Rationally Speaking #189: Stephan Guyenet on "What causes obesity?"

Julia Galef: Welcome to Rationally Speaking, the podcast where we explore the borderlands between reason and nonsense. I'm your host, Julia Galef, and I'm here with today's guest, Stephan Guyenet.

Stephan is a researcher and a science consultant. His background is in neuroscience. Well, his PhD is in neurobiology. His focus is obesity research, and his recently published book is called *The Hungry Brain*. We're going to be talking today about the science of why people gain weight, why we see obesity rising in the US and elsewhere.

Stephan, welcome to the show.

Stephan Guyenet: Thanks, great to be here.

Julia Galef: I'll admit, before we start talking, that I've been avoiding this topic as a podcast episode for, oh God, a year or two at least. Which is not because I don't think it's interesting or important, it's just so complicated -- and also contentious. And that those things together are a recipe for listeners getting mad at you because you didn't bring up a certain study that was really important, or you didn't challenge a certain factual claim.

I'm sure that's going to happen. But I don't want to avoid all topics in this category forever because of that. So maybe, I should just be clear for you and especially for listeners what my goal is with this episode. I'm not going to be able to cover all of the empirical evidence, Stephan isn't going to be able to either even though he knows far more of it than I do.

What I'm hoping that we can do, is get really clear on what Stephan's leading model is of why people gain weight and where it diverges from other leading hypotheses of weight gain. Then, start to talk about what evidence would help us ambiguate between those theories. Without necessarily being able to actually cover all of the evidence. Does that sound good?

Stephan Guyenet: Mm-hmm.

Julia Galef: Great, all right. Well, then let's jump in. Stephan, what's your overview of why people become obese?

Stephan Guyenet: Yeah. This is a really complex topic and I think we have to find some way to get a toehold on the causal chain before we can start really trying to dissect what the ultimate causes are.

I think one really good way to get a toehold is to just look at it from a thermodynamics perspective which is that you can't accumulate energy in your body unless you have a higher rate of energy entering than the rate of energy that's leaving your body. I think that's a useful starting point,

although certainly not an end point for thinking about how obesity develops. It requires that we are ingesting more calories than we're expending.

I think at that point, you can start thinking about *why* are we ingesting more calories than we're expending. How do we get calories in? We eat food. How do calories leave our body? Metabolic processes, as well as work performed in physical activity and things like that.

I tend to look at things from the perspective of the "energy in" side of the equation, because basically, you can out-eat almost every level of energy expenditure. No matter what your physical activity level is or no matter what your metabolic rate is, it's almost always possible to out-eat that. I tend to think about it as a question of how much are you eating relative to your energy expenditure.

Julia Galef: Well, just on that point -- even though it is *possible* to out-eat, to undermine whatever caloric deficit you built up with exercise, for an obesity researcher trying to study why obesity has gone up over the decades, wouldn't it be more relevant to look at whether the decline in energy expenditure is enough to explain the rise in obesity?

Stephan Guyenet: Yeah, absolutely. There are people who are looking at it from that perspective for sure. I'm not trying to say that energy expenditure is not relevant. But if we look at the history of calorie intake and calorie expenditure in this country, what we see is that, for most of the last hundred years, people have been able to roughly match calorie expenditure with an appropriate calorie intake. If you look at calorie intake a hundred years ago, it was actually pretty high. It was almost as high as it is today, and yet, there was very little obesity.

Presumably, that's because almost everyone was working manual labor jobs, we barely had any automobiles, there weren't washing machines, there weren't automatic dryers. We're doing a lot of things that required physical effort, building things in factories, milking the cows, weeding fields.

What you see over the course of the next 40 or 50 years in the United States is that our calorie intake actually declined. It's what you would expect, in the sense that people were not working up as much of an appetite as things were becoming mechanized and their physical activity expenditure was declining.

Julia Galef: What time period is this roughly?

Stephan Guyenet: When the USDA first started tracking calorie intake was in 1909. That's when calorie intake was relatively high and then, it declined through about the '50s and '60s and then, it started to rise again in the late '70s, early '80s.

