



**Stephan Guyenet, PhD**  
**The Neuroscience of  
Overeating & Regulation of  
Calorie Balance**

**SIGMA**  
NUTRITION  
RADIO

≡ Episode 166 ≡

DANNY LENNON:

Hello and welcome to episode 166 of Sigma Nutrition Radio. I am your host Danny Lennon and as always every week here you get to talk with academic researchers and world class practitioners that are at the forefront of evidence base nutrition and performance. This episode will be no different as I'm going to be talking with Neurobiologist Stephan Guyenet about various issues related to the neurobiology of over eating, obesity development, hyper power ability and other related issues. But before we get into today's episode I just wanted to bring to your attention a couple of things particularly one of those is related to those of you who are looking for information about nutrition courses because one of the most common questions I get asked is what nutrition course I recommend that people do.

And there's obviously a lot of new ounce set to kind of different backgrounds people are coming from. But as I've said many times before on this podcast my default response has been to say Mac-Nutrition Uni which is headed up by probably without doubt one of the most knowledgeable, well respected and genuine folks involved in evidence based nutrition Martin McDonald who many of you who listen to the show regularly will know he's been a couple of times

before and someone who I hold in quite high esteem and someone who has mentored me in the past as well.

So this is like the nutrition course that I recommend that people do. And so the reason why I bring this up is that I wanted to give you the heads up that the enrollment for the next intake of that course is now open. But it's going to be closing soon. I think some time in early March, maybe the first week in March that will be closing. So if you want to jump on that then now is the time to do so. And if you want full details in that I'll just put it at a link free to go. Please go [sigmanutrition.com/mnu](http://sigmanutrition.com/mnu). I'll list everything you need there in terms of details and links to go to – to find more about the course and see if it's for you. So I just thought I'd mention that given the timeframe. So that's [sigmanutrition.com/mnu](http://sigmanutrition.com/mnu). And the second thing I wanted to mention before we get started is a shout-out to everyone who has sent in some feedback about last week's episode with Kevin Hall of DIH. And there's a massive response to that. And it seems that you guys really enjoyed Kevin's insights. And it's an episode that I'm particularly proud of as well because I could think it contains a lot of important discussion and stuff that people need to hear.

So it's good to see that it's being received not light as well. And I actually think today's episode is a really nice follow on progression from that because you'll see a lot of the issues are kind of inherently tied to it. So let's wait for Stephan to introduce some of them. But let's get the author of the new book the Hungry Brain and neurobiologist Dr. Stephan Guyenet on the line.

Stephan Guyenet welcome back to the podcast. How are you doing good sir?

STEPHAN GUYENET: I'm doing great. Good to be here Danny.

DANNY LENNON: Yes, it's great to have you back on and just first off before we even get started. I've been reading your new book which is just launch a couple of days ago. I've been reading that over the past couple of weeks. And I just wanted to start by just saying number one, a massive congratulations on a really excellently put together piece of work. It's been a brilliant

read. Not only is it laid out well but the information as well. So I just wanted to first say congratulations on all the work that's gone into it because it's turned out phenomenally well.

STEPHAN GUYENET: Well thank you very much. I'm glad you like it.

DANNY LENNON: Yeah, it is a fantastic and we're certainly going to touch on a number of things that come in through that book. But just as a way to start us off here. Just in case some of the listeners haven't seen your previous appearance in the show or maybe are new to your work can you maybe give a couple of cliff notes about your background and then how that feeds into the kind of topic of the book and the real I suppose driving force behind you wanting to write this book in particular.

STEPHAN GUYENET: Yeah. So I have background in neurobiology. I went to grad school for neurobiology And after that I applied it to eating behavior and obesity. So I was studying in a lab of Mike Swartz who studies obesity and how the brain changes in a way that favors the obese state and favors maintaining the obese state. And we were studying a part of the brain in particular called the hypothalamus. And this is the part of the brain that regulates body fat. And I think still to this day a lot of people don't realize that the brain actually regulates body fatness. And this brought together two of my big interest which are fitness, health and nutrition and the brain.

And it turns out it dawned on me pretty quickly in my work that we were studying the right organ because the brain governs all behavior including how much we eat, what we eat, how much we move our bodies and it regulates a lot of the physiology of our bodies as well. And so it really is a very logical thing to focus on if you're trying to understand eating behavior and body composition and health. But what I saw is that a lot of people weren't really looking at these problems from the angle of the brain. And I understand that. I mean you can definitely get understanding and you can get practical value without thinking about the brain but I think if you really want to understand those things from first principles you have to understand them from a brain centric perspective.

