Episode 68: Stephan Guyenet

Hosted By: Danny Lennon
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Danny Lennon: Hello and welcome. My name is Danny Lennon and you are listening to Sigma Nutrition Radio. This is the show that is all about getting you the information you need in your pursuit of manipulating body composition, achieving for normal performance or becoming a truly elite level evidence-based coach. Whatever your motivation here you can acquire some invaluable tools from world-class experts in nutrition, sports science and health as they breakdown the latest science and explain how they apply it.

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So here we are at episode 68 and today I'm to be chatting with Dr Stephan Guyenet who is a world-class obesity research. He's a neurobiologist and he is also in the process right now of writing a book which I just know is going to be phenomenal and its due out for at least sometime next year. For those of you who don't know about Stephan Guyenet's work, he's just a phenomenal writer. He's one of the people I have so much respect for. You've probably seen me linking to a lot of his stuff. He blogs over at WholeHealthSource.org and just an amazing amount of objective in-depth commentary on a lot of the research to come out and his background again is just quite impressive. He has his BS in biochemistry, that was from the University of Virginia and then went on to the University of Washington where he did a PhD in neurobiology; and a lot of the topic we're going to dive into today are related to essentially what regulates us to eat or to overeat and how we can try and combat that. There are also things around once we have lost a certain amount of fat mass how do we prevent the weight regain that often happens? And again, looking at this more from a metabolic adaptation and neurobiological perspectives. So really, really fascinating stuff and with that let's just dive straight into today's show and remember all the stuff we discuss here as well as any kind of studies or researchers that we mentioned throughout the episode will be linked up in the show notes and there over @Sigmanutrition.com/episode 68. So if you go there you'll have the full list of links that we mentioned and a bit more about Stephan's background. So let's add jump into episode 68.

Hey Stephan welcome to show. How you doing today?

Stephan Guyenet: Good, good to be here Danny.

Danny Lennon: Yes thanks so much for taking the time to come on. I'm really excited about this one because as most people who follow that the blog and the podcast will know I've linked your stuff many times because I think it's one of the best resources at the moment. So hopefully we can dig deeper into some of the issues that you readily talk about on the blog but first let's start may be by just diving into a bit of your background for those who aren't as familiar in terms of how you kind of got involved with the academic fields you're in now and then the main focus of your current research.

Stephan Guyenet: Yeah so I've always been really interested in science, even when I was a little kid I use to poke around in the backyard and get my hands on textbooks and things. I've always really enjoyed learning about the natural world when I got to high school I became fascinated with the brain and I decided that I wanted to eventually be a neuroscience researcher.

The brain is what makes us who we are a think in many ways and it's also probably the main... probably the largest remaining frontier in the biological sciences I would say. And so when I went to university I studied biochemistry with the idea that that would form a basis for then going into neurobiology and having a really good understanding of kind of the fundamental molecular principles that drive neurobiology. And so I went to University Washington for neurobiology, I did my PhD studying neurodegenerative disease and particularly a rare disease called SEA7 and I had actually just published a paper on that and that's from my thesis work more than six years ago. That kind of just shows you how slow science can work.

Danny Lennon: Exactly that is fascinating actually yeah.

Stephan Guyenet: Yeah so I kind of during that time started to feel like the research I was doing wasn't as applicable to human health and well-being as I wish it would be. I mean certainly it was applicable to a very small patient population but I felt like there was a larger, there were larger impacts that I could have if I studied something more common. And you know people say in science a lot basic researchers and things they say well, you never know what you're going to discover, you never know what your discovery will be relevant to and that's always...that's true but then again you know if you're interested in a particular disease you might as well study that disease instead of studying something else.

So I became really fascinated with obesity in particular but also just kind of lifestyle disorders and this all, a lot of this emerged from a growing understanding of ancestral diet and lifestyle patterns and ancestral health patterns. Once I became introduced to the work of Western price and some others, I kind of realized that, okay the chronic diseases that we're suffering from today, the obesity and many of these other things are really sapping our vitality, our quality-of-life, our lifespan and frankly our wallets are things that don't happen very much in traditionally living cultures and are things that probably never happened much in human history up until very recently. And I think that's a pretty powerful conclusion to come to because then it really sets your mind straight about wow these things are really preventable. There almost completely preventable and that's not to say that ancestral culture didn't have their own problems. I always like to acknowledge their main lifespan were shorter, they had infectious

diseases, they had parasites, they had warfare, homicide, you know they had a lot of things that we don't have today and that we're glad to not have today but in specifically in terms of chronic disease risk they were much better off.

