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 talking all about food and the brain. We are going to talk about foods that are good for your brain in terms of focus, in terms of brain health generally, and the longevity of your brain, your ability to maintain cognition and clear thinking over time. We are also going to talk about why and how you prefer certain foods to others. And I'm going to talk about the three major signals that combine to drive your food choices. I'll give you a little hint of what those are. One of those signals comes from your gut and is completely subconscious. This is not the gut microbiome per se. These are neurons in your gut that are sending signals to your brain that you are unaware of about the nutrient contents of the foods that you're eating. The second signal is how metabolically accessible a given food is, meaning how readily that food can be converted into energy that your brain, not your body, but that your brain can use. And the third signal is perhaps the most interesting one. It's the signal of belief. It's the signal of what you perceive and believe the food that you're eating to contain and what you think it can do for you health wise and energy wise. And that might sound a little wishy washier vague, but we're going to provide mechanistic data to support the fact that you can change what you eat. So much so that you can drive your brain and your body to crave foods that are good for you or at least better for you than the foods you might currently be eating. This isn't an incredibly powerful mechanism that we all have. It's one that I think is very underappreciated. And today I'm going to review the data from both animal models and fortunately more recently human studies that really do underscore the fact that you can control your desire for particular foods. Before we dive into today's topic, I just want to briefly touch on some key takeaways from a previous episode, which is the episode on time restricted feeding, also called intermittent fasting. The key elements of time restricted feeding that will benefit your health the most in terms of weight loss or maintenance, fat loss, organ health, quality sleep and cognition are that the feeding window begin at least one hour after waking. You could push that feeding window out to begin later, but at least one hour after waking and that it end at least two and ideally three hours before going to sleep. Some people can end that feeding window much further away from the beginning of sleep, meaning they're finishing their last bite of food, for instance, at 6 p.m. And they're not going to sleep until midnight, but many people struggle to get quality sleep if that feeding window is set too early relative to when they go to sleep. So begin the feeding window at least one hour after waking and the feeding window at least two hours before going to sleep. And a key feature based on the scientific research is that the feeding window itself fall more or less at the same period of each 24 hour day from day to day, meaning if you are going to eat over an eight hour period, that's your feeding window. You wouldn't want to start that feeding window at 10 a.m. one day and ended at 6 p.m. and then the next day started at noon and ended at 8 p.m. and the next day started at 2 p.m. and ended at 10 p.m. and so forth. As much as is reasonably possible, if you want to extract the maximum benefit from time restricted feeding, the idea is to keep that feeding window at more or less the same phase as it's called of each 24 hour day. If it slides around a little bit for social reasons or whatever reasons, it doesn't seem to be a big deal, but you don't want it sliding around by many hours from day to day because of the way that that feeding window impacts other genes called clock genes that regulate a bunch of other processes in the body. Before we begin, I'd like to emphasize that this podcast is separate from my teaching and research roles at Stanford. It is, however, part of my desire and effort to bring zero cost to consumer information about science and science related tools to the general public. Recently I took part in an event called re-think education that was put on by Logitech. I've got a 20 minute lecture where I describe the classic and modern neuroplasticity literature in both animal models and humans. The neuroplasticity literature is of course the literature that describes how to rewire the brain in order to learn. During that 20 minute talk, I described that literature, but I also spell out what I call the neuroplasticity super protocol, which is nine plus steps of things that teachers can apply in the classroom to teach any sort of information, music, math, sports, anything, and that students of any kind in any age can use to enhance the speed and depth of learning. You can find that talk on YouTube by following the link in the caption to this episode or by simply going to YouTube and entering the search terms Logitech, Huberman. Some of the most frequent questions I get are about food and the brain. Everybody seems to want to know what they should eat and what they shouldn't eat in order to have peak brain function to be able to focus and memorize things and so forth, and in order to maintain brain health over time because nobody wants to lose their memory or have troubles with cognition. Fortunately, there are a lot of data now from really good quality peer reviewed studies that indicate certain things that we can do, including certain foods that we should eat, and perhaps even some foods that we should avoid in order to enhance our brain function. And of course, when I say brain, what I really mean is nervous system function because how we are able to move and remember things, etc. Doesn't just depend on the neurons, the nerve cells that are in our head. It also depends on our spinal cord and the neurons that connect all the organs of our body. So in general, there are two categories of things that are going to improve brain health from the perspective of nutrition. The first category is the general category of things that we eat and avoid and things that we do and avoid doing that will modulate brain health and function. What do I mean by modulate? Well, getting quality sleep on a regular basis, making sure that you're socially connected, making sure that you're not depressed. All these things are vitally important to our overall health, and of course they will impact brain function, but they do it more or less indirectly. Okay, there are a few things that happen in sleep which directly benefit brain function and repair, etc. But today I really want to concentrate not on the things that modulate our overall health, but rather the things that mediate brain health directly. And in particular, how certain foods enhance brain function, and we are going to talk about how we can change our relationship to food, literally how we can start to prefer certain foods that are better for us than others. So just briefly, I want to touch on the modulatory components because they are vital. First of all, getting quality sleep on a regular basis and ample sleep on a regular basis is the foundation of all mental health and physical health. There's no question about that. We've done several episodes, including the Mastery, your Sleep episode, which is episode two of the Human Lab podcast, and we've done a lot of other episodes that are all about sleep and how to get better at sleeping. So I just want to make crystal clear that unless you're sleeping well on a regular basis, your brain will suffer. You won't be able to focus very well, learn very well, and indeed there are data linking poor quality sleep to dementia or at least exacerbating pre-existing dementia and things of that sort. So get your sleep in order. The other, of course, is cardiovascular health and exercise. The general prescription that's out there in the literature, and I think is well supported, is to get somewhere between 150 and 180 minutes of cardiovascular exercise per week. If you choose to also use resistance exercise, that's great. But the 150 to 180 minutes minimum per week of cardiovascular exercise is crucial for heart health and heart health directly relates to brain health because the brain consumes a lot of oxygen, glucose, and other factors that are delivered via the blood. So if your arteries are clogged up and you've got poor vascular supply to the brain, in any region of the brain, your brain will suffer. So get cardiovascular health in order. Now, with those two modulatory elements set forth so that we're all aware that they're there and they are vitally important, now I'd like to turn to the elements that have been shown to be vitally important for directly controlling, for mediating neuron function. Neurons, of course, are nerve cells in the brain and there are other cell types too, of course, that will impact brain function. The most prominent of which are the so-called glia. Glia means glue, but even though for a long time people thought that these cells were just kind of holding things together passively, the glia play a very active role in the metabolism neurons in brain function and probably also in cognition, in thinking, and so forth. So what are the things that directly impact brain health and what are the foods that we can eat that will support brain health? Generally, when we think about neuron function and brain function, we default to a discussion about fuel, the fact that neurons use glucose, which is blood sugar, and that they require a lot of it. In some cases, they'll use ketones, which we will talk about a little bit later, especially in people that are following a low carbohydrate or ketogenic diet. But before we can even consider the fuels that neurons use in order to function, we have to talk about the elements that actually allow those neurons to be there and to stay healthy, what actually makes up those neurons. And that brings us to what I would argue is the most important food element for brain function, and that is fat. And that may come as a surprise, but unless one considers the water content of the brain, which is very high, a lot of our brain and a lot of the integrity of the nerve cells, the so-called neurons in our brain, and the other types of cells comes from fat. And that's because nerve cells and other cells in the brain have an external layer. It's what's sometimes called a double layered membrane. It's essentially two thin layers that serve as a boundary between those cells, and that boundary is very important because how things pass across that boundary actually regulates the electrical activity of neurons, which is the way that neurons fire and communicate and keep you thinking and acting and doing all the good things that those neurons allow us to do. And those membranes are made up of fats, but they're not made up of the fats that are around our belly, around the other organs of our body. They're not made up of storage fat, they are made up of structural fat, and maintaining the so-called integrity of that structural fat, meaning the health of those neurons is going to come in large part from the foods that we eat. Now, this needs to be underscored. What I'm saying is that the foods that we eat actually provide the structural basis, the building blocks of the very neurons that allow us to think over time. And, as I mentioned earlier, the fat that makes up those neurons in other nerve cells is different than the other types of fat in the body. So what type of fat is it, and what should we eat in order to support that fat and those neurons? And