And so I started writing about it and the writing started getting some traction and about three years ago Dan Party mentioned that I should write a book and I kind of tossed around in my head for a long time casually but never really taken the idea seriously until he said that. And then it just kind of yelled in my mind that this was the right time and I have the right ideas and so I decided to write this book. And kind of premise – the premise of the hungry brain is that no one wants to overeat and certainly no one wants to do it for a long time, become overweight and develop chronic health issues. But that's exactly what most people do over the course of their lives and so what is driving that disconnect between our actual behavior and our healthy goals for ourselves. So it's kind of a perplexing question and it's one that can be resolved by considering what are the brain circuits that drive, what are those non-conscious instinctive brain circuits that are driving or eating behavior in a direction that is in the opposite direction of what we consciously rationally want. And so the book is all about the circuits. And we know quite a bit about those circuits in the scientific community. But most of that information has not really trickled down to a General audience. And so my goal with the book was to kind of take a broad brain centric view of what's driving that behavior and as far as I know this is a first book to have done that -- first generalized book

DANNY LENNON:

Yeah, for sure. And I think it's like I said it's really well laid out. But what I really want to do today is particularly to try and pull some of these different ideas together because like you said when you take that overview of what is going on between these kind of regulatory mechanisms that we have that can essentially control energy into this whole energy homeostasis piece and then potentially what's going to cause something to go array with those that's leading to this possibility of overweight and obesity is really getting at the core of the issue and I think and what is particularly fascinating about tying this all together is that you mention for example Mike Swartz and his work already are which regulars as a podcast. Well Remember Mike was on this show talking about some of the specifics there. We've had say Brian Wanting talk about food environment specifically.

And we've had other people consider like leptin and some of the metabolic adaptations.

And then so when you start taking essentially the framework that you put forth in the book of tying all these things and together a nice framework emerges so I'm going to try and get it to the core of that if we can. And maybe a good place to start with that is the whole idea of energy homeostasis, right? Because essentially when we look at the factors that cause us humans over-consume calories on a consistent basis that leads to this excess body fat gain. We know that we have these regulatory feedback mechanisms that should at least in theory prevent excessive and maybe you can kind of give the best kind of summation of this. But really and I know this is – it can get very complex. But at least basic level we can have -- we think of to kind of branches to this where first we have those maybe homeostatic controls and different things are going to influence our intake and expenditure based on that side. And then we also have the other kind of non homeostatic stuff of behaviors and habits environmental factors that can override their controls. So what when where can I get people this could have clear picture new head what's the best place for us to start here? How would you get people to start thinking about that I'm one of the main things I suppose we need to start considering yeah

STEPHAN GUYENET:

Yeah, so I think I think as you said we can kind of divide the processes that are happening with eating behavior into homeostatic in other words trying to meet energy needs as perceived by the brain and non homeostatic which doesn't really have anything to do with energy need. And I think you can kind of intuitively conceptualize those as hunger driven behaviors and non-hunger driven behaviors and so there a lot of situations when we eat because we're hungry. You know it's been awhile since we've had a meal. We've been exercising a lot or you know those types of situations we're going to eat because of the perceived energy need. But they're also a lot of situations where there is no energy needs such as at the end of the large meal when we decide that we want to eat 200 calorie slice of chocolate cake with ice cream and whip cream. So I think you can kind of divide things into those two categories and it's really kind of an interesting

question because when you look at a person with obesity versus a lean person what you see is that the obese state is really it's distinct from the lean state homeostatically.

And what I mean by that is that a person who has obesity defends their obese state against changes just as well or does it -- I don't know if it's exactly just as well they certainly do it the same way that a lean person does it. So a person is obese their brain will resist changes in weight in down and upward direction to some degree. A person who lean will do the same thing. And so there's some process that happens there that causes a person who is defending a lower level of body fat to turn into a person that is defending higher-level body fat. So there's some change that happens in that regulatory system in the brain. And we don't really know exactly why that happens. And I talk about this in my book. I offer some ideas and some speculation but you know if we now switch gears and go to the non-homeostatic side of it there are a lot of things in our environment and there a lot of food properties that can cause us to increase our calorie intake. And so the -- but we don't quite understand what the connection is between that kind of passive overeating, non-homeostatic over eating and what exactly gets us to the obese state where were actually actively defending that higher-level body fatness.

And I think it probably has something to do with over eating itself as well as perhaps the elevated levels of leptin that are produced so in our studies with Mike I think I listened to your interview with Mike. I think he must have talked about this some. We found that people with obesity have this kind of injury response, this inflammatory injury response in parts of the hypothalamus that are regulating body fatness. And so there's some there's some stimulus, there's some trigger that causes this process to occur that we believe may contribute to the fact that they were defending a higher level body fatness. We don't quite understand the link there but we do know that there are certain conditions that cause both passive overeating and the eventual defense of a higher level body fatness. And these are being surrounded by a variety of calorie-dense, refined, highly palatable foods, insufficient

physical activity and possibly also not getting sufficient sleep and not regulating stress well.

DANNY LENNON:

Right, and I think a really nice way to start thinking about some of this was the actually the way you had phrased it in the book when to try and get us to think about this nature of overeating you had this great like that said we need to first answer the fundamental question what is it about food exactly that is reinforcing, right? And from there I think you talked about work on this kind of phenomenon of conditioned flavor preference, right? I found that particularly interesting. Can you maybe perhaps explain some of that for people because I think it's quite a nice piece that gets to the core of this idea of what about food it actually is that leads this kind of idea of food that's easy to over eat.