So anyway, I got interested in that and particularly obesity because I think obesity is really kind of, you know if you had to really put your finger on one thing that was driving a lot of our ill health in the in the world today I think it would be obesity. And so I wanted to understand the mechanisms of obesity. I wanted to get beyond the kind superficial view which is just that people are making these conscious, deliberative decisions to put too much food into their mouths or to not move enough. That never really seemed very satisfying to me and knowing that a lot of what happens in our brain is non conscious, you know things happening outside of our conscious awareness and knowing that a lot of things about the body are regulated. I was really interested to learn more about what other processes in the brain were affecting food intake and body fatness. And so I went to work with Mike Schwartz at the University of Washington and studied body fat regulation by the brain and we were studying the hypothalamus in particularly a piece of the hypothalamus, called the arcuate nucleus which is involved in this negative feedback loop that regulates body fatness and it was really fascinating research and I had a productive four years there and my post op there ended at the end of 2013 and since then I've been working on a book actually.

Danny Lennon: Very cool. Yes that's...I think a few things there that are really important to shape especially when people see a lot of your content putting out. You can see some of that coming through. And I think a big thing that you talked about is the kind of ancestral approach, like so often people think it has to be either looking at it from an ancestral point of view or using modern research, modern science or modern medicine and really I think medicine in general right now just makes a ton more sense when you use that framework of evolutionary biology. I think a lot can be gained from kind of bringing the two together like that. So I think that's huge.

Stephan Guyenet: Yeah I agree.

Danny Lennon: On your research that you've been doing I think. I would really want to dig into some of the stuff you just talked about there. Something like the homeostatic controls because I think it was, I was washing a presentation of yours online maybe a year ago now at this stage and it was really fascinating. It was on this model you had laid out that was really well put together for your homeostatic eating and essentially there was this interplay between satiety system, energy homeostasis system, hedonic system, all this sort of stuff and then in turn this influences food intake and is it perfectly captured the complex nature of all these homeostatic controls going on. So let's dive into some of that stuff but first maybe we should start just by clarifying for people the difference between your homeostatic eating and non-homeostatic eating.

Stephan Guyenet: Yes sure. I think that's...I'm glad you brought that up; I think it's a really important distinction. So essentially you know as many things in the body your food intake is

regulated. So your body has kind of like an optimal window of quantity of food that it wants you to get you in the range of each day just to fill all your regular energy needs. So you know just like in our thermostat will kind of regularly your air-conditioning heating to try to keep your body temperature in the right zone the brain tries to regulate your energy intake and your energy expenditure to keep your energy stores inside your body in the right zone because there is kind of an optimum zone. Too little and your at the risk of starvation and your body processes start to shutdown too much and you're going to lose your ability to forage or escape from predators or fight if you need to or whatever. It's going to reduce your fitness on either end, your reproductive fitness.

So basically homeostatic eating is eating in response to a perceived energy need by the brain. So the brain thinks you need energy and it makes you hungry, it makes you more interested in food. So that can occur due to the activation of either of those systems that you mentioned which is one of them is a short-term system, the satiety system and then there is a long-term system called the energy homeostasis system that regulates body fatness specifically. So ultimately food intake regulation occurs at the level of the meal. It's like how much food are you going to eat at this meal or are you can eat this meal at all. And so you have ground breaking communication that happens as your eating food goes down into your gut and you have sensors in your gut that very specifically detects protein, carbohydrate, fat sensors. In your stomach detects stomach distension, all that information goes back up to your brain mostly by the vagus nerve and then that tells your brain stem that there's a bunch food in your gut and that you don't need to eat anymore because you have enough. And so that process is modulated, it's tweaked by this long-term system which measures the amount of body fat that you have. So that is communication between your fat mass hypothalamus.

So hypothalamus is a part of your brain that's on kind of the bottom of your brain right about the pituitary. So the more fat that you have, the more of this hormone leptin in you produce, hypothalamus hears that and it says okay we've either got enough of that or if we don't have enough fat it talks to your brain stem and it says alright it's going to take you more food to feel full at this meal. So you might have to eat if your body fat stores were low because you haven't been eating enough lately or you've been exercising a lot. Your hypothalamus says well you're going to need to eat 50% more at each meal for the next week until you know to feel like your hunger has been satisfied. So that's hypothalamus eating and that's your body just trying to maintain energy stores and it makes a lot of sense but one thing I'll mention as a little asterisk on this is if you'll note I said that the brain is regulating based on perceived energy needed.