the answer is the so-called essential fatty acids and phospholipids. Now, those are more or less the same thing, but I just want to make a very large literature very crystal clear. Essential fatty acids can include the so-called EPA variety or DHA variety. You hear about omega-3s and omega-6s. Most people are getting enough omega-6s from their diet, not everybody, but most people are getting enough omega-6s. However, most people are not getting enough omega-3s in their diet to support healthy brain function in the short and long term. I've talked before about the benefits of elevating the levels of omega-3s in one's diet for sake of offsetting depression and for enhancing mood. And indeed, there's a wealth of literature now pointing to the fact that ingesting at least one or two or even three grams per day of EPA form of essential fatty acid can have effects, positive effects on mood and well-being that are at least on par with some of the major antidepressant treatments out there, but without similar side effects to those antidepressant treatments. And that for people that are already taking antidepressants that supplementing with one to two to three grams of EPA essential fatty acids can actually allow a lower dose of antidepressant treatment to be used and still be effective. So that's depression, but just in terms of maintaining normal cognitive function in people that aren't depressed, the EPA's and omega-3s seem to play a very important role. Of course, you can supplement EPA's through various fish oils and it could be liquid fish oil or capsule fish oil. Some people, if they're not interested in eating fish for whatever reason, they're allergic or for ethical reasons, they can take krill oil. And if they don't want to use krill oil, they can use algae and other forms of EPA. However, I think it's clear that one can get a lot of EPA from the proper foods and it turns out that those foods, not surprisingly, don't just contain high levels of EPA, but they also contain other things that are beneficial for brain health. So what are foods that are high in omega-3s that we should all probably be consuming at least on a daily basis? The number one is fish, so things like macrol and salmon and herring and oysters and sardines and anchovies and perhaps the heavyweight champion of EPA's per unit volume is caviar. Now, I don't know about you, but I'm not eating a lot of fish. I'm not eating a lot of caviar. I can't remember the last time I had a caviar unless it was sprinkled on a little bit of sushi. I'm not a big fish eater, personally, I will from time to time, but that's one reason why one might want to supplement with EPA's from another source. But also, EPA's are found in chia seeds, in walnuts, in soybeans, and other plant-based foods. You can look these up online and you'll immediately see that there are a lot of sources of EPA's. And many of the foods that I listed off might be appetizing to you, some of them might be un-appetizing to you, or some of them you might be sort of neutral about. But it's very clear that eating foods that are rich in omega-3s and or supplementing with omega-3s to get above that 1.5 grams, and ideally up to 2 or even 3 grams per day of EPA, can be very beneficial for cognitive function in the short and long term. Later in the episode, I'm going to talk about how to actually change your relationship to particular foods so that foods that you don't particularly like, you can actually start to like more. And that might be important for those of you that are thinking macros, sardines, I mean, I'm making this face because, frankly, those are not foods that I naturally like. But again, I want to emphasize that you don't have to consume fish and animal products in order to get sufficient EPA's. You can get them from plants, but I do believe based on the quality peer reviewed research that everybody should be striving to get a minimum threshold of at least a gram and a half of EPA's per day one way or the other. The great thing about omega-3s is that they are also thought to be beneficial for things like cardiovascular health. And although there's some controversy there as to whether or not 2 grams or 3 grams or 6 grams is ideal for cardiovascular health, I think the bulk of evidence points to the fact that getting sufficient omega-3s in the diet is going to support cardiovascular health. Certainly not the only thing people should be doing to support their cardiovascular health, aerobic exercise and so forth being important also, but it does seem to support cardiovascular health and in doing so, supporting brain health. However, what I'm emphasizing is ingestion of omega-3s to support the very cells within the brain that make up our cognition that allow for cognition and for movement and memory and all the other marvelous things that the brain does. The other compound that has been shown to be directly supportive of neuronal function is phosphatidal serine, which is abundant in meats and in fish. So here we are again back to fish being an important source of brain supporting food. Phosphatidal serine is something that nowadays people are supplementing. It's a lipid-like compound that at least in three studies have been shown to improve cognition. These weren't huge effects, but they were statistically significant effects. And as well in more than three, at least five studies to reduce cognitive decline. And this is interesting. In every case, it was 300 milligrams supplemented, phosphatidal serine. But one, again, doesn't need to supplement phosphatidal serine. Phosphatidal serine can be derived as I mentioned from meats and fish and to some extent from cabbage of all things. So I don't know how much cabbage people are ingesting. But later when we talk about gut health and the relationship between gut health and brain health, I'll mention fermented foods. And of course, one of the most readily available fermented foods out there that at least many people find appetizing is sauerkraut, which is of course made from cabbage. It's fermented cabbage. So for those of you that do consume meat and fish, provided you're getting enough fish, you're probably getting enough phosphatidal serine. For those of you that are interested in supplementing phosphatidal serine to get these effects that were reported in these various manuscripts, which by the way I've read and look solid. I mean, I don't think we've seen the landmark study showing that supplementing with phosphatidal serine at 300 milligrams per day is going to create a huge offsetting of a massive cognitive decline or a massive increase in brain function. These seem to be modest effects, but the effects do appear to be real. And for those of you that are interested in supplementing the phosphatidal serine, it's a relatively inexpensive supplement that again is lipid like so it's mimicking some of the same things that you would get from food, but in higher concentration. Now, after EPA fatty acids and phosphatidal serine, I would say third on the list of things that come from food that can readily support brain function would be Colleen. Because of the relationship to Colleen in the biosynthesis pathway for acetyl Colleen acetyl Colleen is a neuromodulator, not a neurotransmitter, but a neuromodulator in the brain. A neuromodulator is a chemical that modulates the function of many brain circuits and also circuits within the body. I'll mention what those are in a moment, but acetyl Colleen as a neuromodulator tends to enhance the activity, the electrical activity and chemical activity of certain sets of neurons. And downplay the activity of other neurons. So it's sort of a conductor of sorts leading to enhanced function and activity in certain brain areas and circuits and not in others. For instance, the brain areas that are involved in focus and alertness, we have multiple clusters of neurons in our brain that make acetyl Colleen two of the most prominent and well known are the so-called nucleus basalis, which is a cluster of neurons deep in the basal form brain. That highlight particular areas of our brain highlight meaning when acetyl Colleen is released from those neurons at their nerve endings in particular areas of the brain, those particular areas of the brain can undergo enhanced levels of activity relative to surrounding areas. So it's kind of a electrical highlighter pen, if you will, by analogy. That is the basis of much of what we call focus or our ability to concentrate on a particular batch of information that's coming in through our eyes, our ears, our nose, or even things that we're just thinking in our head. So having ample Colleen for production of acetyl Colleen allows for focus through, of course, many intervening steps. There are also regions of the brain in the so-called back of the brain, the hind brain that release acetyl Colleen that are involved in general states of alertness and not surprisingly then many of the treatments for Alzheimer's disease, which is an inability or challenges with remembering things and focusing, or drugs that impact the acetyl Colleen pathway and are aimed at enhancing the amount of acetyl Colleen that's available to neurons. And it can do that through a number of different mechanisms. You can do that by enhancing the amount of acetyl Colleen that's created, or you can do that by taking a drug that can reduce the amount of enzyme that gobbles up the acetyl Colleen and in doing so leading to more net acetyl Colleen. But outside of the scenario where somebody has cognitive decline due to Alzheimer's, all of us are able to focus to some degree or not, or are able to be alert to some degree or not based on the amount of acetyl Colleen that we have. Now other processes, of course, are involved, but what this means is that making sure that we have enough of the substrates to create acetyl Colleen is vital if we want to be able to focus. And that's why dietary Colleen is so vital, and the primary source for dietary Colleen would be eggs and in particular egg yolks. And this again has a very interesting relationship to our evolution as well. We're always referred to as hunter gathers, but when one hears hunters we often think about meat and animal sources, and indeed as a species we hunted many many other species of animals to consume them and still do. But we also fished, we talked about that earlier and consumed a lot of fish, and we consumed a lot of eggs. Eggs are an incredibly rich source of nutrients for the brain. And that's because the egg actually, if you think about it, contains all the nutrients that are required in order for an organism to grow. You know, a bird that's in an egg shell, it's got the yolk there and it's using that yolk for a reason. It's using that yolk as a source of fuel. It's using that yolk as a source of literally building blocks in order to create its nervous system. Many years ago I worked on chick embryos and as these amazing experiments you could actually take an egg and you could create a little window in the top. And these were fertilized eggs and you'd see over time you could peer in there, literally look in with a microscope or even with the naked eye, and you would see this little chick embryo sitting on top of that yolk growing and growing and growing and growing and growing and the yolk getting smaller and smaller is really incredible. They're using that as a source for all the building blocks of the body, but in particular the nervous system. So eggs are a rich source of calling. Some people will supplement with calling. However, food sources seem to be the best source of calling. And