OZEMPIC: #36 Stephan Guyenet - Why We Get Fat

Uh Hi everyone Welcome to both conjectures the Paris chopra Today I'm with Doctor Steven go at uh who's a researcher and science communicator in the field of neuroscience of obesity He has written an excellent book on the same topic The Hungry Brain Uh In his book he explains how the brain is the central organ responsible for gaining weight and body fat Uh Stephen finished his phd in Neuroscience from the University of Washington and then he spent 12 years as a full time researcher exploring the science for obesity and uh it's link to the brain Stephen is also the founder and director of nonprofit called Red Pen Reviews uh an online publication where he and his fellow researchers review popular nutrition books on their scientific accuracy Uh Nutrition is a field uh with lots of unfounded claims So I'm very grateful for Stephen and the team to put out um this effort for sifting scientifically grounded nutrition from uh pseudoscience So today my plan is to explore with the Stephen the neuroscience of uh why we get fat and what we can do to stay fit Uh Welcome to the podcast if OK thanks for having me Fantastic So I want to start with the the very basics Um um I know everyone talks about obesity but I'm not sure if uh people understand exactly how it's defined So can you uh help uh help everyone understand what is obesity and generally why should anyone care if they're obese or not Yeah So at the simplest level obesity is excess fat on the body And how do we define what is excess So essentially excess is an amount that is thought to impair health and or quality of life And so there are different ways that this has been defined different cutoffs um for obesity and one common measure that's been used is the body mass index which is weight divided by height squared and it uh typically is So it's essentially your weight corrected for height is a way to think about it And so uh typical cutoffs are a body mass index of 25 or higher or excuse me 25 to 30 is considered overweight and then 30 higher is con is considered to have obesity and there are different classifications even over 30 So 30 to 35 is class one obesity 35 to 40 is class 2 40 higher is is class three And so those are the ways that uh those are common ways that obesity is defined body mass index has limitations because it doesn't really tell you whether the weight is fat or muscle and so someone who is particularly muscular or has particularly low muscle mass could actually have obesity from a fat mass perspective even while not having a very elevated body mass index And in that context uh particularly we know that that can apply to South Asians uh

particularly so um that's relevant in this context And so the reasons why we should be concerned about it are because it increases risks of health conditions particularly type two diabetes which is a very weight sensitive condition but also cardiovascular disease certain types of cancers And then beyond that I think something that is perhaps even more relevant to to most people is quality of life So it impacts your physical performance Uh You know for example a child with obesity may have difficulties playing in the same way as as a child who doesn't have obesity Um adults may have difficulty engaging in sports uh if they have obesity and it affects people's love life it affects their um perceptions of themselves Um it affects their life satisfaction And so there are a lot of very kind of tangible day to day effects of it as well in addition to the um the long term health consequences So I think obesity at this time in history is one of the primary health challenges that uh industrialized nations are are facing right Um You make so many excellent points Let me just pick a few of them Uh One of the points you made was BM I is sometimes ethnicity ethnicity specific So especially for South Asians the BM I guidelines are very different And uh uh I came across this fact only a couple of months back and I was just super surprised uh uh because I'm a like I I'm a South Asian myself particularly you know um uh east uh in Indian ethnicity And in that context my BM I was I think 24 and I was pretty happy that way But when I realized uh that uh for South Asians 24 is actually overweight and after 25 becomes obese it it was sort of like a completely perspective shifting for me And I do think given the obesity in India and South Asia I do not think uh my experience is that most people don't realize that uh we tend to put a lot more body fat uh for the same amount of weight as compared to say Caucasians or uh the Western sort of European descent ethnicities Yeah that's right And I think I think part of the issue is that um as well is that it doesn't take as much fat for the average South Asian to be at higher risk of type two diabetes than other metabolic complications Um there's a lot of genetics that goes into how your body responds to to fat And so um essentially some people have um an ability to store more fat in a healthy way So they can accumulate a higher level of fat without it spilling over onto other tissues and causing metabolic havoc Whereas some other people their fat tissue just doesn't have the ability to store it as as well to hang on to it as tightly And so it kind of spills out um and affects the other organs and that can happen to the people of any uh race However it is more common in people of South Asian origin It's like it just doesn't take as much fat for uh for that to start causing metabolic

complications So that's another reason for the lower BM I cutoffs for South Asians right And and I think um uh in your book you explain how these cutoffs were sort of uh if I'm recalling correctly I mean these cutoffs are there because uh researchers have seen sort of almost a correlation of BM I with different uh increase propensity for different uh health conditions right Like if you have BM I 25 you're much more likely to have diabetes versus BM I 20 And and and it's also like a misnomer to think as soon as you get below 25 cut off all the normal range everything is OK But my understanding is that it's actually just linearly related So lower the better Yeah I think I think what really matters is body composition you know how much fat you have how much muscle you have and body mass index is just kind of a really rough way of of assessing that So you know someone with the low body mass index is not necessarily healthy but it is an indicator that they probably aren't carrying as much fat on their body Um But you know there there's a lot of context and I think when you're when someone is thinking about their own body mass index I think it's good to also consider the context of you know looking at yourself in the mirror and uh thinking about do you work out regularly Do you do strength training Um because that context can help you understand what your body mass index mean means doesn't mean that you have elevated muscle mass doesn't mean you have elevated fat mass What what is your body shape Do you particularly have a lot of fat in your abdominal region your your stomach region which it would correlate with extra risk So I think I think there's you know body mass index is kind of a crude screening tool But in my opinion if you just pair that with a mirror and some common sense you can you can get a pretty good idea of of where you stand excuse me But um I think if we're talking about excess fat masks yes I think that there is a relationship where the more of that you have the higher your risk of certain conditions are And that's particularly true for type two diabetes type two diabetes as I said is very sensitive to fat mass and excess energy intake Um but it also impacts other things like cardiovascular disease risk of certain cancers And then uh all of the related metabolic conditions like liver problems and uh hypertension and and stuff like that Got it Um How well do we understand uh the I mean is it like a a positive link obesity and different health conditions or there is a correlation But we don't understand the mechanism Um I mean how well as as uh as the sort of the state of the art in the science do we understand What exactly is that fat does in the body Which is uh which makes us unhealthy Yeah So I think it is causal I think excess body fat does cause these health