So it's not necessarily that your body needs energy is that your brain thinks you need energy and that process of whether or not that your brain can be tricked basically. You know obese people get hungry just like anyone else even though they have several times more fat than a lean person. They don't need additional fat; they don't even need to maintain their fat storage but their brain believes that they need to maintain fat stores and it will make them hungry if they don't eat. So that's a process of kind of re-regulation of that defended level of fat mass and that's what we studied in our lab. I mean we can get back to that but first I want to get to

non homeostatic eating. Non homeostatic eating is very simply is eating for reasons other than energy needs. So whereas with homeostatic eating it's basically like okay I'm hungry I'm going to eat. Non homeostatic eating is like hey I'm at this party and there is a table with crackers and cheese in front of me and I just had dinner but everyone is eating and I just kind of want to eat it or it tastes really good or I'm drinking a beer. I'm not hungry, I'm not thirsty but I like this alcohol, it's making me feel relaxed, I like alcohol, I'm going to drink this 150 calories of beer. There are many, many reasons. You can eat because you're stressed, you can eat because of out of habit. Its noon, its lunchtime and I always eat at lunchtime. I'm not hungry but I'm going to eat anyway because it's lunchtime. There's many, many reasons why you would eat that don't have anything to do with energy need and I think in many cases that's where we get into trouble because I mean energy homeostasis tries to balance the energy level in your body but if you're constantly eating for reasons other than energy need your going to be pushing, you're going to be pushing more energy into your body than it's really asking for and so you're going to be... either you're going to gain weight if your brain is set up so that it doesn't defend your body fatness very well and you're going to gain weight or if your luck you're not going to gain weight if you're just very resistant to fat gain.

Danny Lennon: Yeah I think that's a super important point because you just mention that energy homeostasis system so if we have an energy homeostasis that would lead someone to conclude well then how is it actually possible to become overweight or obese if you have these controls in place but then again you just talked about how we can almost bypass this through non-homeostatic eating. So of course fat gain is 100% predicated on someone being in a chloric surplus and we totally accept that but the issue is rather than just saying that the civil chloric surplus is the cause then of that fact gain we have to ask what is causing the overconsumption right? And I think this is something you've talked about getting this done route cause what drives overconsumption and really when we're talking about the overconsumption that is non homeostatic eating really. So what are the key things that drive this? I know you said there are tons of different factors and maybe could mention a few. Is it purely a result of the environment we now find our self in or is it down to physiology or is it some sort combination?

Stephan Guyenet: I think it's a combination and overeating can be driven by homeostatic factors. For example when a person becomes obese... so just to kind of set the stage here and obese person requires approximately 20% more calories per day than a lean person to maintain weight. If given the same height gender physical activity level, if you control for those important things each person requires about 20% more calories to maintain weight. It's not a lot of calories. I mean 20% more or less food on a plate is not an extreme amount of food like you may not even notice that you're eating 20% more. People around you may notice what might just be the difference of an extra snack you now. Anyway the point is that they have to eat more to maintain their weight and they do eat more. Obese people are driven to eat more by a homeostatic system that is re-regulated to higher level. So for their brain they're not going to be satisfied and I'm speaking in generalities here can differ by individual but in general there not going to be satisfied until they eat a higher number of calories. They're not going to feel full until they eat a higher number of calories than a lean person would. So that's an example of one stat state is established. It can drive access eating but the other thing is with the satiety

systems, so that's the short term system and the brain stem that regulates your meal intake or the size of the meals. That system can be tricked a little bit as well, so it not only responds to the calories but also to the calorie density to the fiber content into the palatability of the food your eating. So the higher the calorie density the less satiety you're going to experience per calorie and it's a major effect. Oh yeah proteins is another one I forgot to mention.

So the higher calorie density the lower the protein, the lower of the fiber and the higher the palatability. The less satiety you're going to experience per calorie and we're talking about if look at the foods that fulfill those criteria its junk food. It's all junk food. It's pizza, it's ice cream, it's chips. Those are the things that when you eat them they just don't trigger per unit calorie. They don't trigger the same level of fullness in your brain because of how those calories are sensed once they go down into your stomach and the digestive tract.

So those are the ways you can overeat with homeostatic mechanisms but I would say that a lot of the overeating we do is non homeostatic. And I think I've come to believe over the course of working on this book that the personal economics of the food environment and the personal economics at eating play a major, major role in how much food we eat. So basically if you look at hunter gatherer cultures, you can... it's really amazing. I mean you talk these entomologists. They have literally developed mathematical formulas that will predict what resources hunter gatherers will pursue in their environment and they are really simple formulas. So if you know the energy yield of a food resource and you know how much time it takes to get that food resource, you can basically calculate whether or not hunter gatherers are going to be interested in it. What they care about is how many calories does it contain, how many calories do I have to spend to get it and how much time is it going to take me get it. So it's their food choices are very much focused on calorie content because that's the main thing about food that gives them alive and well. Like we now have the luxury of thinking about all these other things vitamins and micro nutrients and fiber and stuff. Hunter gatherers are really concerned about how am I going to shove coal into this into this locomotive in my body? And the micro nutrients follow. That's the thing is there eating all natural foods so it doesn't mean those things aren't important but that's not what they're thinking about.