Julia Galef: Got it, so energy expenditure and energy intake both started declining in the mid 20th century, and then --

Stephan Guyenet: Yeah, exactly.

Julia Galef: Then, intake started going back up but energy expenditure did not?

Stephan Guyenet: Right. Well, it's not quite that simple but ...

Julia Galef: It never is.

Stephan Guyenet: Yeah, I know. I'm sorry, I'm trying to make this clear but ...

Julia Galef: No, no, it's great. Go on.

Stephan Guyenet: Basically, the point I'm trying to make is that there is a relationship between calorie expenditure and calorie intake that is, under ideal circumstances, is maintained non-consciously by circuits in the brain. There's actually a regulation that's happening that's trying to keep body fatness at the right level. You see this coupling of energy intake and energy expenditure -- and then around 1980, those things decoupled.

By the way, it wasn't quite as sudden as that. It started earlier, but in the 1980s is where it really accelerated. You see this decoupling where calorie intake is increasing fast, and calorie expenditure, at least in terms of people being physically active, is not increasing proportionally. That's when you really get the obesity epidemic.

This is why I tend to focus on calorie intake, is because for any calorie expenditure, there is an appropriate calorie intake. Really, it's when those things decouple, when calorie intake becomes disproportionate to expenditure that you start getting problems with obesity.

This comes back to the question of what is obesity, or what causes obesity. Obesity really has two fundamental characteristics and this is something that's been pointed out by my mentor, Mike Schwartz, at the University of Washington. That is, first of all, it developed due to this imbalance between intake and expenditure -- but the second is that you actually have a change in how the brain regulates body fatness and how the brain regulates the amount of energy that is coming in. Essentially the brain, instead of defending a lean state, it begins to defend an obese state against changes.

Julia Galef: The way that it defends a lean or an obese state is in terms of the appetite? Or just that it gives you an order to eat or to stop eating?

Stephan Guyenet: Yeah, exactly. It activates non-conscious circuits that are going to drive you toward food via hunger and via increased cravings and things like that, in order to maintain that high level body fatness. That's why weight loss is so hard, is that once your brain is defending that high level of body fatness, if you try to lose weight, your brain is like, "No, this is not what I want to do."

Just the same way that a lean person losing weight, they would have increased hunger, increased cravings, et cetera.

Those are the fundamental two characteristics of obesity, is you have this thermodynamic change of energy flux, and you also have this neurobiological change, of defending that higher body fatness. It's not just a state that results from passive overeating. If it were, then you could just eat less and it would be easy to lose weight.

Julia Galef: Wait, so you're saying that a) we're eating more than we used to relative to our expenditure, and b) our brains *want* us to eat more. Are those really separate things or does the first thing just follow from the second?

Stephan Guyenet: Well, okay so I feel like I'm not giving you all the context that you need here.

Julia Galef: Okay, feel free to add more context.

Stephan Guyenet: Basically, we can conceptualize eating behavior in two different ways. There is eating behavior that is due to circuits in the brain that are trying to regulate your energy intake like hunger. Then, there are circuits in your brain that are independent of trying to maintain your energy status, like things that make you crave really delicious foods. You don't eat a big fat slice of chocolate cake at the end of a meal because you're still hungry, there's not like an energy you're trying to fill by eating ice cream or drinking beer or ...

Julia Galef: Right. The thing that we used to say in my house, when me and my brother were kids, was: after we'd said we were too full to finish our dinner and then, could we please have dessert. Our mom would be like, "Well, you said you were full. Why do you want dessert?" We'd say, "Well, my dinner tube is full but my dessert tube is still empty." Then, she would laugh and give us dessert, not because we made a good argument but because it was funny.

Stephan Guyenet: It works.

Julia Galef: Yeah.

Stephan Guyenet: Nice. Yeah, so coming back to this question of what causes obesity, there are a bunch of things that make us eat more relative to our calorie expenditure. We don't have very high calorie expenditures needs in modern society. But there's also something that is changing the way our brains work that causes it to actually defend that obese state and make it very difficult to lose weight.

Just to illustrate that a little further, I think an example that really helps is to talk about The Biggest Loser. A lot of people are familiar with this show. In case any of the listeners aren't: they get people to lose enormous amounts of weight. It's a competition to see who can lose the most, and then, there's this really big money prize at the end.

