do realize that it's somewhat unusual and you probably get some strange stares, if you decided to consume broccoli, for instance, along with your chocolate, or with another dessert that would otherwise cause a steep increase in blood sugar and has a high glycemic index. But nonetheless, if your goal is to blunt your sugar cravings, what you really need to do is blunt that dopamine increase. So what we're really talking about here is trying to reduce the dopamine signal that is the consequence of ingesting sweet foods. And we're talking about doing that through these different parallel pathways, not just by preventing sweet taste, but also by preventing the post-ingestive effects of sweet foods. And of course the backdrop to all of this

01:12:08 Sugary Drinks, Highly Refined Sugars

is that most of us, again, most of us, not all of us, should probably be ingesting fewer refined sugars. Certainly there are exceptions to that. But I think the bulk of data point to the fact that ingesting these highly palatable, certainly highly palatable, highly processed foods, or foods that contain a lot of high fructose corn syrup, can be really deleterious to our health, especially in kids. And I'm not going to cite off a bunch of statistics, you've all heard them before, that you know, for hundreds of years, we ingested, you know, the equivalent of a few cups or pounds of sugar per year. And you know, now people are ingesting hundreds of pounds of sugar per year. The major culprit always seems to be sugary drinks, meaning soft drinks, and I think indeed that's the case. I do want to point out the incredible work of Dr. Robert Lustig, who's a pediatric endocrinologist at the University of California San Francisco, who was really early in the game of voicing the

dangers of so-called hidden sugars and highly processed foods, there are other people, of course, now talking about this. His laboratory has done important work showing for instance, that if high fructose corn syrup or even just fructose is replaced with glucose, even if the same number calories is ingested, that there are important meaning significant reductions in type two diabetes, some of the metabolic syndromes associated with high fructose corn syrup and on and on and on. And of course there are other culprits in type two diabetes, there are other factors that are going to lead to obesity. But I think that work from Lustig and others has really illustrated that we should all be trying to reduce our intake of highly refined sugars and high fructose corn syrup. And certainly trying to reduce our intake of very sugary drinks, not just soft drinks, but also fruit juices that contain a lot of sugar. Now, even for people that are of healthy weight and who don't have metabolic syndromes, there may be an additional reason to not want to ingest very sweet foods and highly refined sugars. And this has to do with a new and emerging area of nutrition neuroscience. And I want to point out that these are new data, right, so it's not a lock, the double blind placebo controlled studies in large populations have not been finished. So I want to make sure that that's clear, but I also want to make clear what some of the really exciting data, coming from Dana Small's lab at Yale,

01:14:33 Artificial Sweeteners

and from other laboratories are showing. And this has to do with what's called conditioned taste preference. Using a kind of Pavlovian paradigm, what they do, is they have people, and these studies were done in people, ingest maltodextrin, which increases blood glucose, doesn't have much flavor, but even if it does have a little bit of subtle flavor, the maltodextrin is cloaked by some other flavor. And by cloaking it with that other flavor or pairing it with that other flavor, what they find is that over time, because the maltodextrin increases blood glucose, and they're ingesting a particular flavor along with that maltodextrin, they can then remove the maltodextrin, and the flavor will induce an increase in insulin. The increase in insulin of course, is the consequence of the fact that anytime there's a rise in blood glucose, provided the person isn't diabetic, there's a parallel increase in insulin. Now this is very interesting because what it says is, well at a first pass, it says that we are very Pavlovian in terms of our physiological responses to foods and particular flavors come to be associated with particular patterns of blood glucose increase and hence patterns of insulin increase, because of course,

insulin manages glucose in the bloodstream as I mentioned earlier. This also has implications for understanding things like artificial sweeteners. And here I want to highlight that this is still very controversial work, needs more data, but nonetheless, I'd like to share it with you for consideration. The small laboratory has done studies in humans, both in adults and in children, showing that if the flavor of artificial sweeteners is paired with maltodextrin, and then the maltodextrin is removed, that the artificial sweetener taste itself can subsequently increase insulin in the bloodstream. In other words, taking something that increases blood sugar, attaching a flavor experience to that, having children or adults ingest that thing, allows the nervous system to associate that flavor with that increase in blood glucose. But then you can remove the glucose increasing substance, and the flavor alone will increase insulin because insulin typically follows blood glucose. So this is a conditioning effect. Now, the reason these data are controversial is several fold. First of all, the landscape around the discussion around artificial sweeteners is definitely what I would call a barbed wire topic. And I want to preface what I'm about to say next by saying, I actually ingest artificial sweeteners. I will have the occasional diet soda, not every day, maybe I don't know, once or twice a month. I don't particularly like the taste, but I'll do it just 'cause it's around, and I want some caffeine and I like the carbonation if I'm on a plane or something, I do ingest plant-based non-caloric sweeteners. To my knowledge, there have not been high quality studies of plant-based non-caloric sweeteners in the context that I'm referring to here. Nonetheless, these studies show that particular flavors can be conditioned to cause an insulin increase. And the flavor associated with certain artificial sweeteners is included in that category of flavors that can induce insulin, even in the absence of something that can increase blood glucose. Now the simple takeaway from these studies would be the following, and this is actually one interpretation that Dana Small has offered to her data, but she offers other interpretations as well. One of interpretation is that if people are going to ingest artificial sweeteners, and they do that along with foods that very sharply increase blood glucose, then there is the potential, I highlight the potential, for those same artificial sweeteners to increase insulin, even in the absence of food. In other words, let's just draw the scenario out in the real world. You're having a diet soda along with a cheeseburger and fries. You do that every day for lunch, okay? Somewhat extreme example, but natural world example, you do that every day for lunch. And then you just have a diet soda alone. The extreme interpretation of the data that they've collected says, well, that diet soda alone will increase insulin, even though there's no