You think about, you look at these hunter gatherer cultures, they're not starving. You know most hunter gatherers don't really...starvation is not a major threat in terms of dying of starvation. There are instances of that happening but especially with the tropical cultures there not usually dying of starvation but at the same time the availability of food does influence their reproductive rates and it influences mortality in childhood due to infectious diseases. So if you're not quite as well fed your immune system isn't going to fire on all cylinders and you're going to be more susceptible to these deadly diseases that kill like a third of hunter gatherer infants. Half of hunter gatherers don't even make it to adulthood mostly due to digestive and respiratory diseases. If your immune system is not working right you are...you are not going to make it and so food has a lot to do with that. Just having enough calories has a lot to do with that. So even though they're not starring the amount of food they can get plays a huge role in the reproductive success and what that means is that over revolutionary time it's been selected for, basically calories seeking behaviors have been strongly selected for it and you see this in

the physiological biochemical and neurobiological make-up of the human body and the body of any animal. Basically we are hardwired and it's not just food, we're hardwired to look for deals basically like how can I get this food that has a lot of calories for not much work and for not much time and for not much money? The same way that we talk about you know how can I get paid the most for the least amount of work or you know how can I get the best deal on amazon.com or whatever it is you know.

Danny Lennon: Yes like this constant cost benefit analysis going on.

Stephan Guyenet: Yeah, everything we do is a cost benefit analysis. A lot of what our brain does is basically try to predict the value of future outcomes and choose the best course of action and so we're deeply, deeply hardwired to be economic calculators to try to always get the best deal and we do that with food and we do that with everything. So what that means is if the benefits of the food are very, very high into your brain what constitutes a benefit is that it has live calories, tastes really good and if the costs are low, if it doesn't cost you much in effort, doesn't cost too much in time, doesn't cost too much in your money or risk or whatever all the other downsides are your going to be more likely go for it. And you look at hunter gatherers basically not only is their food like pattern predicted by this formula. The quantity that they eat is predicted by the formula. So if they come across a windfall, the surplus of food that is really easy to get and has a lot of calories they just gorge. I mean it's like ridiculous, like these anthropologists I was talking about. I mean these people chug honey like liters of honey. They eat pounds and pounds of meat especially if it's fatty. It's like they eat amounts of food that would make your jaw drop when it's easy to get and its calorie dense.

So I mean basically... we don't want to go quite to that extent today or at least most of us don't but we still respond in the same way to those principles. So if you have a doughnut in front of you you're going to be more likely to eat a doughnut than if you have to walk across the street and go to the donut shop and pay couple bucks for that doughnut. And this has been tested many different ways and basically if the food is easy and cheap and calorie dense we eat more and I think it really boils down to that, to those economics.

Danny Lennon: Yea I think that's fastening because again going back to this cost benefit analysis we're hardwired to look for these more energy dense foods and then we have this trade-off that revolution would have evolved with but now these days there is no real cost most of the time for most of us like the availability is never an issue. It's fairly cheap to get some, to get a lot of calories for a low amount of money as well and it's at every corner of the street. So that kind of cost has gone all the way down and then it's so much more easy to consume. I think that it was a really good point.

Stephan Guyenet: Yeah, that's absolutely right and you know one of the most interesting people I spoke to on this was Brian Wood. He's a guy is whose been studying the Hadza of the fur for a long time. I think 10 years. Hadza are a hunter gatherer group in Tanzania probably, they really in terms of relevance to our own African ancestors probably the most interesting hunter gatherer group we have at this point and he has applied this formula I was talking about

the optimal foraging theory equation. He's in the process of doing some research to see basically how the value food has changed in the modern environment and you know I think it's obvious from what you said and just common sense that it's the effort cost has gone way down. Every cost is almost a zero and you have basically the food industry plays to human nature. They try to fulfill consumer demand and consumers demand stuff that is easy. It demands food that is easy and so you get things like lunchables where it's got like little crackers and things you can throw. You just buy this thing and you throw it in your kid's lunch box and you don't have to prepare lunch. Pop tarts, things that require any effort, restaurants and then the cost of food has gone way down. So we pay less than half. We pay less than half of the quantity of our disposable income here in the US that we did 70 or 80 years ago on food. So the cost of food has dropped by more than half here in the US over in less than a century.