Researchers had actually followed up on the people who lost these massive amounts of weight, 100+ pounds on The Biggest Loser and they tend to regain most, if not all, of that weight in fairly short order after the show.

That's not really what you would expect if body weight were not regulated. If there was not some change that occurred or some difference in the way that these things are regulated, between someone who's obese and someone who's lean, because they're gaining weight at a much faster rate than you would expect for someone who started off at that lower body weight. Someone who starts off lean and tries to stay lean, it's going to be a lot easier than someone who starts off obese, becomes lean and tries to stay there.

Julia Galef: Why couldn't we just explain that data by saying, well, maybe they started out lean when they were very young. Then, high calorie food was so available that there is just always a temptation to eat more calories than they were burning. So yes, they lost the weight when it was part of this program where there was discipline being imposed. Then when it's over, assuming they just go back to the exact same environment and the exact same behavior they had before, of course, they're going to regain it because they have a surplus. It's just not clear why we need to invoke any kind of "set point."

Stephan Guyenet: Yeah, yeah, sure. I think that what you're saying is probably part of the explanation. Whatever your habits are, or whatever other things like that, are going to be things that it's hard to reset even if there's no set point.

However, there's a lot of evidence independent of that, that there is this regulation of body fat levels that does regulate around a specific preferred level. There's a researcher named Rudy Leibel, for example, who's done a lot of this work. If you take people who are either lean or obese, basically the same either way, and you get them to weight reduce by 10%, you see very profound changes in their physiology and their brain response to food cues. What you'll find is that they will have a decrease in their metabolic rate that is disproportionate to the amount of weight that they lost.

It's not just because their bodies are smaller but there's actually this starvation response that kicks in that actually conserves energy even beyond that, to try to regain the lost fat. That also has neurobiological correlates, where you can put people in an fMRI machine and you see that, basically, all of the brain structures that are responsible for making us crave food light up like a Christmas tree after the weight loss.

Also, you find that when you give them food, the same amount of food is less satiating after they have lost weight. We know a lot about the mechanisms underlying this. This is why I'm so confident about this, is that we actually have a really good picture of how this works.

It relates to a hormone called leptin that's produced by fat tissue and that is a signal to the brain of how much fat is in your body. When a person loses

weight, their leptin goes way down and that's really the key signal to the brain that causes that so-called starvation response that tries to bring the body fat back. The reason we know that that's key signal is that if you replace leptin back up to the pre-weight loss level, you don't get those responses.

Julia Galef: You can just add leptin?

Stephan Guyenet: Yeah, you can just add leptin.

Julia Galef: Whoa, why aren't we all doing that? It just seems like ...

Stephan Guyenet: Yeah, that's a really good question. I think there's a couple of different reasons for that, and one of them is that when leptin was first discovered, it was thought of as this incredible potential miracle weight loss drug. It was very clear that it played a really important role in body fat regulation. There's almost a century of research leading up to the discovery of leptin.

Basically, when you just take people who are overweight or obese and you inject leptin into them, it doesn't really do anything. It doesn't cause them to lose weight. What they figured out is these people already have high-levels of leptin, and increasing those levels further, in other words telling the brain, "Well, actually you have even more fat," doesn't really tell the brain to eat less. The brain is really responsive to decreases of leptin as a starvation signal, but is not really responsive to increases of leptin as an excess signal.

Julia Galef: That's so frustrating.

Stephan Guyenet: I know it's frustrating. You have to think about the evolutionary context of what's the plausible explanation for that. Obesity is just not observed among hunter-gatherers and it's just not an issue. Basically, you have this huge disappointment in the pharmaceutical industry that put leptin on a shelf for a long time, and I'm not sure that it's ever really recovered from that disappointment. I'm not sure if anyone is really looking into it for weight loss maintenance but there's ...

Julia Galef: Ah. Right. It's not about *causing* weight loss, it would be about keeping weight *off*?