increase in blood glucose because you haven't ingested food with it because you conditioned that taste of artificial sweetener to the experience of a rise in glucose and hence insulin. Now the counter argument to this would be, well, that's a very unusual situation, maltodextrin causes big increases in blood glucose, so that's not really a fair experiment or it's not a natural world experiment. And I think that's a decent assessment. Although I will point out that one of the reasons why this study is so controversial or why these data are so controversial, is that the experiment actually had to be stopped. And particularly the experiment in children had to be stopped because the changes in insulin that were observed early in the study were so detrimental, that the institutional review board, quite appropriately, said, we can't do this to these kids. They're experiencing these odd shifts in insulin that are not healthy for them when they're just ingesting artificial sweeteners in the absence of these glucose increasing foods. So once again, I do ingest artificial sweeteners, I'm not saying that they are dangerous, I'm not saying that they are not dangerous, I'm saying that you have to decide for yourself. In previous episodes, I've highlighted that artificial sweeteners have been shown in studies of animals, that when given in very high doses, sucralose in particular, there can be fairly robust disruption to the gut microbiome, which is vital for immune health and brain health, et cetera, et cetera. But thus far, our knowledge of how artificial sweeteners negatively impacts or positively impacts, I should say, the microbiome and other deleterious effects on the body, has mainly been explored in animal studies. Again, the work by Dana Small has been done in humans. There's some parallel work by others in animal models. I bring it up today to illustrate the following point. Normally we have a pathway that we don't have to condition at all, it's there from birth, whereby ingestion of sweet foods causes increases in dopamine. And there are parallel pathways by which neurons in our gut and elsewhere in our body, trigger further increases in dopamine. There's no need for a conditioned response or to become Pavlovian about this, right? You're hardwired to want to eat sweet things, by at least two and probably three parallel pathways. Now the work from Dana Small's lab and others that have illustrated this conditioned flavor preference, I think beautifully show that any flavor that's associated with a glucose spike or a long sustained increase in glucose can also be conditioned. In other words, the circuits for dopamine that reinforce the desire to eat particular things is not unique to the sugar pathway. And this is one of the reasons I believe, why ingestion of sweet foods doesn't just us to want to eat more sweet foods, I think that is absolutely clear based on animal data and on human data, I think that's robust, it's actually the stuff

of textbooks now, but in addition, ingesting sweet foods and/or foods that raise blood glucose, but that we don't perceive as sweet. So for instance, foods with hidden sugars, sugars that have been masked asked by salty or spicy taste, increases our desire for glucose elevating foods and food, generally, I think that's the only logical interpretation of the data that I can arrive at. So for people that struggle with regulating their appetite or with regulating their sugar appetite, I think the understanding of conditioned flavor preference, while a little bit complicated,

01:22:36 ADHD, Omega-3s

ought to be useful in trying to navigate reducing sugar cravings and sugar intake. As a segue into tools to control sugar intake, as a means to both regulate sugar intake itself, as well as food intake overall and steer us towards healthier choices. I'd like to talk about some of the special populations out there that might want to be especially wary of having a dysregulated sugar appetite system. And the group I'm referring to specifically are those with attention deficit hyperactivity disorder or, I should say, and/or, people who have issues with focus and attention, generally. And I think more and more nowadays, I'm hearing that people are having a hard time focusing. This probably has something to do with our interactions with electronic devices. As I always say, if a picture is worth a thousand words, a movie is worth a million pictures, and the fact that we can access so any movies just by scrolling with our thumb, is something that the nervous system has just never contended with before in human history. I'm confident in that. And it's not that it can't deal with it, the question is what's the trade off? What are the consequences of that? So attention and ability to focus is obviously key to success in school, success in relationships, success in the workplace, and success in life. We could probably even go so far as to say one's ability to succeed in anything is proportional to one's ability to focus and then deliberately defocus when the time comes to defocus, right? 'Cause we all need rest and we need to disengage and then reengage, If you look at the sum total of the meta-analysis and the clinical data on ADHD and nutrition, you arrive at a pretty clear answer, which is that sugar consumption, in particular, highly refined sugars, is just not good for people with ADHD or with attentional issues. Now, as I say that, I also want you to recall the earlier study that I referred to, whereby the tuning of neurons in the brain is highly dependent on glucose. So this doesn't mean consuming no glucose is going to be a good idea. It doesn't mean that the ketogenic diet is necessarily the best