as with the EPA's and the Omega-3's, there are plenty of foods that are non-animal based that contain calling. So if you're somebody who doesn't eat eggs or doesn't want to eat eggs, things like potatoes, nuts and seeds and grains and fruit, they don't have as much calling as eggs, but they do contain calling. So you can look up the values of calling that are present in those various foods and make sure that you're reaching the threshold amount of calling for you. In general, most people should probably strive to get somewhere between 500 milligrams and a gram of calling per day, so 1000 milligrams. And some people rely on supplementation in order to hit those levels because they're not eating a lot of egg yolks or they're not eating a lot of other foods, certain fish contain calling. For instance, and the other foods I listed off a few minutes ago from plant based sources. So some people will supplement with 50 to 100 milligrams or whatever amount is necessary to get them up to that one gram or even a two gram dose per day. So we have three things that we know can support nerve cells. EPA in particular, Omega-3 fatty acids, phosphatidal serine and calling. Those three things I would list off as the top three things for enhancing neuron function and the integrity of neuron to eat. And the integrity of neurons in the short and long term. And this is again, is setting aside the vitally important factors of hydration and electrolytes. I've said it before on other podcasts, but if you're not ingesting enough water and you're not getting enough sodium and magnesium and potassium, then obviously your neurons can't run because a lot of the brain is is water. And so the main thing is that they're not going to maintain proper hydration and sodium, potassium and magnesium are important in order for nerve cells to function. In fact, they are actually the components, the ions that pass across those lipid membranes, those little fatty membranes that we're talking about earlier that allow the neurons to generate electrical activity and communicate with one another. Definitely want to hydrate enough. Well, we will do an entire other episode all about hydration and electrolytes, but Omega-3s, the EPA's, phosphatidal serine and calling. It's obvious are going to improve brain function. How much they will improve brain function probably depends on how well your brain was working previously. In fact, many of the studies that have looked at the effectiveness of these compounds have looked in people that are suffering from mild or even severe cognitive decline. And while the outcomes of those studies vary, given the interest in maintaining brain function, given the fact that we don't make new neurons throughout our entire life, and given that everybody has to eat, these are quality healthy foods that we should all be ingesting anyways, and it's clear that they can support brain function to some degree or another. Many people ask what I do in light of this information. And while I can only talk about what works for me, I choose to ingest fish oil in mainly in liquid form, because that turns out to be the easiest way and the most economically affordable way to do it for most people. So there are various forms of liquid fish oil out there, some of them include some lemon flavoring, so it doesn't taste like fish oil, because frankly, fish oil to me is sort of noxious tasting. And I'll take a tablespoon of that or two per day. If I'm traveling, I'll use the capsule form in order to hit that threshold of for me about two, sometimes even three grams per day of EPA. So not just two or three grams per day of fish oil, but two or three grams per day of EPA. Now, if I'm eating fish, which, as I mentioned earlier, is not often, then I might reduce the amount of fish oil that I take. But that's my major source of fish oil. Currently, I do not supplement with phosphatidal serine, a number of people that I know and trust and indeed several colleagues of mine do take phosphatidal serine. I don't have any good explanation for why I don't take it yet, but I have not tried supplementing with it yet. Maybe if some of you have, you can place your experience in the comment section. That would be of interest. And then in terms of calling, in order to get calling in my diet, I do pay attention to the various foods that contain calling and I try and get those foods on a semi-regular basis. I do supplement with something called alpha GPC, which is essentially in the acetacolene pathway or biosynthesis pathway. I don't take it very often, but I will take 300 milligrams of alpha GPC from time to time, from time to time. I mean, anywhere from two to three times per week. I'll generally do it early in the day because it for me can have a little bit of a stimulant effect, although it's not nearly as stimulating, say as a double espresso or triple espresso. But that's one way in which I enhance my colon function. And some people choose to get it from supplementation because it's straightforward. There are a lot of supplements out there that contain alpha GPC. Some people are taking dosages as high as 900 milligrams per day. That sounds very high to me. The studies of offset and cognitive decline using alpha GPC did use quite high dosages of 600 to 900 or even 1200 milligrams per day. So it has been used at those much higher concentrations, but because fortunately, at least not yet or not to my awareness, I'm not suffering from any cognitive decline, I will supplement with 300 milligrams every now and again. Next on my list of compounds that have been shown in pure reviewed research to improve neuronal and brain function is creatine. Creatine can be derived from meat sources. It can also be supplemented. Some of you are probably familiar with creatine or heard about creatine from the context of the health and fitness world where creatine is used to bring more water into muscles, which can enhance the strength of those muscles, as well as bring water into other tissues. It doesn't just draw more water into muscle, it can draw more water into the body generally. Creatine has also been shown to have an important role in brain function. And once again, this is something that came up during the discussion about depression a few episodes back. Creatine can actually be used as a fuel source in the brain and there's some evidence that it can enhance the function of certain frontal cortical circuits that feed down onto or rather connect to areas of the brain that are involved in mood regulation and motivation. And that's where creatine plays a role in depression or rather where creatine supplementation seems to be able to assist in some forms of mild depression. That's an emerging literature. It's still not well established. However, there is now ample evidence that creatine supplementation can enhance brain function in certain contexts. And if you're interested in learning more about what those contexts are, there's an excellent review that just came out. The first author is Rushell, R-O-S-C-H-E-L. We will provide a link to this study, rather this review, excuse me, in the caption. This was published just very recently in 2021. And one thing to make clear is that creatine supplementation has been shown to be especially useful for people that are not consuming any meat or other sources of foods that are rich in creatine. What is the threshold level of creatine to supplement in order to get the cognitive benefit? It appears to be at least 5 grams per day. Now the most typical form of creatine is so-called creatine monohydrate. There are other forms of creatine as well, some of which are thought to not draw as much water into non-muscle tissues. And for some people that's attractive to them, they don't want water sitting below their skin, etc. I should emphasize that the responses to creatine in that sense can differ. Some people get a little bit of water retention, some people experience more. There are some evidence that creatine can impact some of the hormonal pathways that it might enhance levels of so-called dihydrotestosterone DHT. And therefore, because DHT is involved in hair loss, there are these theories that creatine can cause hair loss and indeed for people that are very DHT sensitive, it might. There's going to be a lot of variation in person to person in terms of how much creatine impacts DHT and how many DHT receptors they have on their scalp and therefore whether or not they experience hair loss. I'm just giving you all this information so that you're aware of the various things that creatine can do. Nonetheless, I think it's interesting that creatine supplementation of 5 grams per day, that's creatine monohydrate, has been shown to improve cognition of people that aren't getting creatine from animal sources. And there's some evidence, detailed within the review that I just described, that creatine supplementation can also enhance cognition in people that are also eating animal products. So I personally take creatine 5 grams per day and have for a very long time. I can't say that I've noticed a tremendous benefit because I've actually never really come off it. And so I've never done the control experiment. I take it more as kind of a baseline insurance policy for me. I'm probably losing, I'm certainly losing some of my hair, whether or not that's due to creatine or not. I've never done the analysis, but what I can say is that I generally consume these things like EPA's creatine alpha GPC to set a general context of support for my neurons for my brain. And of course, I also pay attention to the foods that contain these various compounds. So I don't actively eat additional meat just to obtain creatine. I eat a fairly limited amount of meat, I don't restrict it, but I do eat meat. But I don't actively seek out creatine in my diet rather I use supplementation in order to hit that 5 grams per day threshold. Next on the list of foods that are beneficial for brain health is one that you've probably seen pictures of online because there seems to be a practice of putting pictures of blueberries and other dark berries next to any title that says foods that benefit your brain. There are a lot of foods out there that have been purported to improve brain function. The interesting thing about blueberries and other berries, blackberries, dark currents, any of these thin skin berries that are purpleish in color is that they contain what are called anthocyanins. Anthocyanins actually have some really nice data to support the fact that they improve brain function. Now whether or not it is direct effects on neurons or whether or not it is by lowering inflammation or some other modulatory effect isn't quite clear. But by now there's enough data to support the fact that eating a cup or two of blueberries pretty often every day or maybe you have blackberries or maybe it's black currents that these anthocyanins are good for us that they are enhancing our overall well being at a number of different levels. And just to give you a couple examples of where there are actually peer reviewed studies to support those statements. The anthocyanins of which blueberries and other dark berries are rich in have been shown to reduce the amount of DNA damage has been shown to reduce significantly, albeit slightly, excuse me, cognitive decline. And that particular study was supplementation of a blueberry extract. I'll talk about the difference between extract and actual blueberries in a moment. But supplementation of blueberry extract in offsetting cognitive decline in elderly people. So you know what constitutes elderly is