STEPHAN GUYENET:

Yeah yeah, absolutely so high in my book I really try to get at these questions from the angle of first principles and so I really try to understand what is it about food that our brain wants. I mean what's the point of eating and if we can look at this from a couple of different angles. But the one that you're asking about here is looking at which food properties drive our behavior because we know that food is reinforcing. It's rewarding. It's seductive. it's something that we want but we also know that not all foods have that effect on us, right? So some foods like ice cream or pizza or French fries are very, very motivating and seductive to the point where we can even eat them if you're not hungry whereas other foods like plain raw kale and celery sticks and things like that it's like yeah, I might have a nibble but I'm not really going to go out of my way to eat those things and I might not even like them at all.. So what is it about a food that is motivating to us.

And we actually know a lot about how this works so there are – when you eat a food well actually I'll take a step back so the ultimate currency of natural selection is reproductive success. So that's how many offspring you leave that can then leave more offspring. That's the ultimate currency of natural selection. But that's not really what we're thinking about when we eat food. What were thinking about are these more proximate goals that natural selection has hardwired

into our brains as a substitute for reproductive success. And so one of those hardwired goals is obtaining and eating sufficient food. But what we can see is that and so because of that food is reinforcing. So basically we learn over the course of our Lives how to obtain it more and more effectively. And so but the interesting thing is that it's not food in general that were looking for.

We're looking for specific food properties and those are also things that are hard-wired in the brain. And so the brain is hardwired to look for fat and starch and sugar and protein as well as salt and particularly amino acid glutamate which is that meaty umami flavor. So when you eat a food there are sensors in your mouth and in your digestive tract especially in your in your small intestine that detect those specific chemicals in food and they report back to your brain and tell you how much of it was there. And so if you eat a slice of pizza for example your brain gets a report that says hey this is a really good dense source of starch and fat and to some extent protein. And that causes dopamine to start spiking in your ventral striatum otherwise known as your nucleus accumbens and what that part of your brain does is it determines your basic motivations and your drives, your cravings.

And so when that happens when those nutrients get detected and a start spiking dopamine in your brain what that does is it reinforces your behaviors of seeking and eating those foods. So you have pizza for the first time your brain gets wind of the fact that it's full of these awesome nutrients that it really, really wants and then the next time you experience the sensory cues that are associated with that like the smell and the taste and the appearance you're going to have this drive. You're going to have this desire or this craving to eat that food. And if that craving is strong enough it can even drive you to eat it even when you're not hungry. And so this explains why we like certain foods, why we don't like other foods and why we learn to like things like a vegetables as they're repeatedly associated with salt and fat because vegetables on their own don't really contain anything that the brain really cares about intuitively. They care – they contain things that we care about rationally and cognitively

because they have fiber in vitamins and things we know are healthy. But that's not what your intuitive brain cares about. What your intuitive brain cares about is things that deliver calories and protein and salt.

And if we look at and those are the things that drive our cravings and if we look at again if we look at hunter-gatherer foraging behavior and in fact not just hunter-gatherer foraging behavior but foraging behavior in any omnivorous free living animal what you find is that the number one driver of their foraging behavior is the calorie return rate. So number of calories that a food item will deliver minus the number that it takes to attain it divided by time. And this is just a very simple economic, you know, equation straight from economics. But what we see is that animals including humans in the wild behave according to this principle and the reason -- so it's just kind of -- excuse me. It's like a cost-benefit analysis that your brain is doing in response to the calorie value of those foods. And your brain knows the calorie of those foods because of that process that I was just talking about how it detects the calorie containing nutrients it's spikes dopamine in your brain and your motivational value, your motivational drive according to the calorie value roughly speaking according to the calorie value of those foods.

DANNY LENNON:

Right. yeah. I think that's just a really important point and again if we're considering this kind of first principles and we're looking at well from an evolution perspective at least it makes sense that were kind of seeking out something that's going to be calorie-dense to provide enough energy and then what when you mention in the that it's going to respond there for to carbohydrate fat as well as protein and then look salt and glutamate as well. So really those things that it's going to know are going to give a certain amount of these macronutrients and there for calories. I think there's two particularly fascinating things that I find about that that are important to this whole discussion whether than this when we talked about getting body fat and obesity. I think the first is that particularly when we look at the conversations that happened quite a lot online and different communities around demonizing certain macronutrients that goes on. I

think this important thing to realize that this condition flavor preference there's a response to not just sugar but it's carbohydrate, fat and protein due to the calorie density primarily that's going this sort of response. And then second that the response is to the macronutrient composition or the signal at least that there's calories coming in rather than micro nutrition. So really we could say that it is the brain is really just looking incoming calories is not too concerned about micro nutrition from that perspective at least would that be fair?

STEPHAN GUYENET:

Yeah, absolutely. So there's a couple of interesting topics here. One of them is as you said brain is concerned with macro nutrients and calories. I mean really that your reward system in your brain the system that determines your food motivation it's pretty good at figuring out how many calories overall are in food and motivating you accordingly. And I think that's very consistent with the evidence that we see from hunter-gatherers that the number one thing that's driving their foraging behavior, the number one thing that motivates them to seek one food over another is that food's calorie return rate. I think our brains are very good at determining how many calories of food has in it and motivating us accordingly. And so you know and this is really interesting because like there's so many essential nutrients in food, right? There so many things micronutrients that if we don't have them we literally die and so why don't our brains care about those things that are absolutely essential to our survival and I think the answer and this is me speculating but I think it's pretty reasonable thing to speculate is that in a wild environment where the only thing you can possibly eat is a diverse omnivorous whole food diet.