Danny Lennon: That kind of leads me into something I did want to get to around food choices or a broader kind of idea of food quality because like we alluded to earlier that body weight changes are of course determined by energy imbalance either in whatever direction depending on the change and then that might lead some people who kind of make these like straw man arguments to jump to the assertion that well food quality doesn't really matter at all. Purity if talking about say body composition and like we've seen this, we've seen like the now infamous Twinkie diet where as long as you control calories you can lose weight and that's completely true. That's like maintaining the laws of energy balance but as we've mentioned... you talked about a couple of things there Stephan around like hyper palatability of foods and we've talked about the food rewards centre. So they are obviously heavily, heavily influenced by the food choices we make independent of the caloric value of those foods. So how far do we take this when we're considering food choices? Like for most people just how important is food quality in successful long-term weight management?

Stephan Guyenet: I think it's you know food quality in combination with the food environment I think is really where it's at. I think that's number one and what it boils down to really is well first of all what you said that food quality impacts quantity and has a very strong impact on the quantity of calories that you absorb into your body that you can absorb so to a large extent quantity follows quality but also I mean really I think what it boils down to is that balancing and counting calories is not intuitive. It's not the way we normally interact with food. The way that we intuitively interact with food is we eat food when we want food and we stop eating food when we don't want it anymore. You know the qualitative side of it, of counting the calories and balancing, that stuff is all done by our brain naturally on an unconscious level and or on an unconscious level and again I always say this, I don't knock people who want to count calories. I think you know there are a lot of different ways to get where you're trying to go and some people have found that that's useful for them and that's great if someone does it. You know it does work if you can actually do it, it works but I think the problem with it is that it's very difficult to do accurately. Even professional dietitians have a hard time getting within 10% of their actual calorie intake and 10%, that's the difference between a lean person and an overweight person in terms of the amount of energy their eating and as I said before 20% is the difference between a lean person and an obese person. So you imagine professional dietitians are off by 10 or more percent, how much is the average person going to be off by who's not a

professional dietician. So it's difficult to get that degree of accuracy and it's as I said, it's not the way that we normally interact with food and I think that what most people want, what I want and I believe what most people want is to have an easy natural way of interacting with food. They don't want to have to over think every bite of every meal and they don't want to have to exert willpower to stop themselves from eating that bite that they want to eat.

So if you can design your food environment and the actual ingredients that you're using in a way where your behavior naturally leads to just eating that food and feeling satisfied naturally leads to an appropriate weight. I think that's the ideal way to do it and I believe that is something that is accessible to most people, although you know I don't want to say everyone because I think we're all dealt a different deck of cards and we're all dealt a different hand in terms of our genetics and our background and all that, but I think that's an approach that most people are going to find more sustainable, more satisfying than the quantitative approach of counting calories.

Danny Lennon: Yeah, completely agree because like if you take example of again an extreme example of someone asking well if I have just all my diet on highly refined processed foods but I keep them under certain calorie level will I start losing body weight and like technically yes you will but then issue then becomes then just as you've touched on that if you're going to go that route you have two count calories, you will have to probably resort to being more hungry and less satiated than otherwise and you can't go down into the eating room and I think that's huge when we're looking at the long-term prospective of this. So that actually kind of brings me to something around...we're getting round the idea of body fat regulation and I think it's useful maybe for a minute just to trace it back to what actually regulates thing at the level of the cell because personally I think a lot of the confusion that's out there around nutrition right now stems from either a lack of understanding but probably more so even people who have a really good understanding but they go too far and zero in on like one specific action of one specific mechanism at one point in time and that leads to like to illogical conclusions and I think that the most obvious example of this right now is probably around insulin is a fat storage hormone therefore just keep it constantly low and you lose more fat. This kind of metabolic advantage for a low-carb diet and such which is evidently probably not the case. So do you think there is a big issue there with people like zeroing in on what one of those aspects of body fat regulation and then if so what is the kind of even like...obviously it's a big detailed area but there kind of any cliff notes things that we can keep in mind when trying to look at this stuff?

Stephan Guyenet: Well I think the point you're making is spot on. I think that people...if I can boil it down to the essential problem as I see it, it's people focusing too much on mechanism and not enough on empirical data because I mean the human body is incredibly complicated place and there are millions and millions of research studies out there on many different aspects of the function of the human body and I mean you can go through and find a mechanism that sounds awesome. I mean there are tons of mechanisms that sound awesome and you can construct a story and say hey you this process really looks like it should be impacting cardiovascular disease or obesity or whatever. This makes so much sense with the way this mechanism works but then when you look at the empirical data, when you look at data

where people have actually manipulated those processes and measured body fat and really dug down deep into not just what the mechanism is but what impact the mechanism has directly on your process of interest. Then oftentimes those mechanisms proved to be unimportant or you know maybe there one player in a more complex system. And I think that people in terms of right general audience science writing coherence is king.

So if you can make one point and build up a big story with these different points that all seem to converge on it that's a very effective way of convincing people that your write. That this thing is important but often that requires ignoring a lot of other complicating details or interpreting evidence in a way that creates coherence where there may not actually be coherence and it's a very convincing way to put together an argument because the human brain responds strongly to coherence but often in the natural world it is simply more complicated than that.