always a little bit of a debate and a discussion. But in this case what they what they did is they supplemented with somewhere between 428. I don't know why they selected 428 and 598 milligrams of anthocyanins daily for 12 weeks was associated with improvements on verbal learning and memory. And they had some other beneficial changes that were within the bodily organs and blood glucose regulation and so forth positive changes. But that's one study in this case elderly meant 65 or older that study and a number of studies like it looking at things like mildly enhanced memory reduced insulin levels reduced oxidation of LDL these sorts of things have basically create a situation where anytime you Google or look up foods that enhanced brain function you're going to see a picture of a blueberry or some other berry because of these anthocyanins. I personally don't supplement anthocyanins. I do like blueberries I eat blueberries when they're in season. I love them. I'm what you would call a drive by blueberry eater like if there are blueberries in a bowl on a table and I'm walking by I just have to scoop them up like some sort of bearer or other animal and pop them on mouth. So blueberries don't last long around me. One of the issues with berries like blueberries and blackberries and so forth is that quality sources of them can be pretty expensive and then of course when they're not in season they're hard to get and so that's why some people will supplement with them. So that range of about 400 to about 600 milligrams per day seems to be the minimum threshold for getting a cognitive effect in these elderly patients in that case they were patients. A good review about the anthocyanins potentially contributing to offsetting cognitive decline in things like Alzheimer's and also enhancing brain function in people that don't have Alzheimer's is a review by off-zal AFZAL that was published in 2019. We will also provide a link to that study in the caption. When one looks across the total batch of studies that are out there on this it appears that if one is going to supplement with blueberry extract to get the anthocyanin effect on cognition. Doses of somewhere between five and a half or about 11 grams seem optimal with the higher end closer to 10 or 11 grams being more beneficial. The blueberry eaters out there like me who prefer to get their anthocyanins from the actual berries appears that somewhere between 60 to 120 grams of fresh blueberries each day is the way that you can get sufficient anthocyanins to shift your system or bias your brain towards these enhanced cognitive effects so we've got EPA fatty acids we've got phosphididal serine we've got coline we've got creatine and we have the anthocyanins and the last item that I'd like to place in this list of food derived things that can enhance brain function is glutamine. Glutamine is a very interesting amino acid I've talked about glutamine one here before there's some evidence although somewhat scant there's some evidence that glutamine can enhance immune system function so people will supplement with glutamine or people can get glutamine from foods foods they contain a lot of glutamine are things like cottage cheese there are also other sources of glutamine glutamine is rich in protein rich foods things like beef chicken fish dairy products eggs but also for you non animal food consuming people out there vegetables including beans cabbage once again spinach parsley things of that sort so those foods contain glutamine for people that supplement with glutamine generally they will take anywhere from a gram as much as 10 grams per day why would they want to do that well there's also some evidence starting to emerge that glutamine can help offset sugar cravings I've talked about this on the podcast before we're going to talk more about the basis for this a little bit later but in brief we all have neurons in our gut that sense the amino acid content the fat content and the sugar content of the foods that we and signal in a subconscious way to our brain whether or not the food is not the food that we eat we are eating contain certain levels of certain amino acids and so we actually have glutamine sensing neurons in our gut that actually have their little processes their little axons and dendrites as we call them in the mucus alighting of the gut they're not just sensing glutamine but when they do sense glutamine they respond and they send signals to the brain that are signals of satiation of satisfaction and in doing so can offset some of the sugar cravings that many people suffer from now here we're talking about glutamine for sake of enhancing cognitive function and this is interesting because it's been shown that glutamine supplementation can offset some of the negative effects on cognition caused by altitude and oxygen deprivation of other sorts well that's kind of a strange and unique situation if you're going up to altitude should you supplement with glutamine in order to be able to think more clearly well it appears that there's good rationale for doing that but the reason I bring this up assuming that most people including me are not going up to high altitudes very often is that it's been well established that apnea failure to breathe properly during sleep can contribute to age related and even non age related cognitive function non age related cognitive decline there are a lot of reasons for apnea's ranging from obesity to obstruction of the airways for other reasons there are tremendous number of underlying causes of apnea and it's something to be taken seriously I mean heart attacks all sorts of metabolic issues are caused by apnea apnea is a serious issue that disrupts the depth of sleep and it's a serious health issue in general in any event apnea is associated with cognitive decline and cognitive dysfunction even in young people and it does appear that glutamine supplementation can offset some of the cognitive deficits that are associated with reduced oxygenation of the brain if you'd like to learn more about how apnea can negatively impact cognition there's an excellent paper that was published on this in 2018 the first author is Sharma sh-a-r-m-a it should be easy to find the title of the paper is obstructive sleep apnea severity affects amyloid burden in cognitively normal elderly this was a longitudinal study amyloid burden is a correlate of Alzheimer's and other forms of neurodegeneration and cognitive decline associated with memory deficits so obstructive sleep apnea excuse me is a very serious issue for which glutamine appears to be able to offset some of the negative symptomology so how is it that glutamine either from food or through supplementation can offset some of these so-called hypoxic effects caused by sleep apnea, hypoxia being a lack of oxygen for the brain that relate to cognitive decline it appears to have this positive impact by way of reducing inflammation so if you want to look more deeply into the various biological pathways and the supplementation regimes for this the paper that I think is really spectacular is a paper last author is kwar-resma q-u-a-r-e-s-m-a that's q-u-a-r-e-s-m-a it's a review the possible importance of glutamine supplementation to mood and cognition in hypoxia from high altitude and even though paper is about high altitude induced hypoxia it does seem to have direct relevance to the sorts of apnea that are related to Alzheimer's and other forms of cognitive decline now I've been taking glutamine as a supplement as I was in college mostly because I felt either by superstition or by reality that it protected me from various flus and colds and things of that sort because of the purported immune enhancing effects again those immune enhancing effects have some data to support them not a ton however I got into the habit of taking glutamine and now that I've learned that glutamine seems to also have some cognitive enhancing effects possibly it's a supplement that I continue to take I take very small amounts of it but I do take it on a regular basis so that more or less completes the list of things that at least by my read of the literature are things that are supported by at least three and in some cases as many as hundreds of studies in various populations that have been explored in mouse studies often but also in a number of human studies I want to emphasize again that all of the things I listed out whether or not it's EPA's whether or not it's phosphatidal serine whether or not it's coaling whether or not it's the various compounds that are in berries etc all of those can be extracted from food there is not any law that says that you have to get them from supplementation supplementation can help you get to the very high levels of those things if you want to work on the higher end if that's right for you obviously check with your doctor before taking anything or removing anything from your diet or supplement regime but in general you can get these things from foods it's just so happens that for some of these compounds the foods that they're contained in like fish are not foods that I particularly enjoy and so I rely on excuse me I rely on supplements in order to get sufficient levels for me but again you can get these levels from food and the reason I made this list the reason that I emphasize these things in this particular order is that they support the structure of neurons they support the structure of the other cells of the brain that make up our cognition and that are important for our focus and our ability to remember things and so forth and they are less so in the category of so called modulatory effects they will also have modulatory effects on sleep on inflammation or reducing inflammation throughout the body on cardiovascular function all of which I believe our positive effects at least what the literature tells us is that none of these compounds are harming other systems of the body provided they are taken at reasonable levels but everything in this list is directed towards answering the question what can I eat what can I ingest by way of food and or food supplement that can support brain function in the short term and in the long term so I hope you find that list beneficial for you if not for use at least for consideration so now having talked about some of the foods and micronutrients that are beneficial to our immediate and long term brain health I'd like to shift gears somewhat and talk about why it is that we like the foods that we like we've all heard before that we are hardwired to pursue sugar and to like fatty foods and that calorie rich foods are attractive to us for all sorts of reasons you know surviving famines and things of that sort and while that is true the actual mechanisms that underlie food seeking and food preference are far more interesting than that they're basically three channels in our body and nervous system by which we decide what foods to pursue how much to eat and whether or not we will find a particular food attractive whether we want to consume more of it whether or not we want to avoid it or whether or not it's just sort of so so what I refer to as the yum yuck or me analysis and indeed that's what our nervous system is doing with respect to food it's trying to figure out whether or not yum I want more of this yuck I want to avoid this or me it's so so now while that may seem like a overly simplified version of food seeking and food preference it's actually not that far from the truth it actually correctly captures much of the biology of food preference so let's talk about what these three channels for food