problems Um However I don't wanna state that with 100% confidence and I also uh don't wanna uh imply 100% certainty that that's the only mechanism So um I think research is ongoing on this but I feel um pretty convinced that it is a cause and effect relationship from fat mass to to health problems And and basically the way the the way I think it works is that uh insulin resistance and resulting increase in insulin secretion So insulin is a hormone secreted by the pancreas that's really important in metabolism People think of it as regulating blood sugar but it regulates a lot of other stuff um as well related to the energy refluxes in the body And that seems to be a real cornerstone of metabolic dysfunction and health problems is when your insulin stops working as well So you become insulin resistant you get higher levels of insulin secretion and that contributes to uh type two diabetes risk cardiovascular disease cancers all all of those health conditions at a minimum seem to correlate pretty tightly with that type of metabolic dysfunction But we think that's probably causal And if you look at what's causing that insulin resistance a key factor seems to be what I call energy poisoning And what what I mean by that is that the tissues in your body are being exposed to excess energy in the form of glucose fatty acids amino acids Those are the three primary types of energy circulating in the in the body particularly the glucose and fatty acids which is carbohydrate and fat And um insulin resistance is essentially a cellular defense mechanism against excess energy because insulin is is a hormone that tells your cells to take up glucose And so when your cells are full of energy because they've been exposed to too much they say that's one of the ways that they start limiting their uptake of additional nutrients And you can see that there's there's a lot of evidence to support this So um if you take cells in a Petri dish and you expose them to high concentrations of glucose fatty acids or amino acids they will develop insulin resistance If you infuse high levels of glucose uh fatty acids or amino acids into a person via the blood stream experimentally they will quickly develop insulin resistance And um if you then um cause someone to if you reduce their energy intake they will increase their insulin sensitivity if they're someone who carries excess fat So basically over consumption of energy relative to your needs it creates this energy load on your body and your fat tissue can handle that for a while As long as your fat tissue is healthy and you don't have too much of it it can absorb that extra energy and protect the rest of your tissues from that excess energy But once your fat tissue starts to reach its capacity which is seems to be very genetically determined then it just can't expand anymore And that excess

energy is not being mopped up and it starts to accumulate in your other tissues And you see this in the form of what's called ectopic fat deposition So you see that fat starts to accumulate in the liver starts to accumulate in the pancreas in the muscles in places where it's not supposed to be And that correlates a lot with insulin resistance It's a marker of that excess energy exposure And then at that point your tissues are just overloaded and they're doing everything they can to refuse this excess energy but it's still kind of being crammed down their throats uh because there's nowhere else for it to go And so that starts to cause that causes insulin resistance It probably causes um your pancreatic beta cells which secrete insulin to become dysfunctional Once they they start to become dysfunctional once they're exposed to excess energy for a long time and then they stop secreting insulin effectively And then the situation just gets even worse spirals out of control and then you have type two diabetes So that's that's kind of um what I think is the the main thing that's happening Um And I could go I could go in more detail on the evidence but I'll just leave it there for now and uh if there's anything you want to follow up on I'll I'll give you a chance to do that Yeah I mean it it's um and what you described um is essentially if if we eat a lot of uh the all the energy uh that's been taken up by the cells and uh insulin gets secreted in response of the sort of the energy that needs to be metabolized in the body But after a period of time uh since so much of energy is coming in and cells cannot uh take all of it Um there is say uh unmetabolized uh energy out there in the body say in the bloodstream and the insulin keeps on rising and the cells have to become insulin resistance because they just can't take anything uh more Uh for some reason I always thought it was the other way around which is maybe the beta cells in pancreas uh they start becoming dysfunctional and sort of uh increase a lot of insulin and the cells have to become insulin resistance because there is a lot of insulin out there But what I hear from you it's probably the other way around Yeah So I mean that this is a nuanced area So it could be both it's not necessarily one or the other Um Those are not mutually exclusive and there is some evidence for the scenario that that you said um I tend to think the main factor is the one that I described Um and if you look at the genetic studies in humans of um the the genetics of insulin resistance and the genetics of type two diabetes what you see primarily for insulin resistance are genes relating to the adipose tissue capacity So that suggests that the main determinant of insulin resistance in humans is how well your adipose tissue can your your fat tissue can mop up that excess energy that you're that most of us are consuming in industrialized