Stephan Guyenet: Exactly, you'd have to lose the weight, and then, it would help you stay there. I don't really know if anyone is looking into it but it's certainly a really plausible idea. There's also some practical issues…

Julia Galef: Setting that aside for a minute -- we skipped over this elephant in the room, which is that you started talking about how there's some change to our brains at some point in the mid or later part of the 20th Century, that caused our brains to want to defend higher weights than we had before. So what was the change?

Stephan Guyenet: Yeah, that's a really, really good and really tough question. I don't want to give you the impression that we understand it very well because we don't. There is not really a lot known. We know that if you overeat calories, you'll gain body fat, but that doesn't necessarily increase the defended level of body fat. If you overfeed someone and they gain fat, then you stop overfeeding them, they will lose that fat usually. It doesn't really mimic what we see in actual obesity where people's set point really resets to a higher level like turning up a thermostat.

The research that I did and that Mike Schwartz did, when I was in his lab, and that's ongoing, is looking into one possible mechanism for that. What we found is that there was actually this inflammatory process occurring in the hypothalamus which is the part of the brain that regulates body fat and receives that leptin signal.

It turns out, from other groups as well, that this is part of a generalized stress response that occurs in the hypothalamus of animals that are becoming obese. There's increasing evidence that it actually plays a causal role. If you can prevent that inflammation from happening in the hypothalamus and these other associated stress response changes, you can actually attenuate the fat gain that occurs in experimental models of dietary obesity.

We actually were able to extend that into humans. At least, observationally, using non-invasive MRI techniques, with my colleague, Ellen Schur. She was the one who led that research and she was able to demonstrate that people who have obesity actually have MRI signals in their hypothalamus that look a lot like they are also inflamed. The more signal you have in your hypothalamus that looks like inflammation, the higher your body fat in this level is likely to be.

Again, I want to emphasize that we don't know all the details of how this happens. Another really important part of this that we don't understand yet is what causes that inflammation. That's obviously a key question. I can give some general information, we know that when we put animals or humans on certain types of diets, they tend to gain weight and it also tends to produces this inflammatory response.

Julia Galef: What kinds of diets?

Stephan Guyenet: They tend to be refined, palatable, calorie dense diets.

Julia Galef: By palatable, you mean like tasty?

Stephan Guyenet: Yeah, exactly. Diets that are motivating, that animals will tend to eat a lot of or humans will tend to eat a lot of.

Julia Galef: Are you using motivating and palatable as synonyms, or are those different things?

Stephan Guyenet: Those are different things, and it's actually sometimes tough to talk about with a general audience because the concept ...

Julia Galef: My audience is special! Go ahead, give it a shot.

Stephan Guyenet: All right, so the concept I'm really trying to get at is this concept of *reward* which represents three things: it represents motivation, pleasure and learning, reinforcement learning. Really, the main part of that that I'm referring to is the motivational component. What is your motivational level to eat? Honestly, it doesn't really matter how much you enjoy a food, what matters is what your motivational drive is to eat that food, in terms of the consequences.

Julia Galef: Like, for example, to separate those concepts a bit -- there are some drug addicts who don't actually derive pleasure anymore from the drug that they're taking, but they still crave it strongly. That would be strong motivation, low pleasure, or palatability. Or maybe high reinforcement. Reinforcement is just how much each time of consuming the thing causes you to want it more in the future?

Stephan Guyenet: Yeah, exactly. It still would be strongly reinforcing.

Julia Galef: Got it, just low pleasure.

Stephan Guyenet: Yeah, exactly.

Julia Galef: I think there are some foods that I actually get a lot of pleasure out of but I just never crave, like apples, for example. Every time I end up eating an apple, because there's nothing else around, I'm like, "I forgot how good these are," but I just never want one again in the future.

Stephan Guyenet: Interesting, interesting. Yeah, those things, in everyday life, tend to be fairly closely linked to one another but you can come up with examples where they're not that closely linked.

Julia Galef: Sorry, I sidetracked you, but we were talking about theories of what causes the inflammation that we see in MRIs that is associated with the drive to consume more calories than one is expending.

Stephan Guyenet: That's right.

Julia Galef: Or associated with obesity, maybe, as you were saying.