preference are the first one is an obvious one it's taste on the mouth it is the sensation that we have of the foods that we eat while we're chewing them and those sensations which are literally just some add a sensory touch sensations you know the the palatability of food as it relates to the consistency of food that's important and as you've all heard before we have sensors on our tongue and elsewhere in our mouth that detect the various chemicals contained within food and lead to the senses of taste which we call bitter sweet umami salty and sour now most of us are familiar with the sense of bitterness that comes from something like a raw radish sweet which comes obviously from sugars of different kinds fructose glucose etc salty salty and sour think lemon or lemon juice for instance and then I mentioned umami the umami receptor is a receptor that responds to the savory taste of things so that's what you might find in a really wonderfully rich tomato sauce for those of you that eat meat and like meat really well cooked not so well done but properly cooked I should say steak if that's your thing and umami is present in both plant and animal foods and gives us that sensation of savouriness it almost has a kind of little bit of a briny taste to it or braised taste to it and indeed braising of meats and braising of vegetables is done specifically to activate that umami receptor so we have those five basic tastes those are chemical sensors on the tongue that what we call transduce those chemicals those chemicals literally infood bind to those receptors and it is transduced meaning the binding of those chemicals the receptors is converted into an electrical signal that travels in from the tongue along what's called the gustatory nerve the gustatory nerve then synapses meaning it makes connections in our brain stem in the so-called nucleus of the solitary tract there are other nuclei back there nuclei are just aggregates of neurons and then it sends information up to the so-called insular cortex to the insula I want to highlight the insula this episode because we are going to return to the insula again and again in this episode and later the insular cortex is a incredible structure that we all have that mainly is concerned with so-called interoception or our perception of what's going on inside our body so it could be the amount of pressure in our gut because of how much food we've eaten it could be the acidity of our gut if we're having a little bit of indigestion for instance it can also be the case that neurons within the insula are paying attention to how stressed you are or how alert you are or how tired you are so it's really an inward focusing structure it focuses on how we feel internally and not surprisingly the taste system sends information up to the insular cortex to give us a sense literally of what we've ingested whether or not what we're tasting tastes good or not we return to insular cortex in a few moments a very important thing to understand is that the neurons in the areas of the cortex your cortex in mind that respond to particular taste are providing an internal representation of an external sense what do I mean by that I don't want to be at all abstract we take these foods we break them down in our mouth by chewing them or sucking on them whatever it is the food happens to be those chemicals bind to those receptors and electrical signals are sent into the brain but they are just electrical signals just like notes being played on the keys of a piano there's no unique signature for salty or sweet it is the relative activation of one set of neurons that was activated by sweet or another set of neurons that was activated by umami it's that relative activation traveling into the brain in essentially the same form the same electrical signals this is really incredible right electrical signals are sent into the brain and you say aha that sweet and I want more of it or that's bitter I want less of it or that's umami flavored and I really really like that really really like that really like savory foods as I happen to that should immediately strike you as incredible because it means that your representation of what you want more of our less of is electrical in nature and to really tamp this issue down studies that were done by Charles Zucker ZU KER is a absolutely phenomenal neuroscientist at Columbia University in New York studies done by the soccer lab have shown that first of all they could identify the neurons in the cortex deep in the brain that respond to a sweet taste or to a bitter taste it turns out they are non overlapping populations of neurons and then using some molecular tricks they were able to either silence or activate the neurons that for instance respond to sweet when they do this they see incredible consequences on perception that indeed occur in your brain and my brain as well all the time without these kind of manipulations here's the experiment they have a subject drink water that contains sugar or drink water that contains a salty substance or drink water that contains a bitter substance for instance okay I'm sort of paraphrasing a large amount of work they identify the neurons that respond to sweet taste they see as many researchers have seen that subjects prefer sweet taste to other tastes and certainly sweet taste to bitter or sweet taste to nothing so to plain water and then they go in and they are able to selectively silence the neurons that represent sweet and when they do that they eliminate the preference for that sweet taste now that might seem obvious the neurons respond to sweet you silence those neurons they no longer seek out sweet but that should strike you also as incredible because they're not actually changing what's happening on the tongue or in the deeper layers of the brain conversely they can have subjects drink bitter water or plain water while activating selectively activating the neurons that respond to sweet and what they find is that then subjects will actively prefer bitter or plain water to actual preferences such as sweet so what this means is that your perception of what you like is a central meaning with it deep within the brain phenomenon it's not about how things taste on your mouth now of course under normal conditions where there aren't these experimental manipulations being done those things are positively correlated sweet taste trigger the activation of sweet neurons for instance neurons in the mouth that respond to umami trigger the activation of neurons in the brain that respond to umami and so forth so they're correlated in a way that makes you seek out the things that you like and avoid the things that you don't like but as we'll see in a few minutes turns out that that is not a direct relationship that is hard wired you can actually uncouple the preference for particular taste with the reward systems in the brain in a way that for instance would allow you to eat or I should use myself as an example because I don't particularly like fish I've had a few you know meals that include a fish that were pretty good but none of them were memorable in the kind of positive way like some other events in my life are memorable but by way of these circuitries and the way they link up with one another it's actually possible to rewire one sense of taste and preference for particular foods if this is seeming at all vague to you just hang in with me a little bit longer because I will provide you with the information tools and resources with which to navigate this process but the most important thing to understand is that like with our hearing like with vision like with smell taste is an internal representation that has particular goals for you your sense of what taste good is related to particular things that are occurring in your brain and body and that are likely to give your brain and body the things that it needs it is not simply a matter of what you quote unquote like or what taste good or what doesn't taste good let me give you a relatively simple example of how your body and your brain are acting in a coordinated way to make you prefer certain foods and indeed to pursue certain foods more so I just mentioned you have neurons on your tongue that respond to different tastes but of course your digestive tract isn't just your tongue it's also your throat goes all the way down to your stomach and of course your intestines it was a long tube of digestion all along that tube there are neurons some of the neurons are responding to the mechanical size of whatever portion of the digestive tract it happens to be so for instance how distended or empty or full rather and doesn't have to be descended how depends how much you ate but how full or empty your gut happens to be whether not something you just ate is temperature hot you know as hot in the sense of hot to the touch or whether or not it's spicy hot whether or not it's soothing whether or not it's kind of hard to swallow this kind of thing so you have neurons all along your gut that are responding to the mechanics related to food and digestion and that are related to the chemistry of food and digestion there's a population of neurons nerve cells in your gut that are exquisitely tuned to the chemistry of whatever it is in your gut and these are neurons called neuropod cells they were discovered many many years ago but really defined with and classified with modern tools by Diego Borrez I hope I'm pronouncing your name correctly Diego we've spoken many times but I can't ever seem to quite capture the proper pronunciation just right but Diego Borrez at Duke University who discovered that these cells reside within the gut and place little processes their little axons and dendrites within the mucosal lining of the gut and there they are paying attention to meaning they respond to amino acids sugars and fatty acids so as your food is digested as food lands within your gut neurons there are sensing what types of foods are available and what types of things are making their way through the gut environment now those neurons aren't actually taking those foods and doing much with them what they're doing is they're they're essentially surveying what qualities of food are there and these particular neurons that Diego and his group discovered send electrical signals up into the brain through a little passage that we call the Angleon that no does ganglia is a cluster of neurons that then go for send up their own process into the brain and trigger the release of dopamine which is a molecule that inspires motivation reward and more seeking for whatever it is led to their activation these are super interesting neurons because what they're essentially doing is they are providing a subconscious signal about the quality of the food that you're eating what it contains and then triggering the release of a molecule within your brain dopamine that leads you to go seek more of those foods now this has profound impact on a number of things first of all there's the consideration of so-called hidden sugars dr Robert Lustig who's a pediatric endocrinologist at University of California San Francisco has been among the most prominent researchers to talk about the fact that they're the so-called hidden sugars in foods now these are not just sugars that they sneak in just to be sneaky these are sugars that are literally snuck in in a way that you can't taste them that's why they're called hidden sugars it's not that they just put them in there for fun these are sugars that are placed into process foods that are designed to trigger activation of these mechanisms to