diet for ADHD. Although there are some people pursuing that and exploring that, and we'll do yet another episode on ADHD at some point that goes a little bit deeper into that, because there's some new data. I did do a very long and fairly extensive episode on ADHD. You're welcome to look that up if you like in our archive, excuse me, in our archive at hubermanlab.com, it's all timestamped. So, you know, because the number of people said, oh, you know, it's an episode on ADHD and you made it two and a half hours long. Yes we did, because we wanted it to be as comprehensive as we could at the time. But it is timestamped, you can just jump to the particular topics of interest and there's short little cassettes there. Now, if you'd like to know upon what I'm basing this statement that sugar consumption and highly refined sugar consumption is potentially bad for ADHD, I'm basing this mainly on the conclusions of a really nice paper, the title of the paper is "Sugar Consumption, Sugar Sweetened Beverages, and Attention Deficit Hyperactivity Disorder: A Systematic Review and Meta-Analysis." And this is a paper, we'll put a link to this in the caption. This was published in *Complementary Therapies in Medicine* which is a bit of an atypical journal in some sense. But I really like this meta-analysis. The sum total of this meta-analysis is really that when, especially kids, get beyond four sugary drinks per week, so four sodas of a typical 12 ounce soda, when they get past four 12 ounce sugary sodas, they didn't, as far as I know, look at artificially sweetened sodas. That's when you start to see a shift towards more negative outcomes, more symptoms of existing ADHD. Now where the controversy comes in is whether or not sugar consumption can actually trigger or cause ADHD. And I don't think we can conclude that at all at this time. And this review, if you decide to check it out, review/meta-analysis, I should say, if you decide to check it out, goes into some of the nuance around that. What's also interesting in terms of ADHD and sugar intake, and it probably has relevance to all of us, is that they also cover some of the interesting data showing that supplementation with omega-3 fatty acids can actually be beneficial for people, in particular kids with ADHD, I've talked before about the utility of omega-3s, that's been shown in various studies that have compared omega-3 fatty acid intake to say prescription antidepressants, like SSRIs, like Prozac, Zoloft, and similar, Fluoxetine, and the results of those studies are pretty clear, at least to me, that provided that one gets at least one gram of EPA, essential fatty acids, so it's not just getting one gram per day, but one or more grams per day of the EPA form of essential fatty acid, can rival some prescription antidepressants and/or decrease the amount of antidepressants that's required to take. Which for a lot of people can be a very useful thing because of the side

effect profile of many of those antidepressants. Of course, talk to your psychiatrist, talk to your doctor, but the omega-3s are no doubt powerful. And then of course there's a whole story about omega-3s and heart health. And of course, like anything else, there's some controversy around omega-3s, but I think the data are clear enough to me around mood and cardiovascular health, that certainly I personally ingest them. But as always, I always say, anytime you're going to add or remove anything from your nutrition, supplementation, exercise, or otherwise your lifestyle, definitely consult with a board certified physician. I don't just say that to protect me, I say that to protect you, you are responsible for your health ultimately. So omega-3 supplementation has been shown to be beneficial for ADHD. Why am I talking about this in the context of an episode on sugar and the nervous system? Well, if you remember those neuropod cells, those cells in your gut that respond to sugar and send signals up to the brain to cause the release of dopamine. Well, it turns out that neuropod cells also respond to amino acids and to fatty acids, in particular, essential fatty acids. So these cells that we call neuropod cells, have three jobs. One is to levels of sugar in the gut, the other is to detect levels of amino acids, and to detect levels of particular essential fatty acids, and communicate that information to the brain. And I should point out when I say communicate that information, they're not actually saying, hey, there's amino acids here, or hey, there's sugar here, or, hey, there's essential fatty acids, because the language of these cells is somewhat generic. It's just the firing of electrical potentials. But that's the key point, it's generic and all three or any of those three, sugar, essential fatty acids, or amino acids, will trigger these neurons to signal to the brain to increase dopamine. And it is not coincidental that omega-3 fatty acid supplementation can help ameliorate some of the symptoms of ADHD by way of presumably increasing dopamine in this neuropod to dopamine pathway that we talked about earlier. The whole thing has a very nice logical structure to it. And points to yet again, the immense value of bringing the proper amounts, maybe even supplementing the proper amounts of omega-3 fatty acids and the proper amounts of amino acids into the gut as a way to supplant some of the stimulation of these pathways that would otherwise be caused by sugar. There's actually a version of this where one could say, if you want to reduce sugar cravings, you might consider increasing certain forms