societies um rather than genes that cause people to over secrete insulin So that those are not primarily the the genes that are popping up And if we look at the genes that relate to type two diabetes they're mostly genes that affect either insulin resistance or that actually reduce insulin secretion by the beta cells or that have some kind of effect on beta cell development or function that would be expected to reduce their resilience to metabolic insults So I think as I said I think the scenario that you outlined is totally plausible and could be part of the explanation I think right now the evidence is primarily pointing toward um this scenario that I described but they're not necessarily mutually exclusive So maybe the driving or the major factor is insulin resistance happens first and then uh dysfunction of beta cells causes uh less and less since we need to be secreted And then I mean a lot all other sort of metabolic conditions uh are a downstream of these two things Well I think type two diabetes it the scenario that you just described is type two diabetes So basically what what has to happen is or what typically happens is you get insulin resistance and then after a while your beta cells just kind of fail and they can't to create enough insulin to to keep up with the insulin resistance And it's kind of that two hit scenario because some people they can become insulin resistance insulin resistant but their beta cells just keep cranking out insulin and they're making enough that they're able to maintain metabolic control and then their beta cells never fail They just stay super insulin resistant and they're fine it I say they're fine Uh What I mean is they don't develop type two diabetes but that person could still have the metabolic syndrome So you know they could still have abdominal obesity they could still have hypertension they could still have blood lipid abnormalities So it doesn't mean you're off the hook But if you don't experience that beta cell failure you're not gonna develop type two diabetes Specifically Got it And all the um conditions that you described even if your beta cells are fine they're because of elevated insulin levels because the body's insulin resistance like hypertension or other conditions of such Yeah that that's a great question and I really wish I could give you a definitive answer Um I it's been a while since I have reviewed the evidence on this Um I know that uh some people like Gerald Riven for example the Stanford endocrinologist who was the discoverer of the metabolic syndrome He believed that elevated insulin secretion in itself was a key driver of um of the health consequences of insulin resistance So um but I think it might be more complex than that I think maybe some is some of the problem is due to the elevated insulin some of it is due to the insulin resistance Um but it's been a while since I've

reviewed the evidence So I'm I'm also a little a little fuzzy on where exactly the evidence stands there Um But I will say I think there are good arguments to be made by um good arguments have been made by good researchers that the elevated insulin itself is at least part of the problem Got it Got it Um All right So we know that um body fat excess body fat is just generally not good for health And uh we also know that uh if you keep on consuming more calories than the body needs it gets converted into fat I mean before I mean I wanted to get into why we eat so much and why we get fat but maybe perhaps you can spend some time talking about uh how everything that we eat the excess calories how how does it ultimately just end up uh into the fat cells irrespective of what we Yeah So it's essentially the types of foods that we eat have only a pretty modest impact on the amount of energy that our bodies burn And so you and it's it's not nothing So if you go if you go on a very low carbohydrate diet there is some evidence that your body might start burning a little bit more than it did before However within the range that people are typically eating in it the effect size is is trivial So basically you know if your body is burning the same number of calories than the amount of uh the change in the energy content of your body at the end of the day is going to be determined by how much you're eating relative to how much you're expending And if you're eating more than your body needs more than your body is expending that energy has to go somewhere And ultimately there's only one place for it to go And that's fat mass because your body fat your fat tissue is the only place in your body where large amounts of excess energy can go There's no other energy storage site that has nearly the same capacity So we have we do have some carbohydrate stores in this form of glycogen But that's the kind of thing that can buffer like a day or two of of energy and carbohydrate intake but it doesn't contain it barely contains a tiny fraction of the amount of energy that your fat tissue contains and can contain And so your fat tissue is really that long term storage and long term buffer of long term energy intake And so um and so that's the place where it goes And the way this happens in the body mechanistically is that when you eat uh excess calories what your body will do is it will take the uh it'll take a portion of the fat that you ate and it will shuttle that directly into your fat tissue So if you it almost doesn't depend it almost is irrelevant what you're eating how much fat and carbohydrate et cetera unless you're eating like almost zero fat And there's literally like not enough to cover that that excess that intake that you took which is very very rare to have a diet that's that low in fat Your body simply takes that dietary fat whatever covers that excess

calories that you took in and just shuttles it right into your fat tissue And so um on a mechanistic level that's that's how it works And we have lots of studies demonstrating this that energy intake is a powerful determinant of changes in in fat mass Got it And even if we are eating um I mean a lot of carbohydrate we I mean a mix of carbohydrate and fats My understanding is that even carbohydrates uh get converted and stored as fat And perhaps if it's like a very very high protein diet maybe even proteins get broken down and stored at fat Am I correct So um carbohydrate can get converted into fat by the body but typically it's a very only very very small amount of it that does uh under normal conditions It's really only under pretty extreme experimental conditions that a significant amount of it starts to be converted to fat So like for example feeding people experimentally on extremely low uh low fat high carbohydrate diets that are really high in simple sugars Um That kind of a diet you'll start to see more de novo lipogenesis is what it's called So carbohydrate to fat conversion primarily by the liver Um but under normal conditions it's it's really pretty negligible but instead what will happen is your body will just shunt dietary fat into your into your fat tissue And so if you like let's say you are eating a diet just just for simplicity let's say half carbohydrate and half fat 50 50 Um And you're you're in energy balance So you're eating the same amount that you're burning and then you add 100 calories of carbohydrate on top of that So now you're eating 100 calories more than your body needs And that's coming entirely from carbohydrate What your body will do is it'll just take 100 calories of fat of the fat you're eating and put that into your fat source So so eating more carbohydrate definitely does increase your body fat storage But it does that by displacing fat oxidation Interesting That makes sense Yeah that makes sense So it's sort of like uh the body you first utilizes all the fat that you're eating uh for storage of fat But if that's so bad I'm I'm curious why is this ketogenic diet so popular where it's just excess fat and people believe and I think there have been success stories also of uh people losing weight on ketogenic diet Yeah absolutely So the reason is that their energy intake goes down so their total energy intake declines so that you don't store fat if you're in negative energy balance if if you're eating less than you're burning regardless of whether that's fat or carbohydrate So um you know if your energy needs are 2500 calories per day and you go on a ketogenic diet and now you're only eating 2000 calories a day then it it doesn't matter that that's mostly fat You're still gonna be losing body fat because you're in a calorie deficit of 500 calories per day Um and so it really you know if you look at