lead you to want to eat more of these foods but not because they necessarily taste sweet or delicious but because they are activating these subconscious mechanisms that are driving you to pursue more of these foods sounds like a very diabolical strategy and indeed it is somewhat of a diabolical strategy however these neurons are also involved in signaling to your brain when for instance you are eating a food that is rich in omega three fatty acids the fatty acids that we were talking about earlier so why is it that you don't crave salmon why is it that I don't sit around daydreaming about macro well because there's also the influence of the actual taste on the mouth under normal conditions it's a combination of the taste of the thing on the mouth plus the subconscious signaling from the gut and while this isn't a discussion about gut microbiome I should just mention that it's very clear that having a healthy gut microbiome allows these neurons to function in a way that serves our seeking of healthy foods in positive ways and without getting into a lot of detail about this the best way to ensure a healthy gut microbiome that I am aware of is not necessarily to take supplemental prebiotics or probiotics there are actually some reasons why you might not want to do that but rather to ingest two to four servings of fermented foods that are low in sugar each day there is a recent study published in cell showing that the ingestion of fermented foods two to four servings each day can enhance the quality of the mucosal lining of the gut that allows certain gut microbiota to flourish and the gut microbiota that are not good for us to not flourish because that's the environment that they settle down into this is work that was carried out by my colleagues Justin Sonnenberg which is in the laboratory upstairs for me as well as Chris Gardner and others at Stanford there certainly not the only researchers exploring this but it does appear that two to four servings of fermented foods each day so these would be things like not to sour crowd low sugar fermented foods is great for the gut microbiome and separate studies not their study but separate studies have shown that the correct gut microbiome conditions allow these neurons that signal to the brain to signal the right at the right times and in the right ways to promote healthy food seeking many people opt to supplement with capsule form probiotics there are some data that suggests that maybe those don't contain the correct prebiotics and probiotics for setting the correct gut microbiota conditions that's a little bit of a controversial issue nonetheless getting probiotics from fermented foods is probably the simplest and most straightforward way it's also the way that we evolved to do that over you know many at least hundreds and probably thousands or even tensed or hundreds of thousands of years people have been ingesting fermented foods not just for their taste but for their health benefits as well so now I've mentioned two of the three mechanisms by which we prefer certain foods one is from the actual taste that we're familiar with the taste on our tongue and in our mouth and the sensations that make us go mmm or or the yum yuk me responses as I referred to them earlier and then there's this subconscious signaling coming from the gut that's really based on the nutrient content of the foods there's a third pathway which is the learned association of a particular taste with the particular quality or value that a food has and this is where things get really interesting and where there's actually a leverage point for you to rewire what it is that you find tasty and that you want to seek more of the work I'd like to talk about next has been carried out in mouse models and has been carried out in parallel experiments in humans this is largely not exclusively but largely the work of Ivan De Arrujo and Dana Small Ivan De Arrujo is at Mount Sinai School of Medicine and Dana Small is at Yale and they and others in their field have done incredible experiments exploring how taste and food value the nutritional value of food and the impact of that food on metabolism in the brain drives our food choices and allows us to change our food choices for the better their groups have done some really amazing studies involving ingestion of a particular substance that either contains sugar and thereby can elevate glucose blood sugar or not and varying meaning changing the taste associated with that ingestion of sugar so let me just give you a simple example where they have subjects these could be mice or these could be humans because they've done both sets of studies drink sweet water as an alternative or a choice to non-sweetened water or bitter water or some other flavor what they find is that mice and humans will prefer to consume the sweet beverage now it's not always sweet water mice like sweet water but humans will prefer for instance a milkshake fatty sweet drink they'll consume more of that and not surprisingly dopamine levels in the brain increase in response to that so the taste and the nutrient content of what it is that their ingesting are aligned they are matched they've also done experiments where they have no taste but subjects are being infused with sugar directly into the gut and not surprisingly based on everything I've told you up until now subjects will pursue more of that thing relative to some other taste either neutral or negative taste because that sugar in the gut is triggering the activation of the neurons I mentioned earlier which is signaling to the brain to pursue more of that thing so this tells us something important it tells us that we are driven meaning we have mechanisms in our brain that make us motivated to pursue more of what brings both a taste of sweetness but also that brings actual changes in blood glucose levels up okay so we are motivated to eat sweet things not just because they taste good but because they change our blood sugar level they increase our blood sugar level this is important because it need to be the case it could have been that we were just wired to pursue things that taste good but what this tells us is that we are actually wired to pursue things that increase our blood glucose so much so that when the small lab it's not a small lab it's actually a big lab but when Dana Smalls lab and or Ivan Darryl Ruchos lab have done experiments where they use a compound called 2-deoxy glucose this is a compound that can prevent glucose from being metabolized by neurons so blood glucose is going up but neurons can't use it what they find is that the reinforcing or the rewarding properties of a food or taste are eliminated put simply it is not sufficient for a food to taste good consciously it is not sufficient for a food to increase blood sugar you need blood sugar to go up and that blood sugar glucose has to be utilized by the neurons even if it's not associated with a good taste and to make it even simpler if this isn't sinking in this should make it very clear what your brain meaning what you are seeking when you eat is not taste it's not dopamine it's not even a rise in blood glucose what you're seeking even though you don't realize it because it's subconscious is you are seeking things that allow your neurons to be metabolically active and this is fundamentally important for understanding why you eat particular foods and how you can change your relationship to those foods now earlier I referred to circuits that are wired for a particular outcome and in biology and in particular neuroscience we refer to things that are either hardwired meaning immutable and unchangeable or softwired a good example of softwiring would be the areas of your brain that are responsible for speech and language are always more or less in the same place in your brain and everyone else's brain however they are not hardwired to speak French or to speak English or to speak Chinese or to speak German because depending on where you were born and the parents that you're born to you need to be able to speak one or maybe even more languages the taste system and this general system of seeking particular foods similarly is hardwired to obtain certain types of nutrients it tends to like sweet things most children naturally like sweet things some more than others but naturally most people from childhood onward don't particularly create very bitter substances maybe mildly bitter but not very bitter so there's some hardwiring of preference but there's also some softwiring in the system that allows it to change the group I mentioned earlier have done some really beautiful experiments looking at how artificial sweeteners interact with the actual sweet sensing system and this gets right down to a number of issues first of all it gets to the issue of how we can rewire our taste system in ways that serve us for better or for worse second of all it gets right down to the issue of whether or not artificial sweeteners are good for us or bad for us and indeed as of just this last year we now an answer to that question and turns out it depends and I will tell you in a few minutes when it is okay to ingest artificial sweeteners and when it is very detrimental to ingest artificial sweeteners of any kind regardless I'm not going to name off brand names but there are different forms of these artificial sweeteners nowadays and there are various forms of non-caloric plant-based sweeteners for which the same information that I'm about to tell you applies okay so the experiments that were done beautifully illustrate that you seek out particular foods because of the way they taste because of their impact on blood glucose levels but also on their impact on the dopamine system even if your blood glucose levels don't change so here's the experiment one group of subjects is given a sweet taste of a substance that also raises blood glucose levels blood sugar and dopamine goes up not surprisingly second condition separate subjects consume an artificial sweetener or a non-caloric sweetener it is not preferred much over other substances but it is sweet so it's preferred somewhat and it does not cause an increase in blood glucose levels and not surprisingly dopamine levels don't go up so initially we don't tend to like artificial sweeteners that much that's the simple way of putting it however if subjects continue to ingest artificial sweeteners even though there's no increase in blood glucose level and therefore no increase in brain metabolism dopamine levels eventually start to rise and when those dopamine levels eventually start to rise you've essentially conditioned or reinforced that artificial or non-caloric sweetener and then subjects start to consume more of it and they actually get a dopamine increase from it so that's interesting it says that consuming more of these artificial sweeteners or consuming them for a longer period of time can start to tap into the dopamine system and lead us to seek out or consume more of these artificial sweeteners many people are probably familiar with this because we tend to or I should say people report that when they ingest these artificial sweeteners at first they don't taste very good but then over time they seem kind of tolerable and then maybe even pleasurable and then some people feel quote-unquote addicted to various diet sodas and things of that sort now there's another condition that's been explored and that's the really interesting condition and it's the condition where an artificial sweetener is paired with a substance that can increase blood sugar but not because it tastes sugary like a normal