01:30:18 Tools: Reduce Sugar Cravings with EPA Omega-3s & Glutamine

of amino acid intake or certain forms of fatty acid intake. So what are some ways that we can reduce our sugar cravings, and ideally ways that we can do that, that also benefit us in other ways, both nutritionally and from the neuroscience standpoint? Well, these neuropod cells that respond to and signal the brain when we ingest sugar, as I mentioned, also respond to amino acids and essential fatty acids. We already talked about the essential fatty acids. I make it a particular point to ingest anywhere from one to three grams, that's grams, of EPA essential fatty acid per day. I make it a point to do that with the ingestion of high quality omega-3s. For me, the simplest way to do that, and I think for most people, the lowest cost way to do that, is to use some liquid form of fish oil or some capsule form of fish oil. You really do have to see how much essential fatty acid in the form of EPA is in those. If you try and do that only through capsules, it can get kind of expensive, depending on which particular brands you use, some have more EPA, some less. You can, of course also do this through foods, you can do this with non fish sources, through things like algae, and there's some other forms, you can look it up online now, plant-based sources of EPAs, you can do this with high quality fish oil. In any case, that does seem at least based on a modest amount, but nonetheless solid literature, to reduce sugar cravings somewhat, but that could easily be by mere replacement of calories. So we don't know yet based on human studies, whether or not the ingestion of those EPAs is specifically activating the neuropod cells, which specifically activates dopamine release and bypasses the need for, or the craving for sugar. We don't know that yet. But logically, it holds up to assume that. The fact that these neuropod cells and I should say other neurons within the gut respond very robustly to the presence of particular amino acids is also a potential lever by which one could reduce sugar cravings. And there's an interesting literature around the amino acid, glutamine, in particular supplementing with the amino acid, glutamine, as it relates to sugar cravings, and certainly as it relates to other aspects of the gut, in particular leaky gut. The use of supplemental glutamine to try and treat leaky gut is not a new phenomenon. There are other approaches too, of course. But there are many people who are experimenting with supplementing with glutamine, several grams per day, often even, you know, five grams distributed through three or four different servings throughout the day as a way to blunt their sugar cravings. Now there has not yet been a large scale clinical trial using glutamine to reduce sugar cravings, but the results of the few studies that I looked at, as well as my understanding of the logic of these neuro circuits, including the neuropod cells, brings us to a conclusion that it makes sense why

if there's a population of neurons within our gut, that responds very robustly to the presence of sugar, fatty acids, or amino acids, that the intake of particular amino acids would allow the dopamine pathways that might otherwise be triggered by sugar to be triggered by something like glutamine, which has very few or no calories. And in fact, having talked about this previously, a number of people that I know went out and tried this, now this is of course is what I call anecdotal data, right? This is not a quality peer reviewed study, this is anecdotal data. Many of them have reported back that they actually feel as if their sugar cravings are reduced. I know some people who actually take glutamine and mix it with full fat cream and take it kind of like a shot of full fat cream, which sounds absolutely delicious by the way, glutamine is a little bit chalky, so it's not that great tasting to ingest with sugar. I should mention, if you do try and take this approach of ingesting glutamine to reduce sugar cravings, you want to increase the amount of glutamine that you take somewhat gradually. It can create some gastric distress if you just, you know, I certainly wouldn't take a big table spoon of it, throw it in water and chug it down three times a day. Some of you with very hardy stomachs can probably tolerate that. You know, if you're like my bulldog, which unfortunately passed away, but Costello, I always imagine that if ever we did an autopsy on him, he'd have like a license plate and like a human being in his gut, 'cause it seemed like he could ingest anything with no issues, but of course, many people have kind of sensitive guts. So if you're going to try taking glutamine as a means to reduce sugar cravings, just know that the studies are still ongoing. Some people have achieved benefit. Please also realize that there's an entire literature devoted to the potential hazards of increasing glutamine if you have a preexisting cancer. So if you have cancer or you're cancer prone, I would really discourage you from this approach. And in any case, as always, talk to your doctor. The logic nonetheless is there, why increasing amino acid intake or fatty acid intake might decrease sugar craving.