the studies that have highly controlled diets like metabolic ward studies and then they're measuring fat mass changes it really seems to not matter at all It doesn't matter measurably whether the calories are coming from fat or carbohydrate all that matters is the energy balance And I'm not saying you know it's possible that if we did bigger bigger studies longer studies maybe there would be a difference that could be detected but under the conditions that have been studied both overfeeding and underfeeding um there's really little or no detectable effect of fat versus carbohydrate that is independent of the calorie value of that Got it Um So um I I know in um in some of your review papers you talk about models of obesity So generally um again the natural question is if um eating more than what the body requires is so bad for health why are we doing it Uh Most a lot of us are overweight or obese So why is that So and you know I'm setting you up for this uh very very broad time But uh this is what um uh the whole I mean this is sort of the gist of what I was trying to get to in the podcast Yeah absolutely I think this is really a key question and a great starting point because it doesn't make a lot of sense Right Like nobody wants to overconsume people don't want to have overweight they don't want to have obesity And yet we do that most of us do that every day And so how is that possible for us to not want to do that And yet we do it anyway So it I think it um really illustrates that our brains are composed of different functions and those functions are not always agreeing with one another right So there's a part of your brain that wants to remain slim and wants to remain healthy and wants to implement would prefer to implement behaviors to to do that And then there's another part of your brain that just wants to eat too much And those two parts of your brain are disagreeing with each other right And the one that wants to eat too much is usually winning And so how exactly does that work I mean first of all that's kind of an interesting observation in and of itself right Because we kind of like to think of ourselves as this uh you know unitary mind that is thinking and making decisions But I think it's more complicated than that I think we we we have different parts with different motivations that are competing with one another And essentially uh one way to think about this is using Daniel Conman's framework of system one and system two system one are the parts of our brain that are automatic and intuitive and uh mostly nonconscious So we're not really controlling them we might experience some of their outputs but we're not really controlling them And then there's a system too which is the conscious effortful part that we used for thinking and willpower And uh the the things that we do control consciously and the parts of our brain that

cause us to overeat are system one Those are things like you know what part of your brain makes you feel hungry You're not in control of that you experience hunger but you don't decide I want to be hungry now and then turn that on right That's just something that arises that you experience And the same with a craving If you're if you see freshly baked cookies in front of you you don't consciously flip a switch in your brain that says I want to start desiring these cookies now right That's something that arises on its own because of sensory inputs that are entering your brain and triggering something non conscious And so there's a lot of stuff like this in our brains that if you think about it makes logical sense Right That that's what's going on that there's all this nonconscious stuff that's impacting our eating behavior But I think most of us just haven't really sat down and and thought about that and thought about the implications And so my book is all about what are these nonconscious brain regions that are impacting our eating behavior in such a way that drives us to overeat And so um my so it's it's the book is kind of an attempt to catalog and describe these systems Um And I think you know neuroscience is really complicated So there's no way that I could cover everything in one book even if I knew how it all worked Um But I've done my best to cover the important stuff in the book And um so I think there are different reasons for why we overconsume and we can put those into two main categories Um So and again the framing here is I'm talking about nonconscious brain regions that in the modern food environment push us to overconsume That's that's kind of the framing here The two categories are what we can call homeostatic systems and non homeostatic systems So homeostatic systems are systems that evolved to try to regulate our energy status So those are systems that regulate like our body fat mass and regulate our appetite on a meal to meal level Like those systems are trying to make sure that your body has the right amount of energy in the fat stores in your digestive system but not too much That's that's what those systems are doing And then the non homeostatic systems is all the stuff that is makes you eat for other reasons So reasons that don't have anything to do with like for example the reward system that decides that certain foods are particularly valuable and creates a motivation to eat those foods So for example you know we were more interested in eating like let's say French fries than celery sticks right Like French fries or ice cream those are more appealing foods to the brain than celery sticks If you put ice cream next to celery sticks on a plate and hand it to a kid which one are they gonna eat You know so there are intrinsic differences in the motivational value of of foods to the brain

And so that's an example of a non homeostatic system And so um let's start by talking about the homeostatic systems So we can break that down into two categories One is the short term regulation of energy status and one is the long term regulation of energy status So the short term regulation is the circuits primarily in our brain stem that regulate our uh satiety So the fullness that we experience satiation and satiety the fullness that we experience as we consume a meal So we sit down to the meal we feel hungry we start to eat and then with each bite we take our motivation to continue eating declines a little bit Right And then at some point we get to the point where we're not motivated to eat anymore at all and we terminate the meal and do something else So that's called that point is called satiation And then we're not interested in eating for a while After that we feel full that's called satiety And so there are brain circuits that regulate that we intuitively we kind of think oh you know my stomach is full of food and that's why I don't want to eat anymore But actually usually your stomach's not even close to full human stomach is huge It can usually eat a lot more than we typically eat Um What happens instead is that your brain decides that you've had enough and it sends a signal So and that's a very complex regulated process that occurs as I said primarily in the brain stem as a result of ascending neural signals primarily from the vagus nerve but also from other sensory systems um throughout the digestive tract And so as it turns out different foods impact that system in different ways So if you have if you're eating a food that is uh very calorie dense in other words it has a lot of calories per unit mass or per unit volume So think about like um something like cheese would be very calorie dense something like a fruit would be less calorie dense It has a lot of water Chocolate Very calorie dense right Um those foods do not create as much satiety and satiation per unit calorie as foods excuse me that are lower calorie density So food like a piece of fruit that has a lower calorie density more water So the calories are diluted for the same number of calories It stretches your stomach more and that is part of the signal that goes up and gets processed in your brain and makes you feel more full per calorie that you've consumed Also higher protein creates more satiety and satiation Um higher fiber as well and um higher palatability creates lower satiety and satiation So the better something tastes the more your brain is like Hm I think we could have more of this and it kind of takes the brakes off a little bit And so what ends up if you put all this together What ends up happening is foods that have high calorie density low protein low fiber um and high palatability Those are foods that per unit calorie don't generate much