I think it's very difficult to meet your calorie needs without also meeting your micronutrient needs. And so what you see is that hunter-gatherers rarely have nutrient deficiencies where you see I'm talking about micronutrients like vitamins and minerals where you see -- and proteins. Where you see deficiencies is in non-industrial cultures that primarily have agricultural diets that are not sufficiently diverse. So they have diets that are very, very focused on grains, the exclusion

of almost everything else or very, very focused on tubers to the exclusion of everything else. And they are the ones who will develop deficiencies in protein or specific micronutrients. But that's not something you very often in hunter-gatherers. And so I just don't think the brain is set up to really care about those things because it didn't matter. Like that was not something that needed to guide our behavior because it was something that came naturally with getting enough calories. And so that's one side of what you brought up and the other one is talking about this sugar idea. And I think it's definitely true that sugar is a highly motivating substance for humans. It's palatable. It's rewarding. It's seductive. But I think the bigger picture is that sugar is only one of the things that has those properties and has those effects on the brain and eating behavior. So and so and you know what the brain is -- is very deeply hardwired to like sugar. You can put sugar on a baby's tongue and it will make facial expressions that are consistent with pleasure. And it will also kind of dampen pain. They actually use sugar solutions to dampen pain in infants. And so there's definitely something going on there. I mean the brain really likes sugar and it's not surprising if you think about it. Sugar in an ancestral environment is a signal of fruit and honey. Those were the two forms of sugar that were available in a natural environment. And they were both extremely valuable sources of nutrition to our hunter-gatherer ancestors. If you look at hunter-gatherers right now at well I say right now. There aren't very many hunter-gatherers left but right now and historical hunter-gatherers what you see is that the ones that are living in the parts of Africa that our distant ancestors were thought to have lived in they get a lot of their calories from sugar. I mean the Hadza for example that live in the African Rift Valley which is called the Cradle of humankind. These people, you know, there's fossils stretching back for millions of years. I mean we've been in that location for a long, long time and when we emerged from Africa and went around the globe we came in large part from that location. And so this is really profoundly significant place for the evolution of the human species.

What we see is in the Hadza which are probably the closest, you know, existing group that we have to our ancient hunter-gatherer ancestors they get a lot of sugar in their diets. And it's mostly from honey. They get about 15 percent of their calories on average year-round from honey. And then they eat fruit on top of that so that like similar or even higher to the amount of sugar that is good Americans eat. And for them this is good nutrition where Because hunter gatherers are in a situation where there in a challenging environment and they're having to work hard to meet their calorie needs. And so when they find a food like honey that's extremely rich in calories and very easy to get it's like amazing. I'm going to drink a quarter – I'm going to drink quarter of this right now. I'm just going to drink it straight liter of honey right now and that's what they do. And this is like seems an amazingly gluttonous to us. But it was actually good for them because it supports their survival and reproduction. And it's not good for us today but that's only because we're in an environment of excess of calories, excess of nutrients and excess of refined foods. So anyway I'm just trying to put this into a broader context that the human brain and human eating behavior is definitely motivated by sugar. But it's also motivated by fat and protein. And I think that if you leave those out of the equation then you're really not seeing the big picture.

DANNY LENNON:

Yes and that can't be emphasized enough. It's so important because that's when this whole discussion around say sugar in particular comes up and how maybe some people will and again rightly say that a lot of the people in the general population consume too much sugar. And I'm sure we can make that point but trying to demonize a certain compound and an this one nutrient as the issue driving obesity or the this is a sure that's going to make someone gain body fat independently of other factors is just completely illogical and it's only when people start disconnecting sugar inherently being fattening versus if sugar or adding sugar into a certain particular type of food makes that's food then hyper palatable then leading to an excessive calorie consumption that is one way of saying okay there's a role at least maybe it's playing there as opposed to it being the one thing, right?

So it's only because you're mixing it with probably fat and starch and then food that's maybe low in fiber and low in protein and so those tiny value et cetera, et cetera. And then share these foods are the issue so it's a disconnect between people saying sugar in of itself is this evil thing versus saying okay maybe at certain high level that's playing a role in increasing the hyper palatable of certain foods which people tend to overeat on, right?

STEPHAN GUYENET:

And, you know, I think sugar -- sugar is a refined food. It contains no nutrients other than carbohydrate and so you know if you're going to eat a whole food diet it's not a part of that and I support that and I eat very little refined sugar myself. But I mean I don't think that it is the nutritional demon and, you know, I have never observed someone sit down to a bowl of plain white granulated sugar and dig into that you know. And I've never had any urge to do that myself and I think it's not just sugar there's a bigger picture there. Like if you consider ice cream what is ice cream without sugar it probably tastes good but not great. What is ice cream without fat? I don't think I would even enjoy ice cream without fat. And so I think there is there's a bigger picture there of different nutrients that come together and produced that effect. But I will say you know what sugar it's definitely empty calories. It's not just empty calories and I think I didn't this is where guys like Gary Tubbs have someone of a point is that in excess particularly in the context of calorie excess it does disproportionately overload the liver and that can result in some adverse metabolic effects and I know you had Stanhope – Kimber Stanhope, am I getting that name right? I know you had her on the podcast a while back, I listened to that and enjoyed it. And there are adverse metabolic effects that can occur from too much refined sugar. But I think that, the thing that often gets lost in this conversations is that – that's – and I'm not saying this got lost in the conversation with Dr. Stanhope but in the – in the public conversations I think what gets often lost is that that's part of a context, a broader context of people eating too many calories, of people eating refined food, of people not getting enough physical activity, of people consuming

excess drugs like cigarettes and alcohol and all sorts of other lifestyle factors that can plug in to this.