sweet substance so now there's an artificial sweetener that's coupled with an actual increase in blood glucose the natural world scenario where this would happen would be drinking a diet soda which contains no calories and therefore would not increase blood glucose but is sweet with a food that increases blood glucose and when that happens what you're essentially doing is tapping into the dopamine system this nonchloric sweet taste is paired with it and there's an increase in neuron metabolism so you have all of the components for reinforcement and as a consequence you get in a sort of Pavlovian conditioning way a situation where later when you ingest that artificial sweetener you actually get not only the increase in dopamine but you get alterations in blood sugar management now blood sugar cannot go up if you don't ingest something that makes blood sugar go up so it's not as if you ingest artificial sweetener with some food that contains calories or sugar and then later you remove the food and you just drink the soda and your blood glucose goes up rather it's a much worse situation if you I'll make this in the natural world context if you ingest an artificial sweetener say drink diet soda while consuming foods that increase blood glucose then later even if you just drink the diet soda it's been shown that you secrete much more insulin the hormone that regulates blood glucose in response to that diet soda studies have been done in both adult humans and in human children general when we say children we mean human children but just to be very clear what we're talking about exploring consuming diet soda with or without food then later consuming just the diet soda and what they found was having previously consumed diet soda with food and then later only consuming the diet soda of course there isn't an increase in blood glucose because they're not bringing in any calories when they just drink the diet soda but there is a significant increase in insulin release and that is serious in a terrible way because increased release of insulin and so-called insulin sensitivity is the basis for type 2 diabetes so much so that in the study with the children consuming nonchaloric beverages in this way first with food and then on their own led to increases in insulin that made them prediabetic and they actually had to halt the study so want to zoom out from this and just really illustrate the major findings and then talk about how this can be applied in the positive sense I also want to mention what this means in terms of your consumption of artificial sweeteners of any kind so first of all the direct takeaway about artificial sweeteners artificial sweeteners are not bad for you I'm not going to say that what I am going to say is that whether or not you would ingest them alone or you ingest them in combination with foods or as part of foods that raise blood glucose is vitally important for your insulin management and the simple extract or tool from this is if you're going to consume artificial sweeteners it's very likely best to consume those away from any food that raises blood glucose levels so if you're going to enjoy diet soda be my guest but do it while not while consuming food in particular foods that raise blood glucose because what these studies show and I will provide references for these is that they can vastly disrupt blood sugar management by way of the insulin glucose system okay and actually I'll just give you the reference now this is a paper from Dana Small's lab the first author is Dallanberg D-A-L-E-N-B-E-R-G and the title of the paper is short term consumption of sucralose with but not without carbohydrate impairs neural and metabolic sensitivity to sugar in humans this is a paper published in cell metabolism in March of 2020 I think it's a very important paper and similar findings have been addressed in mice and in other studies and now because of this paper there's now a bunch of other groups working on this this issue there's some evidence previously published in nature excellent top tier journal among the Super Bowl of top three journals being nature science and cell paper publishing nature a few years back showing that particular artificial sweeteners can disrupt the gut microbiome and have deleterious health effects that result I think stands although there's some results that may not agree with that depending on whether or not the artificial sweetener is saccharin or sucralose or aspera or stevia that's the gut microbiome but what we are talking about here is independent of the form of artificial or nonchloric sweetener because it has everything to do with whether or not there is a match or a mismatch between the perceived taste and the effect of the thing that you are consuming on blood sugar and metabolism so the first takeaway from this is if you're going to consume artificial sweeteners it's really important that you do that not in conjunction with foods that increase blood glucose second of all it points to the fact that the foods that we prefer and the activation of the dopamine system both through the gut and at the level of conscious taste what in other words what we like is the same as the other like is very plastic it's mutable and we can change it how can we change it well earlier I mentioned a structure in the brain called the insula this incredible structure that's involved in interoception and interoception of all kinds in fact just as an aside you're so go my lab published a paper showing that activity within certain compartments of the insula of humans is responding to a heightened state of anxiety in the body it can respond to changes in our respiration changes in our heart rate so this is again it's a read out of our internal state not just of taste but of many many different aspects of the mechanics and chemistry of our internal milieu within our body all of the work that I was describing previously has also been addressed at the neural level and using a broad brush to explain these results what we can say is when there is dopamine increase one sees activation of the so called nucleus accumbens which is part of the so called mesolimbic reward pathway if you'd like to learn more about the mesolimbic reward pathway and dopamine in general and humans and in animal studies and all the various incredible and challenging things that dopamine can do for us there's a episode all about dopamine that you can look up it's easy to find at ubermanlab.com the increases in dopamine associated with sweet taste and or blood glucose elevating foods and drinks cause activation of the nucleus accumbens that's not surprising also in the circuit is activation of the so called arqueuit nuclei within the hypothalamus these are areas of the hypothalamus that respond to hormones from the body and respond to hormones and neuropeptides in the brain as well as neural signals in the brain to drive us to eat more or to stop eating so it's hypothalamus nucleus accumbens these are sort of the hypothalamus and the arqueuit being the motivating to eat or motivating to stop eating both sets of neurons are contained there there are other areas like the lateral hypothalamus as well but hypothalamus is sort of the accelerator and the break on eating and then the nucleus accumbens and dopamine release can be thought of as kind of a a nitro boost if you will like the kids say to the kids say that anymore anyway a nitro boost to increase what we call the gain or the volume of how much you want more of something okay when dopamine is present it's this kind of generic signal to go seek out more of whatever caused that release and then there's the insula this very thoughtful rational not really it's not thinking it's a brain area you're thinking but it's part of the areas of your brain that are interpreting what's going on in your body whether not you feel good or not good whether not you feel anxious excited or fearful it's integrating all that information and fed into this entire circuit as well are the inputs from your prefrontal cortex which is your thinking rational neuronal structure if you will informing you for instance ah I don't really like salmon very much or I'm not so crazy about kale but it has omega threes or it's rich in these polyphenols that are good for me and if one decides that they are going to eat these things not just because they are good for them but believe it or not if one takes the perception or adopts the perception that they are both good for you and that in being good for you they are good for your brain metabolism and that you desire to be healthy as crazy as it sounds those subjective signals of what you tell yourself about the foods that you're eating can actually impact how those foods will taste maybe not immediately but eventually and can impact the way in which your body utilizes those foods now that might be a little bit more interesting now that might seem like a absolute pipe dream if I just imagine that I like macro macro will start to taste good I'm not saying that I didn't say that you could override the academic way You can create a authentic lifestyle that їp Pat син is a dense captain a high risk gaming gaming recreational games up ahead fish all Good morning take on a different value based on the activation of the dopamine system. Now knowing what you know, there are a couple of ways that you could imagine doing that. First of all, you could, in this so-called Giduncan or Thought Experiment, you could, for instance, swap out sucralose because sucralose is just a taste. It's an artificial sweet taste. You could swap that out and insert kale, but eat the kale with something that raises blood glucose to some degree or another. Now, I'm not encouraging anyone to run out there and spike their blood glucose like crazy. And in fact, blood glucose isn't really the goal. If you recall, the goal is to get neurons to be metabolically active with that blood glucose. That's what's actually rewarded at a sub-subconscious level, meaning at a deep subconscious level. But consuming these foods with other foods that increase blood glucose in thereby brain metabolism, or I suppose if you're ketogenic here in the ketosis, I don't know what the range of foods that are allowed on ketosis are, so I don't want to misspeak here and, you know, say cracker, which would probably be a sin in the context of ketosis. And no knock against ketosis. I'm offering this in part because I think that there are a number of people that have and can positively benefit from a ketogenic diet. But for instance, if there's a food that you want to consume more of, but that you find somewhat meh or mildly, ya, yuck, even, pairing it with ketones. If indeed you are using ketones for your brain metabolism, because that's what happens on the ketogenic diet, over time, that food will be reinforced by the dopamine pathway. We know this from these studies where sucralose was the substance paired with the glucose elevating. In other words, metabolically elevating food substance or liquid substance. So how does one go about doing this? Well, first of all, I want to emphasize that this experiment actually has been done in a slightly different context. Studies by my colleague, Alia Crum, in the psychology department at Stanford have explored the bodily response in terms of insulin release and the release of other food and eating related hormones, as well as overall feelings of satisfaction, et cetera. In groups of people that drink a milk shake and are either told that it's a low calorie shake that contains various nutrients that are good for them or a higher