satiation in her satiety So those brain circuits in your brain stem that determine all this stuff they're just not firing as much per unit calorie And so you have to eat more calories to reach that point where you feel full and your motivation to continue eating ends And since that feeling is what we typically use to determine whether we've eaten it enough I mean normally we just sit down and we eat till we're full Right You can reach that point with dramatically different number of calories depending on the type of food that you're eating And so those properties that I just described correspond to highly processed calorie dense refined industrial foods things like pizza and uh French fries and cookies and cake Those are the types of things that are gonna create very little satiety and satiation per unit calorie And that are going to just naturally lead to an over consumption on a meal to meal basis Without you even noticing conversely more lower calorie density more natural unrefined foods like fruit fresh meats um eggs um vegetables um whole grain foods Those types of foods will tend to create more satiety per unit calorie and you will consume less on a meal to meal basis without even noticing or thinking about it So that's that's the relevance of that short term regulation system Then on the long term regulation we have what's called the lipostat And this is a system in the hypothalamus that regulates your body fat mass And so uh essentially what it does is it measures the amount of fat on your body using the hormone leptin that is secreted by fat tissue in proportion to how much fat you have So the more fat you have the more leptin you have in your blood your hypothalamus measures that and decides whether it's enough essentially And if it's enough then you're cool But if it decides that it's not enough then it starts to activate a starvation response makes you feel hungry It makes you feel um more motivated to eat calorie dense foods It biases your attention toward food and eating rather than other activities It uh can curtail your energy expenditure So lowers your metabolic rate to conserve energy and it does all that and it shunts the energy into your fat tissue and it keeps doing that until your leptin goes up enough so that it's satisfied And so that's a key reason why it's hard to lose fat and keep it off is that the system opposes fat loss And the the the cruelty of it is that this system seems to work just as hard in people with obesity as lean people So the system in people with obesity has decided that obesity is the new normal and it's going to defend that state against fat loss So you see that people with obesity when they lose weight they experience this starvation response activated by the brain just like if a living person tried to lose weight So the body is saying no I don't want to do this You're starving yourself Even

though in reality a person with obesity is not starving themselves by going on a diet they still have excess fat mass But the brain perceives that the person is starving themselves because of how this regulatory system works And so essentially what will happen what happens is that in a person with obesity that system um pushes them to continue over consuming calories to maintain that obese state And it opposes attempts to reduce calorie intake And so that's why it's a key contributor to overconsumption Um because it is it's it's telling you to to maintain that higher level of energy intake so that you can maintain that elevated fat mass which it has decided is what it wants you know and this is not conscious Again these are like totally nonconscious circuits just like the ones that are regulating your blood pressure and your heart rate and your digestion Like this is not under your conscious control You're not consciously or morally responsible for what these circuits are doing This is just a thing that is arising physiologically from your brain and that makes weight loss difficult and makes people pushes them to over consume on a on a daily basis So that's the homeostatic side of things I I had one question for you Yeah Yeah Before is uh there's a lot to sort of unpack but I'll sort of uh um rephrase what you said from a meal to meal uh association point of view And I was curious So I mean it seems what you're describing is brain is trying to estimate calories that you're ingesting while you're having a meal but it's in sort of an inaccurate estimator But why is that brain generally uh is tending to underestimate calories instead of overestimating it It could I mean in theory it should go either way Right But generally it seems we are tending to overeat rather than under eat Yeah It's a really good question I mean I think there are some some mysteries that remain and I don't have a confident answer to this I can I can do a little bit of speculating Um but I think you know these systems are very complex and they evolved for a very different context than the modern world These systems evolved for a hunter gatherer context that existed thousands millions of years ago And even these systems actually primarily evolved even long before humans existed before primates existed I mean a lot of these circuits you can find them in lampreys that is the most ancient living vertebrate our most distant vertebrate ancestor that separated from us hundreds of millions of years ago You can find most of this stuff Lampreys are uh are cyclostomes which means they don't even have jaws So they this is before the evolution of even jaws So this is like incredibly ancient and they already have a lot of the circuitry So I think that um there is an evolutionary context here that is very different than the one that we're currently finding ourselves in And I think