Danny Lennon: Just on a couple of recent episodes people have heard us talking about some of the metabolic adaptations that accompany weight loss and leptin obviously being a major role in that. So I would just love to get your thoughts on this because people have heard about the actual leptin and the role of the hyperthalamus, etc. So what do you feel these adaptations mean for someone who has lost weight already and do we have any well understood strategies that at least might mitigate the potential for these metabolic adaptations to drive weight regain because like that's clearly the biggest problem for most diets right?

Stephan Guyenet: Yeah, yeah I agree. Well to just really briefly explain for people who might not be familiar with this. I talked a little bit about that feedback loop between fat mass and hypothalamus in the brain. Hypothalamus listens to the level of leptin in the blood, tells it how much fat you have. When the fat goes down the leptin goes down and your hypothalamus essentially initiates a starvation response. So the hypothalamus's in control of basically all of the major energy consuming processes of the body and it also is to a large extent in control of your food seeking behavior and so it tries to bring the fat back and it activates a whole suite of responses that are designed both to increase your food intake and to decrease the amount of energy that's leaving your body. And so basically the more your fat drops, the more your level of fat drops, the harder your hypothalamus works to try to get the fat back and the more of these responses it activates to try to restore balance. So that's how it works in theory, at least that's the kind of typical, canonical view of it, and that's true. To a large extent that's true and you come across a lot of people who have lost a lot of weight and they feel cold, they feel sluggish, there hungry all the time and that's normal. That's the brain trying to get fat back. Its shutdown there, not shutdown but reduced their thyroid hormone signaling to reduce their sympathetic nervous system activity, increased their muscular efficiencies so that there burning fewer calories per contraction. It's activated their hunger centers; it has activated their food rewards centers. Basically anything you can do to get that energy balance restored and has, like I said has a lot to do with leptin and reliable has done some awesome research on this where he makes people lose weight and then he replaces their leptin levels through leptin injections to the pre-weight loss level. All of that stuff I was talking about is normalized. Like people don't

have brain responses when you put in an FMRI machine and look at their brain, they're not having these excessive responses to palpable food anymore.

Their thyroid hormone normalizes, their sympathetic nervous system normalizes. It's just like this response very much depends on leptin according to his research. Okay so now to get to the more practical question which I kind of what can we do about this because as you said this is a really big question. This is a really big issue. For most people it's easier to lose weight than it is to maintain that weight loss. You look in the studies and people will gradually regain their weight over the course of you know a few years and that's the main reason why it's weight losses considered to not be very effective. At least you know typical dietary and exercise weight loss strategies. So I mean the question is how can you affect this homeostatic mechanism? And I believe there are ways that we can affect it to make it support your goals rather than fight against your goals and you know when it's working with you then that means that your intuitive eating is helping your goals and that you are naturally going to be gravitating toward the weight that you want as opposed to your cognitive deliberative willpower mind having to fight your intuitive mind which is what often happens.

So one of the things that I think has a big impact is protein. So we know that high-protein diets can mitigate many of these responses I was talking about that the brain activates in response to weight loss. So the reduction on energy expenditure that you see the increase in hunger, that you see those things are both mitigated with high protein diets and we know that amino acids have effects on the brain on the hypothalamus that could plausibly account for this this effect. So I think high-protein is one way to help maintain leaner weight and physical activity is something that's repeatedly and studied to help maintain weight loss. It's one of the best tools for weight loss maintenance even though it might not be one of the best tools for weight loss to begin with. Not seeing its ineffective but most studies show it to not be highly effective tool for weight loss to begin with. I think diet quality makes a big difference and some of that relates to the protein.

I think some of it relates to the palatability and the fibre but basically my research has shown in rodents that you can take obese rodents. We make them obese on these refined calorie dense high-fat diets. You can put them back on regular healthy rodent chow which is unrefined high-fibre lower calorie density and they just lose the weight and they start eating a normal mount again. It's like there homeostatic mechanisms just re-regulate and this has been shown over and over again that the level of body fat that animals defend depends to a large extent on the type of food that they're eating. So basically the level of food intake that they will intuitively eat and the level of body fat that they will intuitively settle at depends to a very large extent on food quality and there is not as much evidence in humans on that but I would be pretty surprised if that wasn't true in humans and you see this all the time. I mean people, they go on a new diet, they're not...sometimes their thinking about calories, portion size, often they are not. You know you see people going on low-carb diets or paleo diets and their like oh calories are BS because I didn't think about calories I just ate my food and I lost weight and that's true but if you measure their calorie intake they are eating less calories, it's just that that' the

number of calories that their brain is intuitively telling them to eat in the context of the food choices and the food environment that they have selected.