01:35:15 Tool: Blunt Sugar Peaks & Craving with Lemon Juice

Now there are other ways to reduce sugar craving and there are certainly ways to reduce the sharp rise in blood glucose that can occur when we ingest sugary sweet foods or even just an abundance of carbohydrate foods, and there are a huge number of these things. I'm going to sort of layer up through the ones that you might find in your cupboard, at the grocery store, and then get into some of the more extravagant or I

should say, esoteric ones, many of which however can be quite potent. The first of which is simple lemon juice, right, or lime juice. There was an old lore and actually some papers, pointing to the idea that the ingestion of vinegar, either white vinegar or wine vinegar, could somehow blunt blood glucose after the ingestion of sugary foods or the ingestion of a lot of carbohydrate foods, or even just a big meal. Actually, Tim Ferris, I should say the great Tim Ferris, 'cause I do have great respect for the fact that he seems to be about 10 years ahead of everything, both in terms of nutrition and skill learning and things of that sort, many of the things that he predicted in his books, "The Four Hour Body" and "The Four Hour Chef" actually turned out to be true based on scientific data, some of which only exists in the animal models, but now also some predictions that played out to be true in both the animal models and the human models. So I think that Tim certainly deserves a hat tip for the fact that he experimented with these methods and reported his experiences with those methods and that now some of them, many of them, have been validated by what I perceive to be quality science. He talked about the fact that, at least in his experiments on himself, the ingestion of vinegar did not seem to blunt blood glucose, and he was using continuous glucose monitors. These incidentally, another example of where Ferris was early to the game and the rest of us are kind of just in his wake. He talked about the use of blood glucose monitors, those, I think at the time were implanted below the skin. Nowadays there are less invasive blood glucose monitors, things like Levels and so forth, and these are actually becoming pretty popular. I've worn one of these before. They're actually pretty informative. I learned for instance, that when I go in the sauna that I experience a sharp rise in blood glucose. And that makes sense because of the dehydration associated with being in the sauna, a lot of sweating, the concentration of sugar in the bloodstream goes up. So there's some other things that certain foods affect my blood glucose one way or another. It's kind of an interesting and fun experiment that some of you might be interested in doing as well. Regardless, there are now data pointing to the fact that lemon juice and lime juice, a couple tablespoons or so, if ingested before, or even during, or even after, consumption of sugary foods, or I should say foods that sharply increase blood glucose or large carbohydrate meals, can actually blunt the blood glucose response. And I did see that when I did my own experiments on myself with a continuous glucose monitor, it was kind of fun to do those experiments. I preferred to do those experiments by eating somewhat larger meals of things that didn't contain a lot of sugar. I saw some big increases in blood glucose in certain instances, and then I would ingest some lemon juice or lime juice,

typically mixed in with water. And sure enough, you could see a blunting of the blood glucose response. And of course this was real time, continuous, hence continuous, blood glucose monitoring. So for those of you that are interested in blunting your blood sugar response, certain foods, that's a simple, low cost way to do that, if you want to explore it. I will say, if you are fasting and you already have low blood glucose, and you ingest lemon juice, or I should say some lemon juice and water or lime juice and water, be careful because you can actually become hypoglycemic. For the very same reasons that that lemon juice and lime juice can blunt blood glucose when your blood glucose levels are moderate to high, you can also reduce blood glucose levels even further when blood glucose levels are low. Now that's lemon juice and lime juice there. But we can't say that has to do with acidic things, generally. And just as a side point, many of you have probably seen in the store, so called adjusted pH waters or foods and drinks that are supposed to adjust your pH. Hate to break it to you, but your pH is very tightly regulated throughout your brain and body. You do not want this to change. It is entirely impossible, at least in any safe way, that you would become quote unquote more alkaline by ingesting an alkaline water or something like that. It is true that the pH, your alkalinity and acidity varies in different compartments in your body, that's important. Unless you are hemorrhaging or vomiting, or there's something badly wrong with you, health wise, and you're in a really dire circumstance, you don't want big shifts in your body pH and your body has all sorts of ways of buffering against changes in pH. So I encourage you not to fall on the, or hop on the bandwagon of adjusting pH and becoming less acidic, and that kind of thing. When you ingest lemon juice or lime juice, the mechanism by which it blunts blood glucose is probably twofold. One is probably through the post-ingestive effects of glucose in the gut, meaning the way in which sugars are interacting with neurons and other components of your gut circuitry to impact things like gastric emptying time, to impact things like the firing of those neuropod cells and their signaling to the brain. But almost certainly it has something to do also with the perception of sour taste on the tongue. We didn't go into this too much today, but you, of course, don't just have sweet taste receptors in your mouth, you also have bitter taste receptors, you have salty taste receptors, you have sour taste receptors in your mouth and of course, that means your tongue and palate. And those are interacting. If you ingest a substance that's just sweet or mostly sweet, that causes a certain set of effects on your blood glucose, but also your brain, dopamine, and the other neuro circuits of your brain. If you also ingest something that's sour like lemon juice or lime juice, it