calorie shake that has a lot of nutrients, et cetera. And what they found was that the different groups, and here again, I'm being very general with my description of these studies, but what they found is that the physiological response, the insulin response, the blood glucose response, and the subjective measures of whether or not people enjoyed something or not, were heavily influenced by what they were told were in these milk shakes. So blood glucose would go up, insulin would go up, when people were told it was a high calorie shake with lots of nutrients, less so when people ingested a shake that was, you know, that they were told had less nutrients and so forth. When in reality, it was the identical shake. This is incredible. This is a belief effect. This is not placebo, right? A placebo effect is different. A placebo effect is in comparison. It's where the control condition actually influences outcomes to a same or to some degree, just like the experimental condition. This is not a placebo effect. This is a belief effect where the belief and the subjective thoughts about what a given food will do has a direct impact on a physiological measure, like blood sugar and blood glucose. Okay. So let's zoom out from this for a second and think about how we can incorporate this into adopting consumption of healthy foods that serve our brain health in the immediate and long term. And if you're wondering what those are, I listed them out at the beginning of the episode and their justification for being on that list. What this means is obviously you want to consume foods that you like, but because brain health is very important and many of the foods that promote brain health, perhaps are not the most palatable to you or desirable to you, the key would be to ingest the foods that you want to ingest more of simply because they're good for you and not because they taste good to you. Alongside foods that increase whatever fuel system you happen to be relying on, I think that's the most nutritionally politically correct way to say it. So if you're keto, that would mean ketones. Okay. If you're not ketogenic and I think most people probably are not in ketosis or trying to maintain ketosis, but for instance, people that are on a purely plant-based diet, that would be one set of foods for people that are omnivores, a different set of foods and for people that are carnivores yet, another set of foods. If you want to eat more of a particular food because it's good for you, parot with something in the same meal, you don't have to hide it physically or in the flavor sense. You don't have to hide it within that other food, but parot with that other food that provides you a shift in brain metabolism because that's really what your brain and you are seeking even though you don't realize it. How long will this take? Well, according to the data in humans on sucralose and the conditioning for sucralose to have these effects, which in many cases were detrimental, because they were increasing insulin. But in this case, you're trying to hijack this conditioning of food preference for healthy purposes, not with sucralose, but by ingesting things that are good for you. Then the data really point to the fact that even within a short period of time of about seven days, but certainly within 14 days, that food will take on a subjective experience of tasting at least better to you, if not good to you. Now, I believe this has important implications for much of the controversy and food wars that we see out there. Food wars being, of course, these groups that ardently subscribe to the idea that their diet and the things that they are eating are the foods that are good for us and that are the most pleasurable and the things that everyone should be eating. We see this with every community within the nutrition realm. Now, of course, there are studies that point to the fact that certain foods and food components are healthier probably for us and for the planet, but you really see it on both ends of the spectrum. You've got people who are on a pure carnivore diet who are arguing with a lot of biomedical evidence that that's what's best for us and beneficial. And then you've got people that are arguing the same general sets of arguments but for a purely plant-based diet and then I think most people fall into the omnivore category. What's very clear, however, is that what we consume on a regular basis and what leads to increases in brain metabolism, leads to increases in dopamine and thereby our motivation to eat them. So what this really says is that what we tend to do regularly becomes reinforcing in and of itself. And I think in large part can explain the fact that yes indeed for certain people a given diet not only feels good but they heavily subscribe to the nutrient and kind of health beneficial effects of that diet and they often will provide evidence for that, whether or not you ask them for it or not. But that's true of every subcategory within the nutrition realm. Again, this is not to take away from some of the beautiful data emphasizing that certain foods and micronutrients, et cetera, are better for us or worse for us and for the planet. That's not a debate I want to get into right now. What this emphasizes is that foods impact our brain and its health but they also impact how our brain functions and responds to food. And that is largely a learned response. We can't completely override for instance that certain foods evoke a strong, the yuck component. Certain foods are truly putrid to us. I should just say certain things are putrid to us and we should not consume them. Right? And that's a at the far end of the spectrum. It's hardwired for us to avoid those because they can be dangerous for us. They can make us very, very sick. But it's also true that if we continue to eat foods that are progressively sweeter and sweeter and highly palatable. It shifts our dopamine system because it activates our dopamine system to make us believe that those foods are the only foods that can trigger this reward system and make us feel good and taste and that they taste good. But after consuming foods that perhaps are less sweet or even less savory that are not what we would call highly, or I would say nowadays, it's super palatable foods, we can adjust our sense literally of what we perceive as an attractive and rewarding food. And indeed the dopamine system will reward those foods accordingly. I can't emphasize enough how much this learning of associated food reward is important for not just understanding why we like the foods that we eat and how to eat more of foods that are healthy for us and enjoy them. But it also speaks to the fact that our brain as a whole is a perceptual device trying to make guesses or estimations about what certain foods are going to do for us. So, put simply, we don't just like sweet foods because they taste good, we like them because they predict a certain kind of metabolic response. This is important also because Dana Small and Ivan Derrorojo and others have been exploring whether or not people, for instance, that have type 2 diabetes or that suffer from any number of different metabolic disorders, whether or not somehow these food reward systems are permanently disrupted and through a beautiful set of experiments that have been done by, mainly by Dana Small's group at Yale, but also by the Derrorojo group and others, exploring how the reward pathways are altered in various metabolic disorders, etc., people suffering from type 2 diabetes. We don't have time to go into all those data now, but the takeaway is that food preference and the ability to reshape these circuits is not disrupted in these people to the point where it can't be rewired. And that's very encouraging because what it means is that for people that are suffering from these syndromes through some simple alterations in dietary choice, provided those are carried out over time and in the correct way by pairing with the foods that will appropriately shift metabolism of the brain, and one can actually rewire what they consider not just palatable but attractive as foods. If you want to learn more about food reward and food reinforcement because it turns out those are slightly different things, there's a wonderful review written by Ivan Derrorojo. They have a middle author, Mark Schacher, and Dana Small. It's called rethinking food reward and it was published in the annual reviews of psychology. You can find it very easily online. It was published in 2019 and it's a beautiful deep dive, although quite accessible to most people about how different foods and the way that we perceive them impacts our brain and body and why we like the things we like and how to reshape what we like. So once again, we've done a fairly extensive deep dive into food and your brain focusing first on how particular foods and compounds within foods that are available also through supplementation can impact immediate and long-term brain health came up with a relatively short list of what I would call superfoods only because there are ample data to support their role in enhancing short and long-term cognition and neuronal health and so on. And we also talked about food preference and why particular tastes and particular events within the gut and particular events within the brain combine to lead us to pursue particular foods and to avoid other foods and how you can leverage those pathways in order to pursue more of the foods that are going to be good for you and good not just for your brain but for your overall body health and to enjoy them along the way. If you're learning from and or enjoying this podcast, please subscribe to our YouTube channel. That's a terrific zero-cost way to support us. In addition, please leave us suggestions for future topics and guess you would like us to host in the comment section on YouTube. As well, please subscribe to the Huberman Lab podcast on Apple and or Spotify and on Apple, you can leave us up to a five-star review. If you're not already following us on Instagram, we are Huberman Lab at Instagram and there I do neuroscience tutorials that sometimes have overlap with the podcast but often are original content altogether. We are also Huberman Lab on Twitter. Another terrific way to support us is by checking out our sponsors that we mentioned at the beginning of the episode. We also have a Patreon. It's patreon.com slash Andrew Huberman and there you can support the podcast at any level that you like. During today's podcast and on many other previous episodes, we talked about various supplements. One of the major issues with supplements is that supplement companies don't always have the highest quality standards and or the amounts of the supplements that they list on the bottle aren't what actually are contained in the capsules and pills and powders of those supplements. For that reason, we partner with Thorn, THORNE, because Thorn has the highest levels of stringency with respect to the quality of the supplements they use and the quantity of the supplements they use. They've partnered with all the major sports teams and with the Mayo Clinic and we have tremendous confidence in the quality of their supplements. If you'd like to see the supplements that I take, you can go to Thorn, THORNE.com slash the letter U slash Huberman. There, you can get 20% off any of those supplements and if you navigate into the main site through that portal of Thorn.com slash U slash Huberman, you can also get 20% off any of the supplements that Thorn makes. And last but not least, thank you for your interest in science.