And I think, you know, I guess to expand on that a little bit, you know, I know Gary Talbot's perspective on this is very popular right now. So, I'll comment a little bit on that. But he's very focused on this concept of insulin resistance. And – and you know what, insulin resistance is really important and this – this is something that I also think is very important and very central to metabolic disease especially diabetes but also cardiovascular disease. But the thing is if – if you – if you are an alien who came down to earth and decided to look at the research and say what causes the insulin resistance; you would not conclude that sugar is the main cause of insulin resistance.

You would conclude that high intakes of refined sugar are contributing to insulin resistance but the main causes are excess body fat and calorie intake and lack of physical activity. I mean there is so much evidence, so much evidence supporting those conclusions and the fact that those are central as well as genetics, genetics is also important. That I think, you know, we can recognize that sugar plays a role in that but I think when we exclude those other factors that are probably even more important than sugar, we're kind of taking the focus off of the main driver of this serious metabolic abnormality that underlies a lot of human disease.

**STEPHAN GUYENET:**

Yeah. Like it's such an important point because again, because again if we just consider just the amount of evidence that we have to that effect of just consider people who are – who are overweight who manages to lose a decent percent of their body weight, right? And so typically we see this number I'd say a decrease of 10 percent of body weight for someone overweight. No matter what method someone uses to achieve that, nearly across the board we see improvements in their insulin sensitivity improvement in various different blood markers. So, it kind of speaks that point that the – the at least one of the main things contributing towards it is probably going to be just the fact that there's overweight or – or obesity present. Then obviously we have like you said physical activity and genetics are probably the next big two.

And so these things are ones we know for sure are playing an impact and we can sometimes take the – the spotlight away from them if we focus on – on things too much in particular. This whole thing of trying to focus on one particular nutrient or the other I think, again this is another great line in your book that I remember highlighting and I think I have it here somewhere. It said in popular media there was a perennial debate about whether sugar or fat is responsible for the obesidemic. This has lead some people to view obesity research as a team sport rather than a scientific discipline. Allow me to end the debate by stating that most researchers find quite obvious, it's both. And – and that was – that was quote was particularly impactful I think because that sums up things pretty well and right were so many people spend time debating different sides of this.

This I suppose argument that isn't really leading anywhere because it's missing the – the other parts of this equation like what or causing this over-consumption of calories. What's – what's the role of food or hyper- palatability, food environment, psychological triggers, et cetera, et cetera. So, I think that's a pretty pinpoint area that – that you've touched on. One thing just before I forget Stephan and maybe going in the slight different direction. We just talked about how there are certain attributes that we can start to piece together of what causes a certain food to be reinforcing. Or what causes certain foods then to be hyper-palatable. We know there's – there's different attributes that – that we've seen in research that point to this. So – so one question that I would have and I don't know if we've got a good answer for this yet. Is at least anecdotally when different people report that they have a “trigger” food or some sort of specific food that for them if they have some of it, it will trigger binge on this stuff or they can seem to have just a small amount of that. And first but for like for some people it could be sweets for other people it's chocolate for -- for some people it's a peanut butter if they get a jar and a spoon they're going to finish the thing. For some people it could be breakfast cereals, whatever. There's all these different preferences that people have but at the same time we see then for one person they may not be triggered at all by certain high sugar foods.

But they again if they have any type of peanut butter they'll just smash the thing down and other people are at the office it was supposed the real thing I've been trying to work out is, is there anything pointing to why different people will find different types of foods that may have different attributes to be the thing that they are most likely to overeat on. And I know there's so many elements that can play in to that but how would you even approach that question

STEPHAN GUYENET: Yes, that's a really interesting question. And I will start off by saying that to my knowledge we don't really know what generates those individual differences. But I can offer a little bit of speculation. So genetics are – genetics is a force that impacts almost everything about our bodies and brains. And if we look at the genetic contribution to body fatness for example, genetics in an affluent nation such as the United States or most other affluent nations genetics explains about 70 percent of the differences in body weight between individuals. So and it goes a lot deeper than that. Because genetics explain even a lot of the details of our eating behavior or I shouldn't say explain they partially explain a lot of the details of our eating behavior. So, the research of John De Castro and other has shown that even some of the pretty fine details of our eating behaviors such as how much of each macro nutrient we gravitate toward at a meal. How much food it takes for us to feel satisfied, how much the seductiveness of food has how much impact that has on our eating behavior.