adjusts the output of those neural circuits in your brain. So again, where you have a situation where you have two parallel pathways, one that's post-ingestive coming from phenomenon within our gut neurons, but also things like gastric emptying time, the clearance and transfer of food, and the conversion of food into particular nutrients and the circulation of glucose in your bloodstream and how it gets into the brain. But also simply by ingesting something sour, you are changing the way that sweet things impact your brain. And so I think it stands to reason that the lemon juice/lime juice effect is not going to be magic. It's going to have everything to do with the way that ingesting sour foods can adjust the taste. Excuse me, can adjust the neural response to taste of sweet foods. And in fact, we know based on the beautiful work of Charles Zuker at Columbia Medical School, that that's exactly what I happens. They've measured the activity of neurons at various locations in the so-called taste pathways of the brain. And they found that when particular tastes like just sweet or just bitter or just sour evoke certain ensembles of neurons to fire in particular sequences, when sweet and sour are co-ingested, when bitter and sour are co-ingested, you get distinct ensembles, meaning distinct patterns of activity of those neurons. And of course, distinct patterns of downstream activity within the brain and body. So while it is still somewhat mysterious as to how exactly things like lemon juice and lime juice can reduce our blood glucose spikes. When we ingest those with sweet foods or carbohydrate laden foods, or with big meals, you can use this as a tool with the understanding that there's a grounding in the biology of the way these circuits work.

01:43:09 Tool: Reduce Sugar Cravings & Spikes with Cinnamon

Now, some of you have probably heard that cinnamon can be a useful tool for controlling blood sugar. And indeed that's the case. It's very clear that cinnamon can adjust the rate of glucose entry into the stream, possibly by changing the rate of gastric emptying, it might slow the rate of gastric emptying and thereby also reduce the glycemic index of particular foods. So I suppose if I were going to eat a mango, and I hadn't just done a bunch of hard training, I might sprinkle some cinnamon on it here. I always enjoy kind of coming up with new ideas of ways that I can eat foods during these podcasts. In any event, there's some debate out there, if you look online as to whether or not Saigon Cinnamon, Cassia cinnamon, excuse me, or Ceylon cinnamon is best for purposes of blunting blood glucose spikes. But I think the, at least by my read of the data and from

what I've found, it doesn't really matter provided it's real cinnamon. And you have to actually look and make sure that it's real cinnamon, because a lot of cinnamon that you buy is not real. I do want to provide a cautionary note about cinnamon however. Cinnamon contains something called coumarin, which can be toxic at high levels. So you don't want to ingest more than about a teaspoon, maybe a teaspoon and a half of cinnamon per day, because you'll start to exceed the threshold at which cinnamon could start to be problematic. But certainly if you're going to have a big meal or a meal that has a lot of sugar in it, or a lot of carbohydrate laden foods, and you don't want an increase in blood glucose, you could put cinnamon in a beverage, you could put cinnamon on food in order to blunt that blood glucose increase, reduce the glycemic index by way of reducing gastric emptying time. Again, just making sure that you don't get out past that one and a half teaspoons per day, 'cause you really don't want to start dealing with any of the toxicity related to coumarin. So we've talked about lemon juice and lime juice and cinnamon, these are kind of commonplace in many kitchens. Then of course we can venture into the more esoteric or I would say the more advanced tools

01:45:10 Berberine, Sustained Low Blood Glucose Levels

for adjusting sugar intake. And the one that comes to mind is of course Berberine. Berberine is a derivative of tree bark and it is a very, very potent substance for reducing blood glucose. So much so that it is on par with Metformin or Glibenclamide, which are prescription drugs specifically used to reduce blood glucose. So using Berberine is a serious step, you should absolutely talk to your doctor about it. I know of a number of people that use it to lower blood glucose when they eat really large meals. I know the number of people that are using it to get to some of the other effects of Metformin that people have discussed, things like activating or tapping into the so-called AMPK pathway, reducing mTOR, these are people that are aiming their activities at increasing longevity, a somewhat controversial approach, still, but I know many people are doing it. It is true that if you ingest Berberine, your blood glucose will plummet. And I point that out because I've actually tried it before, it gave me brutal headaches and I felt really dizzy, and I felt like I couldn't see straight. And actually I couldn't see straight, why did it do that? Well, it made me hypoglycemic. It actually drove my blood glucose down too far. And the reason it did that is that I took Berberine on an empty stomach. I know some people can tolerate it. I would say, be very cautious about ingesting Berberine on an