Stephan Guyenet: Yeah, that would be a better way to put it. We don't really know what causes those things but we do know that certain types of diets cause that, and we don't know exactly what it is in that diet. There are theories. Like some people think it's the saturated fat, some people think it's the lack of fiber that causes changes to the gut, microbiota, but then it has effects on the brain.

Julia Galef: It all goes through the brain, you're saying?

Stephan Guyenet: Yeah, it has to go through the brain, for a couple of different reasons.

First of all, the brain generates all of our behaviors, including our eating behavior. It generates all of our feelings and impulses that influence our eating behavior, as well as our physical activity patterns. It regulates a lot of things about our physiology as well, including our metabolic rate -- not to say it's in complete control, but it influences.

Furthermore, the body fat regulation system that measures your body fat and thus influences appetite and metabolic rate, in order to homeostatically regulate body fatness, is located in the brain. The brain is really very central to all of this.

Julia Galef: Okay. So whatever it is in this diet that is extremely rewarding, and that seems to be associated with inflammation and obesity, that kind of diet started becoming more common in the mid to late part of the 20th Century

Stephan Guyenet: Yeah, because of the uncertainty that we have about the exact mechanisms, I can only really paint this in broad strokes. I still think the broad strokes are really useful. If you look at animal models of obesity, the absolute most fattening thing you can possibly give to a rodent, for example, is to give them a variety of highly palatable human junk foods. Human junk food is insanely fattening to just about any species.

Julia Galef: By fattening, you mean because they're motivated to eat a lot of it, and also, it's high calorie?

Stephan Guyenet: That's a good question. It's definitely related to that, but at least in rodents, I'm not sure that's the full story. You actually see, also, calorie expenditure effects. What I mean by that is, at least, in certain contexts, what you'll see is that they actually burn less energy than they should on those diets. It's not quite that simple in rodents.

Although in humans, you really see a lot of more effects on the energy-in side than on the energy-out side. People who have obesity have a higher level of calorie expenditure, a higher metabolic rate than people who are not obese.

Julia Galef: Just not high enough to make up for the surplus?

Stephan Guyenet: Correct. They have larger bodies that require more energy and therefore, they generally have a higher metabolic rate, when correcting for things like gender and height and that sort of thing.

Julia Galef: How does this model that you've laid out interact with the simplistic “calories in, calories out” model? I know there’s a lot of debate over what causes weight gain and whether the calories in, calories out model is correct. People state it in different ways, but one way people state it is: The only way

you're going to gain weight is if you're consuming more calories than you're burning. And anyone who tells you differently is selling something, basically.

Is this just a specific version of calories in, calories out -- or is it a different thing?

Stephan Guyenet: Yeah, that's right. The idea of calories in, calories out, I think requires defining, because it's used in different ways and different contexts. One of the ways is the way that you just said, which is that the balance between calories in and calories out determines the amount of fat you carry.

Julia Galef: Thermodynamics, basically.

Stephan Guyenet: Yeah, that's almost not different from the First Law of Thermodynamics. That's not in question. Even though some people would debate it that it's not a serious argument.

There is this other idea that some people refer to and that is really that your level of body fatness is determined exclusively or predominantly by voluntary decisions that you make, about how much food you're eating and how much you're exercising. This is the idea that, basically, there's no regulation happening, there's nothing trying to keep you from losing weight and the only thing that's keeping you from losing weight is poor decisions, basically.

Julia Galef: Or willpower, I guess.

Stephan Guyenet: Yeah, willpower, poor voluntary decisions.

There's no doubt that willpower plays a role. If you have a craving to eat something super unhealthy and you can't stop yourself from doing that, of course, that's going to increase your risk of gaining weight.

I think what that version of the calories in, calories out idea misses is that a lot of the things that drive us to eat and that determine our eating behavior are not voluntary conscious processes. Ultimately, we have a conscious gatekeeper over our eating behavior. You can say, "No, I'm not going to eat this."

But when you have impulses arising from non-conscious parts of your brain like hunger and cravings, and those sorts of things telling you to eat, we have a limited capacity to control those things if they're being thrown at us all the time, day after day. Usually, those types of impulses are going to be more influential of people's everyday eating behavior than the conscious, rational "willpower" or whatever, however you want to call those higher-order circuits.