So some people when they're in the presence of really rewarding seductive food they will you know really stuff their faces and other people can really control that pretty easily. And then other things like willpower some people have a better ability to regulate their own behavior through willpower and to kind of like stop their own impulses or prevent those from translating into behavior. Some people do that better than others and that has a genetic component as well. So genetics really influences a lot of the details of our eating behavior and our food preferences and I don't know exactly where those things come from. I don't know exactly what systems in the brain or body are impacted by genetics that causes to have those differences and I'm also not saying

that genetics is the only reason but I strongly suspect that the – that our genetic blueprint is a major reason why we see these individual differences.

DANNY LENNON:

Yes. No, no, no thanks for that. That highlight something that I think is -- is important piece of this. Another again question that maybe slightly vague but I just thought of as you were talking earlier was that when it comes down to brain chemistry or the homeostatic control that we have in place over energy or say changes in leptin for example. When were thinking about the those kind of -- the levels of those circulating hormones or the different mechanisms in place. We know obviously when we compare a lean person versus an obese person we're going to get these differences in that metabolic states so an obese person for example is not just the same set up as a lean person but with more body fat there's complete different stuff going on metabolically. And so if we think of just one example and with leptin resistance right we have so much going on that's tying in to potentially causing future overconsumption or the inability to decrease energy intake because of leptin resistance.

Now so with these different setups, my kind of question that I haven't been able to get that kind of decent answer to is, when we consider someone that was say formerly overweight or formerly obese has lost weight and the -- we know that the biggest issue for most people is trying to maintain that weight lost. It's not the initial weight loss per se that's the most difficult thing, from the research it seems that it's the maintenance of weight loss. So if we have someone that was a formerly obese or formerly overweight that is now at healthier weight, is there a difference in the way those regulatory mechanisms are set up between say that person versus a person that was – that was always lean for example if that question makes any sense.

STEPHAN GUYENET:

Yeah, yeah absolutely. Yeah. There are very profound differences in those homeostatic mechanisms, those feedback loops that are regulating weight. And so you're saying is there a difference between two people one of whom has always been lean and one of whom recently went from overweight to lean. So this -- this gets back to the system in

the hypothalamus that I was talking about earlier that regulates body fatness so it's -- it functions similarly to your home thermostat in the sense that your thermostat has a certain temperature that you set it to that it's going to defend against upward or downward changes if you have both air conditioning and heat. And so if your temperature is -- so let's say you have your thermostat set to 24 and it goes down to 23 your heat's going to kick on and it's going to go back up. So -- and -- and if you -- let's say you leave all the windows open in your house and you're just letting the wind blow through and now it's 15 in your house while your heat is going to keep blowing and blowing and blowing trying to bring it back up even though it's not being successful in doing so because you're not you're not -- you're not letting it.

But that -- that homeostatic mechanism that feedback mechanism is still going to be activated and so that's -- that's basically what you see in people who have lost fat. They -- their brains were -- at their former weight their brains were comfortable at that weight, that is what their brain "wanted." And once they deviate from that and this is -- this is mediated by a drop in the leptin signal once their brain deviate -- once their bodies deviate from that their brain hears about it and initiate a starvation response and that starvation response, if you just -- if you just lose weight by eating fewer calories of the same food you're going to get that starvation response and as far as we currently know it will continue until the fat comes back. So it could be for years and that starvation response causes you to be more hungry, it causes you to have a greater interest in calorie dense foods. So you're paying more attention to food cues, you're craving more, you're having a hard time walking by the ice cream aisle at the grocery store. It also may it reduces your calorie expenditure. It may make you feel sluggish and cold a lot of people have experienced that after they lose weight.

And so -- so that's -- that's really the difference is that this feedback system is not at its set point in a person who has -- who is now lean who used to formerly be heavy and so that in some ways you're actually in a very good metabolic state. Your body feels deprived and what that means is that your metabolism in terms of glucose and fatty acids is actually

going to be very efficient and you're going to have a lower much lower risk of developing diabetes for example that you used to. You're going to have better insulin sensitivity but your brain still doesn't like being in that state because for our hunter - gatherer ancestors, weight loss was a threat to survival and reproduction. And so I think -- so that's -- that's one thing is that -- that response can persist as far as we know it can go on forever. And that's why people -- That's one of the main reasons why people tend to regain weight following weight loss but I think that another thing to recognize is that you're set point or the comfortable level of body fatness that your brain tries to defend depends in part on the cues that it's receiving not only from the leptin but from things in your diet and lifestyle.

And so it's -- this has been very clearly demonstrated in rodent models and I think there is evidence in humans that's pretty consistent with this as well even though it hasn't been as clearly directly demonstrated. But in rodents what you see is that their set point or the level of body fatness that they are trying to defend, that their brain is trying to defend depends on the palatability the seductiveness of that food as well as its calorie density. And so an animal that is placed onto a calorie dense palatable refined diet will gain weight and if you just restrict the number of calories that it has access to it will lose weight but as soon as you take the Restriction off it will bounce back up to the weight of animals that have been eating that the whole time. Whereas if you put that same animal on an unrestricted diet that's an unrefined, calorie-dense, less palatable diet even after it's already become fat it will settle at a lower level of body fatness. And if you perturb its calorie intake again it will bounce back up to that -- to that lower level relative to what it was on when it was eating the other diet.