empty stomach, or if you are in a low carbohydrate diet, unless you really know what you're doing and you have a medical professional to kind of guide you through that. If I took Berberine along with a very large meal, that included a lot of carbohydrates, you know, I can recall the days in which Costello and I would eat a couple of pizzas and then we might get ice cream, that kind of thing. Then I felt perfectly fine on even up to 750 milligrams or a gram of Berberine. It has the kind of unique property of making you feel not overwhelmed by the amount of blood glucose increase that you're experiencing from eating a big meal. I don't quite know how else to describe it. It's almost as if you can keep eating and eating and eating, and of course you have to protect your gastric volume. I mean, you only have so much space in your stomach to ingest food. I wasn't using it to gorge on food, I just heard about it, I was interested in experimenting with it. I don't have any chronic blood sugar issues. But again, when I took it on an empty stomach, it made me hypoglycemic on a low carbohydrate intake, hypoglycemic, not a good experience. And again, an experience I think to avoid. But provided there's a lot of glucose in your bloodstream, and certainly if you are of the experimental type or you're trying to regulate blood glucose, Berberine might be a good option. But again, talk to your doctor. It does have some other interesting effects in terms of lowering total cholesterol that are research supported of reducing insulin a little bit. Well, that's not surprising if you reduce blood glucose, you're going to reduce insulin because of course, insulin manages blood glucose in the bloodstream. So I would place Berberine and of course, Metformin and Glibenclamide in the kind of the heavy hitting potent tools for regulating blood glucose. Now, this is an episode, not about sugar per se, but sugar viewed through the lens of the nervous system. And what's interesting about Berberine, Metformin, Glibenclamide and related substances, is that some of the effects are of course on gastric emptying or buffering blood glucose within the bloodstream, et cetera. But there appeared to also be some neural effects of having chronically low glucose or blunting blood glucose through things like Berberine. And some of those neural effects include longstanding changes in the hormonal cascades that are the consequence of having low blood sugar and thereby, changes in the neural circuits that manage blood glucose overall. The simple way of saying this is that by maintaining low to moderate blood glucose, either by not ingesting heavily carbohydrate laden foods. So here I'm speaking to the low carb or the ketogenic types or by blunting blood glucose through things like Metformin or Berberine, even if ingesting carbohydrates, maybe even some sugars, over time, it seems that there's a adjustment, what we call a homeostatic

regulation of the neural circuits that control things like sugar craving, and indeed, some people report feeling fewer sugar cravings over time. Now I didn't use Berberine for a very long period of time, I've never used Metformin. I have experienced a somewhat odd but welcome phenomenon of with each progressive year of my life, I have fewer and fewer sugar cravings. Why that is, I don't know. I suspect it might have something to do with my sleep. And I'll talk about that in a few minutes. But if you're going to explore Berberine or Metformin or otherwise, in addition to working with a doctor, I think you should understand why you're doing it, right. I think that many of the effects can be quite potent. They can happen in both the immediate term in terms of regulating blood glucose, they can send you hypoglycemic if you aren't careful, they can also cause longstanding changes to the neural circuitry that regulates blood sugar over time. Some of which might be welcome changes, right? Reduce sugar cravings for instance. And if you are really, really serious about modulating blood glucose through things like Berberine, the typical dose range, again, is anywhere from half a gram to 1.5 grams daily, that's the typical dosages that have been explored. And there are some other substances like sodium caprate which are known to augment the effects of Berberine via the AMPK pathways. They basically can increase the ability for Berberine to have its glucose lowering actions. But that of course is getting into the really potent, what I would call sharp blade tools for controlling blood glucose. And listen, anytime you're dealing with blood glucose, you are dealing with the brain's preferred source of fuel. And anytime you're dealing with the brain's preferred source of fuel, you have to be especially cautious about depriving the brain of what it needs. So whether or not you're low carb, high carb, you know, keto, vegan, carnivore, these substances, like Berberine, are very, very potent and you need to take them seriously.

01:51:24 Tool: Sleep & Sugar Cravings

There is yet another tool for controlling sugar cravings and the neural circuits that regulate sugar craving and its downstream consequences. And this tool is what I would call a high performance tool, but it's one that you probably didn't suspect and that's sleep. I've done extensive episodes about sleep, and we actually have an episode called master your sleep. You can find that episode easily at hubermanlab.com. It's available in all the various formats, YouTube, Apple, Spotify, et cetera. and it provides a lot of tools. And on social media, I provide a lot of tools, often we have a newsletter that provides