the the basic problem is that we have an evolutionary mismatch we have circuits that are outside of their natural context and that's causing them to to misfire essentially And a key aspect of the natural context that contrasts with what we have today is how easy it is to get energy and how easy it is to get calorie dense highly digestible energy in in food And so I think as a general principle these circuits are calibrated to tend to err on the side of getting us to eat more because that was really you know not eating enough was a threat Historically was a major threat to survival and reproduction which are the currency of natural selection But eating too much wasn't much of a threat I don't wanna say it didn't was irrelevant completely but it was just a lot less relevant than eating too little If you think about a hunter gatherer you don't you know like the modern context getting food is trivial You you know as as long as you have enough money I guess But you know for most people in affluent industrialized societies you go to the grocery store it takes a few minutes and then your house is full of food You can eat tons whenever you want Right But a hunter gatherer if you need to eat you have to go out and work to procure that food at the time that you want to eat And so it's a very very different context It's not like you can just reach out and grab something and put it in your mouth And so the idea that they needed to be protected against eating too much is almost like nonsensical Why would they you know how would that scenario even arise Right Um And so I think these systems these systems I don't want to say that I I do think we actually do have some systems to protect us against overeating I just think they're a lot weaker they're a lot weaker than the systems that um protect us against undereating and tend to push us to err on the side of eating more because that evolutionarily speaking was was extremely valuable for our survival and and reproduction right And perhaps this uh also explains the lipostat system wherein if if if the brain knows it's possible to get calories and that's how you've gotten fat Uh then it would drive you motivate you to sort of get to the level because it somehow senses that your environment has potential to get you the energy that you currently sort of stored in your fat So it would fight against you trying to sort of shake it off Yeah that's an interesting idea I mean I think so you're suggesting that the brain like has a sense of how easy it is to get calories Yeah I mean when I was reading when I was reading your book that's what I was trying to imagine that perhaps brain has this sense that it's for the environment is rich with food So it motivates to seek the food if whenever the fat reserves go low Yeah I mean I don't know whether that's true or not but I think that's certainly very logical and um it wouldn't surprise

me if it was true I think that one of the things we're figuring out is that these systems even the very you know what we used to think of as simple systems like in the hypothalamus and the brain stem that are just kind of regulating energy balance We we used to think ok there's these circuits in the hypothalamus Um There's a couple of important cell types and they're receiving this leptin signal and maybe like one or two other hormones And it's a negative feedback circuit kind of like your thermostat and and then that regulates appetite and stuff But it's turning out that those circuits receive a lot of other inputs It's actually a lot more complicated than we thought And so just as one example these circuits in the hypothalamus that regulate fat mass they are actually regulated very rapidly by food availability in in mice So if you put food in front of a mouse even I if I'm recalling correctly even before they start eating it as soon as their brain knows that they're about to be able to eat this food there's already signals going to those neurons and their activity patterns are changing and they're basically staying OK we don't need to keep seeking food anymore And so I think that so the the reason I'm explaining this is that I think that we are going to continue the discovering that there are a lot of inputs that are going into the activity of these neurons probably from all levels of the brain and things like you know anything you can think of that could have been relevant to energy regulation in the ancestral environment is a candidate for the kind of input that would be integrated into the circuit Because you know if you think about it like just think about like an engineer like how would you design an animal You could probably in terms of how it regulates energy you probably want to factor in a lot of different variables into how it's regulating energy Like you know some kind of assessment of the value of the food is consuming Like does it have what does it have like certain kinds of toxins in it If it does maybe I should only eat a little bit and maintain a lower level of fat mass or is it like really great nutritious food In which case maybe I should eat more of it You know how hard do I have to work for it How abundant Probably there's like lots of different signals that are impacting the system that we just haven't characterized yet So um what I just said is is speculative Um but I think that that's kind of the direction that we are going in And so I think it would be very logical if what you said was true Uh it wouldn't surprise me if that was the case Yeah I mean in general it's a really hard to wrap your head around Uh what say hundreds of millions of years of evolution can do uh especially for a system as complex as a brain and a body where everything is just going into everything else I mean I sometimes I even wonder how difficult it is for

a science communicator like you to even describe because everyone wants a mechanistic answer Our brain is sort of uh wired to seek simple A to b sort of connections But in complex systems almost everything impacts everything else Yeah that's that's right And you know I as a science communicator like I also about neuroscience there's also just a lot that nobody knows and a lot that I don't know So I just try to respect that Um I just try to respect that uh those limitations But yeah I mean the brain is unbelievably complex and I I think that is something that we're finding that everything does impact everything else If you think about you know I specialize in the the hypothalamus that's what I was trained in And even you know these circuits that we used to think were pretty simple they're receiving inputs from a lot of different places they're sending inputs to a lot of different places and each one of those places that it's receiving and sending information to is also getting and sending information to a ton of different places And and that's just the hypothalamus which is a tiny part of the brain And that's just I'm talking about two cell types out of like a dozen that's in the hypothalamus So thinking about even the complexity of how that even develops during development how all this stuff gets wired is is unbelievable to to think that the brain could even exist Yeah I mean it's so awe inspiring Uh but back to the topic um what about this non homo static systems that make us overeat Yeah So I think there are a number of non homeostatic influences and I talked about influences on uh calorie intake and I talk about a few of them in the book Um The biggest one that I focus on is the reward system And I think this one is really important This is the system that um sets our motivational drive to seek and consume food with certain specific properties So basically to some state it simply some food is a lot more seductive than other kinds of food And that will cause us to seek the seductive food more than the non seductive food and consume more of the seductive food And not only is some food more intrinsically seductive but it has properties that cause our brains to learn um to prefer certain things over time as we consume that food multiple times and also to develop and stamp in certain eating habits And so that all revolves around a brain chemical called dopamine which is our learning and motivation chemical And it's it's very central to that process This kind of like uh intuitive gut motivation to eat which is independent or at least partially independent of hunger and which we can call craving That's one way to describe it And so the way this works there's there's actually a lot that's been learned about this even since I wrote my book And um the key way that this works or a key that the the way that this works is when you