So I think that's really important and I think what that suggests and I believe based on a lot of indirect evidence that the way that your hypothalamus defends your body fat level is modifiable, it's plastic so depending on the type of food your giving your body depending on the food environment probably, your hypothalamus can defend different levels of body fatness against changes. So you will intuitively gravitate toward different levels of body fatness depending on what you're introducing into your body and into your food environment.

And so I mention the fiber thing now is kind of a shout out to the microbiota. Microbiotas is really hot right now and frankly there is not a whole lot of evidence in humans that it has a large impact on body weight but given the animal research I think that there certainly is high potential for that to be important and I think we're going to know more about that coming up but I think certainly it's a good idea to feed the little microorganisms, a variety of fermentable fiber's which means whole plant foods basically. I think sleep and circadian rhythm is also important. We've seen very consistent strong associations coming out of observational studies where people who don't sleep enough tend to gain more weight and I mean I think one could question those whether that reflects causality but it has been very consistent and we're having an increasing number of randomized controlled trials coming out that are supporting those conclusions. One of the ones that I thought was really interesting; they found that people who aren't sleeping enough and who go on a diet tend to lose weight as lean mass more than fat mass. Whereas people who are sleeping enough tend to lose fat mass and less as lean mass. So I think there are things going on there and more and more research is suggesting that those little parts of the brain that regulate circadian rhythm like the suprachiasmatic nucleus have connections with the hypothalamus and the brain stem and those things affect each other. And when you're not giving your body, you know I would argue evolutionarily appropriate circadian stimulus that probably can have downstream effects that effect possibly some homeostatic regulation but it also affects I'll mention non-homeostatic factors. So Dan Pardi has done some research on this that is interesting and his work and other people's work shows that when people haven't slept enough they just make poor decisions. When you're not rested its common sense when you're not rested you don't have the mental capacity to exert cognitive deliberative control over decisions and so you're going to act impulsively. It's like I want to eat that doughnut, I'm going to eat that doughnut, right now because I want it right now. As opposed to okay well wait a minute what's going to happen if I eat that doughnut? Maybe I'll feel like crap in 15 minutes, maybe I'll gain a little bit of weight, maybe this is not consistent with my goals of leanness and health of how I want to feel, of how I want to look of what my desired disease risk is down the road. Those are the kinds of things that are of the kind of like an effortful decision-making processes that require your brain to have enough to be fueled up. If your depleted because you didn't sleep enough or you've been working all day or you've been making important decisions all day, you don't that reserve capacity to make constructive decisions about things that involve your long-term abstract interests such as body weight and health. So those are just some factors to think about.

Danny Lennon: Yeah I think that was a brilliant breakdown of so much in there and I actually had Dan on the podcast before and I think a few things around his research that I think was really fascinating that actually just linked to something you said earlier that's a sparked of was I think when he was looking at the impact of poor sleep on people's food intake. One really interesting thing that he did I believe on one of his studies that others hadn't done was he based on what people perceived as healthy food as opposed to judging on what the researchers thought as because everyone has this kind of subjective thing and I think and again it goes back to earlier you were saying its people's perception of things that changes and I think that was huge and then the second thing around physical activity it's actually interesting because I was talking...I think it was episode 65 recently and we got into this again leptin and action hypothalamus and we see that physical activity... you will of course know more than me on this.

I think it was the increase in either interleukin-6 or interleukin-10 I can't remember which one in this particular paper that I was reading. The increase in that from regular training actually increased leptin sensitivity in the hypothalamus. So and again you start to see all this stuff start to feedback and how everything is integrated, it's just so fascinating.

Stephan Guyenet: Right, that's right. Yeah I think the exercise thing... I think exercises may be more valuable for weight control than some people realize and I think a lot of it relates to prevention. Maintaining leptin sensitivity of the hypothalamus and allowing your body to kind of absorb calorie excesses a little bit more effectively but yes so the muscle produces IL-6 and that goes into the hypothalamus and I think there might have been an IL-10 in there somewhere like it causes IL-10 to be released but the signal from the muscle to the hypothalamus that's been explored is IL-6.

Danny Lennon: Yeah and potential that is why we see that exercise being so effective for any weight loss that someone has had keeping that from regaining as opposed to this being the primary driver of the weight loss is probably because once they lose all that weight we know they have this big massive drop in leptin so they'll not be able to get back up to that same level I'm guessing because they want me to put on that same amount of fat mass but if they can increase their sensitivity then maybe they can get better kind of communication there even on this reduced amount of leptin.

Stephan Guyenet: Yeah I mean it makes a lot of sense and you know it's something that we're going to need to explorer experimentally but at least on a theoretical level that makes a lot of sense too.