tools on how to maximize sleep. What is the role of sleep in sugar metabolism, sugar, hunger, and the way that the brain regulates those things? Well, there's a really exciting study that came out just last year. This study was published in the journal, Cell Report, a Cell Press journal, excellent journal. And the reason I love this study so much, is it involved having people, so yes, this was done in humans, sleep in the laboratory. That's not unusual, there's a sleep lab at Stanford, there's sleep labs elsewhere. But what they did was they actually measured from the breath of these people, and they extracted from their breath, the metabolites that would allow them to understand what sorts of metabolism was occurring in these people's bodies at different phases of sleep. And this is a really remarkable study. They actually did this every 10 seconds throughout the entire night. So in little tiny 10 second bits, meaning at very high resolution, they could evaluate what is the metabolism in the brain and body that people experience as they go from REM sleep, rapid eye movement sleep to slow wave, sleep, and so on. And I'll go deeper into the study again in the future, because it's so interesting, and I think so important. But what they discovered was that each stage of sleep was associated with a very particular signature pattern of metabolism and particular phases of sleep are associated with sugar metabolism, or more with fat metabolism, or more with other aspects of metabolism. And the reason why I think this study is important to discuss in the context of today's discussion about sugar in the brain, is that many people have experienced the effects of disrupted sleep on their appetite. And in particular, it's been reported that when people are sleep deprived or the quality of their sleep is disrupted, that their appetite for sugary food increases. Now that was always assumed to be due to some metabolic need that was triggered by the sleep deprivation or by the poor sleep. But in reading over this study, some of the more important points made by the authors relate to the fact that well, sleep is known to have incredibly important effects on brain and body, for a variety of systems, immune system, neural functioning, et cetera. This very organized sequence of particular forms of metabolism being active during particular phases of sleep, which are very, very well orchestrated, as we know, slow wave sleep, and REM sleep being orchestrated in 90 minutes, so-called ultradian cycles and so on and so forth, is thought to of perhaps set up the brain and body to be able to regulate itself in the waking hours. And therefore, when people are sleep deprived or deprived of certain forms or states within sleep, such as rapid eye movement sleep, that it creates a disruption in a particular set of metabolic pathways. Now we don't a leap too far from this study to sugar metabolism and the neural circuits controlling sugar metabolism. But I will

say this, if you look at the sum total of the data on obesity or on type two diabetes or on metabolic syndromes of any kind, you almost always see disruptions in sleep. Now, some of those could be you do to sleep apnea caused by even just the size of somebody's neck or the weight of their body. In other words, we don't know the direction of the effect, metabolic syndromes could disrupt sleep, which disrupt metabolic syndromes. And indeed the authors point out quite appropriately, that they don't understand the direction of the effects that they observe either. But there is now a plethora of data pointing to the fact that getting quality sleep each night helps regulate not only appetite, but also the specific forms of metabolism that drive specific appetites. So the takeaway is, while there are extravagant and potent and interesting ways to regulate blood glucose, everything from cinnamon to lemon juice, to Berberine, to sodium caprate, to behavioral tools, to the mere understanding of how the direct and indirect pathways go from the gut to dopamine, et cetera, if you're not establishing the firm foundation of proper metabolism, all of those things are going to be sort of rearranging deck chairs on the Titanic as it's sometimes described. So we can't overstate the importance of getting regular sufficient amount of high quality sleep, at least 80% of the time, not for sake of immune system function, for clear thinking, et cetera, but also for properly regulating our metabolism,

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including our sugar metabolism. Thank you for joining me for this discussion about sugar and the nervous system and how they are regulating each other in both the brain and body. If you're enjoying and/or learning from this podcast, please subscribe to our YouTube channel. That's a terrific zero cost way to support us. Please also subscribe to our podcast on Apple and Spotify. And on Apple, you have the opportunity to leave us up to a five star review. If you have comments and feedback or suggestions for future topics and guests, please leave those in the comments section on YouTube. In addition, please check out the sponsors mentioned at the beginning of today's podcast, that's best way to support us. In addition, we have a Patreon, it's patreon.com/andrewhuberman. And there you can support the podcast at any level that you like. If you're not already following Huberman Lab on Instagram or Twitter, please do so. There I cover science and science-based tools that sometimes overlap with the content of the podcast, but

often is distinct from the content of the podcast. During today's episode, and on many previous episodes of The Huberman Lab Podcast, I've discussed supplements. While supplements aren't necessary for everybody, many people derive tremendous benefit from them. One issue with supplements is that if you're going to take them, you want to make sure that they have the absolute highest quality. For that reason, we've partnered with Thorne, that's T-H-O-R-N-E, 'cause Thorne has partnered for instance, with all the major sports teams and the Mayo Clinic. There's tremendous trust in the fact that Thorne supplements contain the specific amounts of supplements that are listed on the bottle and that the quality of the ingredients they include are of the very highest standards. If you want to see the supplements that I take, you can go to thorne.com/U/Huberman, and you can get 20% off any of the supplements listed there. Also, if you navigate further into the Thorne site, through that portal, thorne.com/U/Huberman, you can also get 20% off any of the other supplements that Thorne makes. Also, if you haven't yet signed up for the Huberman Lab Neural Network Newsletter, it's a semimonthly newsletter that includes summaries of various podcasts, it has some actionable protocols, it's completely cost free. You simply provide your email. We have a very clear privacy policy. We do not share your email. If you want to get the newsletter, you can go to Hubermanlab.com. Just go to the menu, you can find the sign up there easily. You can also see some examples of previous newsletters without having to sign up at all. And last, but certainly not least, thank you for your interest in science.