consume food there are receptors primarily in your small intestine that detect the chemical composition of what you ate These cells are called neurop pod cells It's a a type of entero endocrine cell and it is directly these cells are directly hooked up to neurons And when they detect fat carbohydrate and protein they start sending signals to those neurons that send signals up your vagus nerve up to your brain stem that tells your brain what you ate And that that signal goes to many parts of your brain But for our purposes one of the key places it goes is to or two places ventral tech mental area and the substantial not substantial Nigra which are dopamine producing parts of the brain And when those cells detect um higher concentrations of fat carbohydrate and protein they start releasing more dopamine into parts of your brain that regulate motivation and learning particularly your striatum but also other associated parts of your brain and what that does So let's say let's say you ate a slice of pizza that has high concentrations of fat and carbohydrate and some protein and also a lot of salt which seems to be relevant You get a lot of activity in in this pathway you get a lot of dopamine release and then that motivates you to eat more of that But most importantly what it does is it sets your future motivational level to acquire and consume pizza So it causes your brain to learn to be motivated And the way that works is that your brain will record all the sensory attributes of the pizza and that situation So it'll your brain says hm I'm gonna remember this you know cheesy smell and this texture and the way the box looks and where you were when you ate it and who you were with and what the situation was what the brand was All that stuff gets stamped in as motivational triggers and the next time you smell that smell or you see the box or you see a slice or you're walking past that same pizza joint that is gonna get your dopamine spiking again So your brain recognizes that cue that predicts the acquisition of that calorie dense food your dopamine starts spiking again and then you experience a craving a motivational drive to acquire that food And so that process happens with any food So it's not necessarily a bad thing This is just a natural way that our brain motivates us to eat But the problem is that you get higher levels of reward with more calorie dense foods that combine multiple dopamine spiking ingredients And so when you have something like ice cream which has the sugar and the fat it's particularly combinations of sugar and fat that really drive the system So ice cream fried foods like French fries pizza cookies cakes any kind of like sweet and fatty dessert Those are the things that really get the system going And again it's not inherently bad to have a food spike your dopamine that's a natural process

But the more dopamine spikes the higher your level of motivation is to consume that food And the higher your level of motivation is the more likely you are to seek and consume that food when you don't really need it So maybe you would be willing to eat it between meals when you aren't really that hungry just as a snack or maybe you'd be willing to eat it at the end of a meal like when you're full So if you imagine let's say you have you know beans and rice for dinner and you eat as much as you eat until you're full You you if somebody put more beans and rice in front of you you wouldn't eat any more beans and rice But then somebody brings out a delicious dessert and suddenly you're re ready to eat hundreds more calories right And part of the explanation for that is that the very high reward value of that dessert There's also a sensory specific satiety which we haven't talked about but we could get into that later And um so yeah and and you know it let's say the beans and rice was like especially delicious and especially fatty you're probably gonna eat more of that than you would if it was pretty plain and and bland and and lower in calorie density So I think that um it's not inherently bad for food to spike your dopamine But the more of that that happens the more it drives your food intake the stronger the cravings you're gonna have and the harder the time you are to the harder it's going to be to control your intake The other thing it does is it causes you to develop habits So if this process goes on for a while and your dopamine keeps spiking and you're consuming that food habitually it stamps it in and it becomes kind of automatic and then that food just becomes a thing that you eat regularly in your diet So maybe like every day when you're sitting in front of the TV at night you eat chips That's just what you do now or you have a can of soda in the afternoon That's just what you do now And it's just automatic because that reward um rewarding behavior has just kind of become stamped into your brain as a result of repeated reinforcement And that can be it can be very difficult to change those kinds of deeply ingrained uh reward based habits right Uh I guess I mean that's what probably what most people call is comfort foods which is sort of like the default foods they gravitate towards in certain situations But uh this this brings me to the whole question of food addiction and I've sort of realized the more I've read about it the more I realize it's a very sort of sensitive topic Uh Some people think there is food addiction some people think there's no food addiction So what's your view on it And how common are the mechanisms you just described with uh other addictions sort of mechanisms such as nicotine or alcohol Yeah So as far as I can tell uh all addiction is very similar in terms of the basic mechanism It is

over stimulation of the dopamine system leading to access motivation to consume or to engage in a particular rewarding behavior So all habit forming drugs all drugs of abuse stimulate the dopamine system even ones that we don't consider harmful like caffeine that also stimulates the same system It just doesn't do it uh to an extreme degree But if you look at highly addictive drugs like um like heroin and methamphetamine cocaine crack cocaine they drive very high levels of dopamine release that lead to very high levels of motivation to engage in drug seeking and consumption behavior And then you get this rep prioritization of behaviors where the most important thing in your life is getting and consuming that drug Other things like you know maybe holding a job and social ties and taking care of yourself just moved down on in importance because they've been replaced by this thing that your brain now views as the most important because it's been so heavily reinforced by that dopamine And so um you know this system didn't evolve to make us seek crack cocaine It evolved to make us seek food and sex and other natural rewards that uh in the evolutionary context were beneficial right The system evolved to help us survive and reproduce not to make us fat and addicted to drugs Um And so but nevertheless this is the same system that gets um activated by food And again that's not necessarily a bad thing where it becomes bad is where the activation becomes excessive and starts to lead to negative consequences And that is what addiction is You know if you experience dopamine mediated reward and it doesn't cause negative consequences in your life then that's not an addiction So even you know some people there are people who even can use heroin from from now now and then and it's not negatively impacting their life They're using it maybe once a month and they enjoy it It's it's not messing their life up and and that's it And that is not classified as addiction So it really depends on what negative consequences Yeah And so coming back around food um there's basically there's two perspectives on this Well there's one from the scientific literature in medical communities And then there's my perspective which is within the spectrum of opinions in the scientific and medical communities But I just want to present those two separately Um This there's no consensus in the scientific or medical communities on whether food addiction is a valid concept And so some people think yes food addiction exists Uh Some people think we shouldn't be talking about this in terms of addiction even if people have disordered eating behavior it's not really the same as having addiction to you know heroin or cigarettes or some or gambling which is now recognized as an addiction uh in the DS M five which is a um American um