Danny Lennon: Stephan this has been amazing so far. Before I get to the final question because I know we're running time here. I'd love for you to tell people where they can find more of your work either through the blog, also any information about that the book would be awesome and I know you developed that idea weight program along with Dan as well. So we can talk about that as well.

Stephan Guyenet: Yeah so my primary blog is wholehelpsource.org and I'm currently in the process of rolling out a new website. It's not really ready for prime time yet but it will be at our www.stephanguyenet.com So that's my name stephanguyenet.com Like I said its not quite ready yet but if you want a laugh you can go over there and see what it looks like in its incomplete state. Then I'm working on this book, so I have a tentative title, the book is called "The Hungry Brain" and it's going to be published through flatiron press which is a division of McMillan and I'm really, really excited about it. My editor told me that I can start telling people what the title is and tell them a little bit about it but it's going to be in 2016 for sure and I would say that optimistic release date would be about mid 2016. So it's going to be a while yet. It's mostly written but there is a lot of stuff that has to happen between now and then.

I didn't quite realize when I got myself into this how long the publishing process takes but I mean when you're trying to make something that is really top-notch and is going to make a big impact I think you know it makes sense to take the time to do it as well is you can. So I will have the professional illustrator and I'll have a couple different editors working on it but I'm really excited about this book. I mean it's going to be nothing like any other book that's ever been published on obesity or overeating and there are some books that I've kind of touched on aspects of what I'm going to write about like David Kessler's book "The End of Overeating", Brian Wansink's book "Mindless Eating" but there is no book that has really tried to offer a comprehensive explanation for overeating and weight gain that really focuses on the brain you now and so it's going to be all about the neuroscience of eating behaviour and particularly about this kind of interplay between our intuitive mind and our conscious deliberative mind. So like why is it that we overeat even though we don't want to overeat? Like nobody wants to eat more than they need, nobody wants to gain weight, at least not many people. Nobody wants to get sick because they ate too much but we do it anyway and why is that and it's really like in the process of learning about that. You learn a lot about how the brain works in general and some of the things I'm going to be talking about are just basic, how the brain selects actions. How that process works on a neurobiological level is just so fascinating and it's been really cool for me to talk to all these different top researchers and put this story together. I mean a lot of this stuff has never been published before in any book or on my blog so I'm super excited about it.

Danny Lennon: Yeah I'm excited just hearing about that. I just can't wait for it now.

Stephan Guyenet: Cool! Awesome! And then there is the ideal weight program which you can find on either the link through my current blog or a on the Dan's plan site.

Danny Lennon: Very cool and for everyone listening I will link up to all that stuff in the show notes. So if you just go over to the show notes page you'll be able to click through to all of that stuff that Stephan has just listed for you. So with that we come to the final question of the show and it's simply if you could advise people to do one thing each and every day that would improve their life in some aspect what would that one thing be?

Stephan Guyenet: Wow! Okay, let's see. Alright I'm going to come from a food perspective because my brain is primed on that and that's probably what people are here to hear but I'm

going to say if I could give people one piece of advice I would say control your food environment. Set up your food environment such that the easy choices are the healthy ones and the difficult choices are the unhealthy ones. So don't have food close within reach. Don't have tempting foods visible and if you have anything in your house that you don't really want to eat make it harder or even better don't even have it in your house at all. Even little, little effort barriers like having to open a cabinet or having to open the refrigerator or having to peel a piece of fruit like an orange, even those things that seem trivial are enough to change the economics of food behavior significantly. So use it to your advantage if you're thinking about your weight.

Danny Lennon: Awesome! A great way to end the show and so honestly this been amazing. I really took a lot from that and I'm sure everyone listening did and hopefully we can get you back in the future because there is so much that I didn't get a chance to ask you about we could have got it to at all more nerdy stuff around hypothalamic information. I know you have a few cool papers on that but maybe some point down the road. So thank you so much for your time.

Stephan Guyenet: Absolutely. Alright thanks Danny it's been a pleasure.

Danny Lennon: So there we have it that was episode 68 with Dr Stephan Guyenet. I hope you took as much value from it as I did. Really, really fascinating stuff and it was great to get inside the mind of Dr. Guyenet. So with that again guys let me know how you find the show. I'm loving getting all the emails and Facebook messages and tweets from you guys. It really makes a difference to see what is working. Let me know what you'd like to see on the show, how we can improve who you'd like to get on, anything that's going to make the show better for you more engaging and more valuable. Please let me know. I'm loving the iTunes reviews coming through at the moment guys. For everyone that does that please know that it's noted and I'm reading every single one and I really, really do appreciate that. So thank you guys and I will talk you in the next podcast.