And so it essentially it will defend a different level of body fatness depending on -- depending on what you feed it and I think he see the same thing in humans when people eat a unrefined, simple less calorie dense diet we tend to be comfortable at a lower weight. It's not just that we passively over eat -- or excuse me. It's not just that we passively eat fewer calories, although I think that's part of it but I think

that we are actually comfortable at a lower weight and we don't activate that starvation response in response to weight loss to the same degree as if we were just restricting calories of calorie-dense, highly palatable food.

DANNY LENNON:

Right. Yes, so I think it was really interesting then when we start to think of the kind of practical implications for the diet or themselves in terms of the long-term view because. Like we said earlier if someone is in a consistent calorie deficit no matter what that means, they're going to decrease body weight, over time, they're going to lose body fat. And we know people that have lost weight by simply just counting their calories and really their food selection doesn't really matter that much once there is that deficit there. They can be eating junk food all the time and still lose body fat. And but based on what we've just talked about there, the likelihood of rebounding or regaining that body fat can very much relate then to, like you said in the hyper palatability of that food and the types of foods that are in the diet. So for a weight maintenance. Or at least maintaining that wait in the long term and that new lower weight, that's when all the factors of food quality and the overall diet quality become more important. Would you think that's kind of a fair assessment as opposed to that the dieting period itself may not matter as much in terms of we know, any diet will kind of work once its calorie restricted.

But the real issue of people trying to maintain that weight loss is where the benefits of having a less palatable maybe more bland meal so to speak but primarily of -- of good quality food is more important?

STEPHAN GUYENET:

Yeah. So I think there are a couple things that we can discuss here and one of them is I mean there's no doubt at all that changes in calorie balanced -- calories coming in or calories leaving or both is what determines changes in fat mass. I mean that -- that's so well established at this point. But I think the question is how do you cause that to happen in the most comfortable and sustainable way possible. And so -- you can -- I mean if you want to eat pizza and twinkies and drink soda you can lose weight while doing that there's no doubt about it and people have demonstrated that that is

true. But I just don't think that easiest way to either lose or maintain and I think -- I think you're right that the maintenance is -- is the more challenging part of the equation but I think it plays into loss as well because I mean when you're -- when you're actively losing weight as opposed to maintaining. If you want to lose at any appreciable rate you're going to have to restrict your calorie intake to below what you need to maintain your ultimate target weight. And so there's a level of restriction there that's pretty substantial and it might last for months and so I think you have to choose a strategy that you're going to be able to sustain.

And you know it some people have success just counting calories and eating less of their regular food and if that's the strategy that works for you I have absolutely no problem with that. But I think that that's the tough sell for a lot of people I think a lot of people who need strategies that's going to make their impulses -- it's going to dampen their impulses to eat more food and to eat more calories. And I think that's where these strategies come into play the help -- to help take those impulses that the brain is generating when it resists that weight loss and to try to dampen them and maybe even recruit them to support your -- your goal. And I think you know the difference between -- probably the main difference between the loss and maintenance is just that maintenance last longer.

I mean you might take, you know, depending on how much weight you want to lose and what your approaches might take you a few months to lose the weight you want to lose but after that you have to maintain it for the rest of your life. And if you're fighting yourself, if you have to fight your impulses everyday and you have the struggle happening everyday, you're just not -- most people are not going to be able to maintain that for years and years and years which is what you have to do. And so I think -- I think it is more important for maintenance but I think the main reason is just that maintenance last longer and your motivation wears out like you start off very motivated to make this change but that's not -- that feeling, that strong feeling is not going to last forever so how do you how do you design a diet and lifestyle

that is going to allow you to maintain those behaviors even when you're not feeling highly motivated.

DANNY LENNON:

And that's so important. It's one thing that we've seen when any kind of debates around the internet; people take the whole -- if it fits your macros diet by philosophy too far or -- or simply saying well you can diet on any food you want as long as you eat a certain amount calories and macro nutrients you're going to lose body fat. And again that's completely true and like we know that that's a fact, you will decrease body weight but the practicality of it becomes just like you say how easy is that going to be in and how doable is that diet. So sure let's assume someone is going to eat 1,500 calories a day if you do that just only from eating Ben & Jerry's then after a few days like how difficult is it to only eat that amount of that highly palatable food and in a very calorie dense manner and make that feel associated versus. eating large volume meals of different lean proteins and lots of fibers, vegetables, et cetera, et cetera. It's going to be a different -- at least even if the calories are the same, you're going to feel like you're eating more food so. I think these are some things that need to be taken into consideration for the practical nature of this.

Stephan we're just coming up close to the time. So, one small little question I did want to bring up to you whilst we're on the topic of brain chemistry and the control of appetite. Is that little aside that was in the book talking about smoking giants and the munchies because I think this is a -- a particularly interesting area. It actually kind relates back to this whole appetite pathway we've mentioned. You wrote about some of the work of Richard Fulton and the effects of smoking marijuana on -- on food intake. Can you maybe just briefly touch on that for people in and how that relates back to some of the brain chemistry and appetite regulation that we've just been discussing.