diagnostic manual for psychiatric disorders And so there's there's not really a consensus Um however there are from people who do believe that there is food addiction there are diagnostic tools that have been developed So there are questionnaires that you can take um like the Yale food addiction scale that will classify people as having addiction or not having food addiction And these are based on the diagnostic criteria for drug addiction So they basically took those and translated it in terms of food and then they applied the same criteria And if you apply those criteria that are established for drugs you see that food addiction does exist according according to this metric and something like 10% of people in the general population qualify And then that goes up If you look at people with obesity and then people with binge eating disorder or extreme obesity you get a pretty high proportion of people have food addiction Um An important point I'll make here is that only something like 25 or 30% of people who have obesity are diagnosed as having food addiction using the scale So even though that's a higher proportion than in lean people it's not the case that there's a 1 to 1 correspondence So I don't think it's accurate to just say obesity is food addiction I don't think I don't think really anybody believes that that's true Um OK so that's that's kind of the scientific and medical communities My personal opinion I believe that food addiction does exist um at the most basic level an addiction is a reward driven behavior that is causing you harm and how many people are experiencing harm due to over consumption of food and consumption of unhealthy food that in part is due to the fact that that food is very rewarding right I mean one of the reasons people are over consuming is because the food is seductive that is currently in our food environment that causes people to engage in purchasing consumption behaviors that they may not have otherwise engaged in just by the nature of how dopamine mediated reinforcement works And so if we take that very simple definition of reward driven behavior that causes harm a lot of people if if we just apply that a lot of people would be classified as being addicted to food And I think part of the reason people are resistant to that idea is because they don't like the implications of it They don't like to think about the fact that if we accept that it means a lot of people have a problem I have an eating problem And I think that's actually true Um That said I think to some extent the concept of addiction is not really necessary um with food because well I shouldn't say it's not necessary I think it can be important because people who really have a big problem controlling their eating behavior because of uh craving and reward driven eating Those people can

seek professional help in the form of um food addiction treatment programs so that it does have value in that sense But I think the thing about addiction is it's pretty arbitrary to call some things addiction and something's not because motivation is a spectrum You know you can go anywhere from being completely unmotivated by of behavior or a stimulus to having such extreme levels of motivation That it's the only thing you care about in your life And there's an entire spectrum from 0 to 100 that humans can be on And it's only when you cross a certain threshold that will say that that's addiction Great That will will label that addiction Got it So since we um sorry II I since we have only a couple of minutes left I want to just wrap up and uh get your views on what people can really do to sort of not gain fat And I know it's like a very very big question to ask at the end when we have just a few minutes left but maybe you know one or two top things that you would sort of give very practical recommendations to people Sure So I'll just give a couple of tips based on things that we talked about Um And there's a lot more in my book Um a lot more detail and and more topics but a couple of things that I think are particularly important that touch on what we've talked about are one eating higher satiety foods So foods that per unit calorie are more filling such that you just naturally consume fewer calories while experiencing the same amount of fullness So this is tends to be unrefined lower calorie density foods that have um lower calorie density higher protein higher fiber um and moderate palatability So they don't have to taste bad But you want to steer clear of those really really seductive foods So these are things like oatmeal uh other whole grains fresh fruit um eggs meat poultry um uh yogurt that those kinds of foods vegetables and uh as opposed to more calorie dense processed foods that naturally promote a higher calorie intake So that's one thing I think people can get a lot of mileage out of that So that is uh you know properties of the actual food that we're eating But I think there's another thing that's really important and that is your food environment So not just what types of food you're eating but the food environment that's surrounding you the kind of cues that you're feeding your brain And that relates back to that reward um that reward system in your brain that dopamine And so essentially what you wanna do the key thing is to control the food you use in your food environment So at home and at work if you're able to you don't want to have the sight or smell of foods throughout your day So you don't want to have food on the counter you don't wanna have it visible easily accessible within arm's reach particularly between meals And another thing you can do is create small effort barriers to make it a little bit

harder for you to get food at times that you shouldn't be eating food So put you know if there's something that you would kind of wander over to and grab a snack put it in a jar with a screw on lid and put it on a high shelf or have the only fruit that's available Be something the only food that's available be a piece of fruit that you have to peel before you can eat like an orange If you're really hungry you can still eat the orange but you're not gonna just casually stuff it in your mouth That's something that you have to engage in some effort to do Um So yeah so controlling your food environment creating small effort barriers and eating higher satiety foods I think that's a strategy that people can get a lot of mileage from Fantastic Uh Thanks so much Uh I know this Uh this went probably longer than uh what we both were sort of initially discussing since you are a bit short on time But uh I hope you're able to make to your next appointment in time But uh this was super wonderful Uh Thank you Steven It's been a pleasure talking to you uh learned a lot and uh hopefully everyone else will learn a lot from uh the podcast and probably go and pick your book The Hungry Brain which I thoroughly thoroughly enjoy Ok Thanks for having me All right Bye-bye Take care Ok Bye