Julia Galef: Maybe a way to distinguish would be to ask you: is there anyone who thinks that you could take people who are obese and put them in a controlled

environment where you're feeding them a controlled diet and they wouldn't gain weight, or they would gain weight very slowly? I'm trying to distinguish between models where the causal arrow that eventually leads to weight gain goes through the node of consuming food, like, calories consumed… Whether we want to call that free will, or us responding to drives that are very difficult or almost impossible to resist. It doesn't really matter.

But, like, "the act of putting food in your body is central to how much weight you gain" versus, on the other hand, theories that there's something about the way our body is *processing* the food that we consume that is maybe more efficient or something like that. That couldn't *possibly* be called a choice because it's just something our body is doing. That is the thing that's causing people to be more likely to be obese now than they were 50 years ago.

Stephan Guyenet: There are differences between individuals in how the body deals with food. There's no doubt about that.

Julia Galef: Yeah, but we're looking for a difference. Presumably, there has always been differences and so, if people are more obese now, then there must have been something that changed, unless the genetics just changed that much over 50 years.

Stephan Guyenet: Basically, the answer has to be either in the calories in side, or in the calories out side, or both.

Julia Galef: But could calories out also involve how efficient your metabolism is?

Stephan Guyenet: Yeah, absolutely. What I'm trying to say is that the difficulty with the calories out argument is that people who have obesity almost invariably have higher calorie expenditure, not a lower calorie expenditure. You can't really explain obesity by saying they have a reduced calorie expenditure because they don't, they have a higher calorie expenditure. The only way you can really explain it thermodynamically is by saying the calorie intake is higher so then, the question becomes why is the calorie intake higher.

Julia Galef: Does that mean that the puzzle of why there's more obesity now than there used to be reduces to the puzzle of why are people consuming more calories than they used to?

Stephan Guyenet: I'm not sure I would quite endorse that statement. I think that, clearly, if all of us were jogging two hours a day and eating the same amount of food as we are right now, there would be less obesity. I don't want to say that there's no role for calorie expenditure but there has been a decoupling of intake from expenditure. Our intake today is, you could say, inappropriate for our level of calorie expenditure. Does that make sense?

Julia Galef: Yes, okay.

Let's talk about other common theories of weight gain that have to do with the *kind* of food that's being eaten. You talked about this a little bit because you compared the super high rewarding modern diet, that has pizza and ice cream sundaes and refined white bread and cookies, and things like that, compared to diets in the past that were less rewarding and maybe somewhat less palatable.

But there's a bunch of other theories of what causes weight gain that get more specific about some calories being good, let's say, and other calories maybe being not so good, or even bad. How does your model differ from those?

Stephan Guyenet: Yeah. As far as we currently know, if you really look at the most tightly controlled studies available in humans, of which there are a number, as far as we currently know, the calorie value of food is the only food property that meaningfully impacts body fatness. There are a number of studies that have varied other things like the carbohydrate to fat ratio, varied things like sugar intake, even varied protein. There are many, many other hypotheses that you could test about how food compositions affects body fatness that haven't been tested yet.

But in terms of the basics like macro-nutrients, it doesn't have any effect. It's independent of calories, is what current evidence suggests. And so we don't really have any evidence, right now, that things other than the calorie value of food impacts that food's effect on your body fat. We do actually have pretty good evidence that the macro-nutrient composition -- that is the fat, carbohydrate and protein composition -- does not affect body fatness independently of calories.

That's not to say that some foods are not more fattening than others -- I think that some are, but I think that relates more to the fact that we tend to eat more calories of some foods than others.

Julia Galef: Right. Yeah, I'm very confused by what people mean when they talk about a food being more or less fattening. How can you even talk about that independently of the amount consumed? It doesn't ...

Stephan Guyenet: I don't think you have to talk about it independently of the amount consumed. I think that's an integral part of it. If I put, or let's say you put, a pizza in front of me, versus a piece of fish and a salad and a potato. I'm going to, just in real life, I'm going to end up eating more calories of that pizza, probably vastly more calories, than I would of the fish and potato and vegetables.