STEPHAN GUYENET:

Yeah, absolutely. I -- I this is a kind of a fun topic because it's -- it's something that I think is interesting and it's something that a lot of people have first-hand experience with but it's also something that really serves to illustrate some of these brain circuits that regulate our -- our cravings and our food

motivation or behavior our eating behavior. So Richard Fulton is a long a drug researcher with a very long career and one of the things that he did was he studied the effects of marijuana on food intake and so obviously you know people who are familiar with this know this as the munchies and he wanted to see how big of an effect this was. So on one of his studies he had people smoke marijuana joints or Placebo joints, I had never heard that term before Placebo joint, I thought that was pretty funny. And – and then he measured their food intake in -- in the setting of I think they were in a metabolic ward or something like where he could really track their calorie intake really accurately. And he found that people who are smoking -- I think it was two joints a day they had a 40 percent increase in calorie intake and it wasn't even at meals it was mostly between meals it was this sweet and savory snacks that they were over eating between meals.

And they gained fat at a rapid rate and it turns out that THC goes in to the brain and one of the things it does is it activates a receptor called the CB1 receptor, cannabinoid receptor type 1. And this is a receptor that is involved in food reward an appetite and when you stimulate it, it makes food and take go up and it increases food reward and food seductiveness and so -- and interestingly there's also a flip side to that so there's this drug called Rimonabant that I called a reverse marijuana because it acts in a fashion that's opposite to THC on the CB1 receptor. And this was developed as a weight loss drug, it's actually one of the more effective weight loss drugs that's been developed, it's pretty effective in a variety of species including humans and went all the way through clinical trials it was even briefly approved as a weight loss drug in Europe but unfortunately reverse marijuana cause people to become depressed and suicidal. And so they took it off the market but still it's a mechanism of action I think really serves to illustrate the impact of those chemical pathways in the brain on our food intake and our food motivation.

DANNY LENNON:

Yeah it is certainly it's a great example and I think it was -- it certainly makes people think about at anyway and it's -- it's a -- I liked reading about that. Stephan we're just up on time here so to finish, let people know where they can find the

## *Ep 166 Stephan Guyenet*

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book your, website that's up and anywhere else or anything else that you want to -- make people aware of.

STEPHAN GUYENET: Yeah sure so the book is available from all major US retailers right now including Amazon. And my new website is StephanGuyenet.com, so that new website has my blog now it has a page for my book it has the ideal weight program and it talks a little bit – it tells a little bit more about who I am. And my Twitter account is @whsource so those are all ways of keeping up with what I'm doing.

DANNY LENNON: Perfect and I'm going to link up to all of that stuff in the show notes for everyone listening so make sure you go and check out Stephan's blog, some tremendous articles on there and of course I highly recommend the book. And having read it like I said at the start it really is a fantastic resource and I think you'll get a ton from that. So, with that Stephan thank you so much for your time today for all the great information and then also for putting together the great work that, now you've done it with the book but the work you continue to put out online and advancing people's knowledge and bringing interesting and fascinating science to people so thank you so much.

STEPHAN GUYENET: Thank you Danny, good to be on the show.

DANNY LENNON: And so that was Stephan Guyenet, the show notes to this episode are going to be over at [Sigma.nutrition.com/episode166](http://Sigma.nutrition.com/episode166). And they are you'll be able to get a transcript to all the episodes you'll be able to find a list of related links, details of Stephan's new book, some things on his background, et cetera, et cetera. And anything related to this particular episode. And of course remember that those of you interested in the Mac - Nutrition Uni-course if you just go to [Sigmanutrition.com/MNU](http://Sigmanutrition.com/MNU) then you will be able to find details of that. And actually on a related note I'm going to be going to the one day Mac-Nutrition conference which is being held on the 11th of March in left brought in Loughborough in the U.K. So if any of you guys listening are going to that conference then make sure you come and say hi if you see me there. It would be good to come to meet you out there for any of you that are attending. And for those you who are maybe

thinking of going or just hearing about it now then I'll put a link to the conference on the on the page that I just mentioned to you.

So just go to [sigmanutrition.com/MNU](http://sigmanutrition.com/MNU) and under the course details I'll put a link to the – the conference as well for anyone's who's interested in – in going. So, that's going to be on the 11th of March and that like I said if you do end up going make sure to let me know and do come and say hello if you see me there. So that is it for this week, over the coming weeks we're going to have another run of big episodes which as you probably seen from February has been quite the run so far in terms of guests and topics that are being on the show. And one of those previous episodes with Dr. Dominic D'Agostino is going to be the subject of a kind of response episode so to speak. So Chad Macias who is from The Institute for Human Kinetics as well as being a post-grad in oncology is going to be on the show to discuss some points of contention that he and many others have with some of the views and I suppose interpretations of the research being put out by add Dominic D'Agostino and others from that research group in University of South Florida as well as kind of related labs who do work in a similar area related to cancer therapies or -- or cancer biology.

And so Chad is going to be on to discuss some of those points contention and where he kind of disagrees on that so again it will be a nice way to have some balance to this discussion. And unrelated to that Dominic D'Agostino himself will be back to talk specifically about traumatic brain injury and related to some of the interesting research in that field as well so they're all coming out soon over the next few weeks. We will also have episodes with a team discussion here from the Sigma coaches. We're going to be talking with Adam Ali from Physiomics and some other cool stuff along the way. So that is pretty much it, I will leave you with that and make sure you hit subscribe on your podcast app so that you don't miss anything. Take care.

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