Julia Galef: So then, if we talk about how fattening one food is relative to another, we're talking about: If given the option to eat as much as we want of food A versus food B, the total amount of weight we will gain as a result of the amount we choose to eat of food A is higher than food B. Therefore, food A is more fattening?

Stephan Guyenet: Yeah, basically. First of all, I don't want to express 100% confidence that there's nothing besides calories that could possibly matter because there are a lot of things that we just haven't tested yet.

Julia Galef: Like what?

Stephan Guyenet: Like the effects of different types of fibers, the effects of palatability per se, or reward value food per se. For example, let's say that you have a diet that's very similar except one version is highly rewarding and the other one is bland. Does that influence how much fat you would gain for the same number of calories perhaps via effects on these brain circuits that regulate your metabolic rate? We don't really know the answers to those questions. And there's a million little sub-hypotheses that you could ask that we haven't asked yet.

Furthermore, in animal experiments, it's not as simple as it is in humans. In rodents, it's not just about how many calories they eat. Food actually does have a more important impact on their calorie expenditure but ...

Julia Galef: Eating 100 calories of food A would cause them to just be motivated to exercise more than eating 100 calories of food B?

Stephan Guyenet: It's not necessarily via exercise, it can also be via just normal metabolic processes. Sometimes, they don't really differentiate, they just know that these animals gained weight when we put them on this refined calorie dense diet even though they didn't actually eat more calories than this other group. That implies that they're burning fewer calories.

Julia Galef: One thing I realized I didn't get clear on earlier is: if eating this high reward diet is causing our brains to regulate the amount of fat in our body to make us want to eat more to maintain a higher weight, is it the *rewardingness* of the food that's causing that change? Or is it the *amount that we're eating* causing that change?

Let's say we took one person and we force them to overeat -- but eating bland foods, not rewarding. They're just eating because we're making them. And they do this for several weeks. Does their brain, now, have a higher set point where it's going to try to make them maintain a higher weight even when we stop holding a gun to their head?

Stephan Guyenet: These experiments have been done in animal models and to some degree, in human experiments, to ask this question…

Julia Galef: Actually, I guess, this isn't an obvious comparison. We should compare that to a person who ate an amount of calories that was enough to just maintain their weight, but they were all rewarding calories. They're eating 2,000 calories a day, or whatever the recommended amount is, but it's all pizza and ice cream and things like that.

Which of those people -- the first person who's overeating bland foods, or the second person who is appropriately consuming their amount of calories but of rewarding foods -- which of them, or both, would end up messing up their set points?

Stephan Guyenet: Yeah. The first way that this was addressed is in animal studies, in rodents, in rats in particular. What they showed is that if you take two groups – or, let's say three groups: One group that gets to eat as much as it wants of some really, really awesome delicious food, gets really fat really fast. Then, you have another comparison group eating healthy diet as much as it wants, it stays lean.

Then, you have a third group that has a restricted calorie intake of the really delicious food. It's being restricted to match the level of the body weight of the group eating the healthy food. It's not gaining weight, it's being restricted, but it's eating the same food as the other group that's getting really fat.

Julia Galef: Right, that's my person B.

Stephan Guyenet: Right. After a little while, you say, "All right, well, now you can eat as much as you want," and what you see is that that group that was previously restricted rapidly bounces up and approximates the curve of the group that was eating that food the whole time.

Julia Galef: Whoa. Wait, that's really weird because that makes it sound like our brains are picking a set point based on, not on how much we are eating, but on how much we *would want to eat* of the food we are eating, and how much we would weigh if we were eating the full amount that we wanted to of the food available.

Stephan Guyenet: That's absolutely right.

Julia Galef: That's creepy, I've got to say.

Stephan Guyenet: This relates to some other things that we could talk about, but it's basically, the brain values food instinctively or non-consciously based on its physical qualities that are evaluated by the gastrointestinal tract in the brain. It places certain value on food. So foods that are really high in fat, sugar and salt and protein or whatever, the brain is like, "Oh, this is really good. We gotta get a bunch of this." That's the stuff that helped their ancestors survive.

What I think is happening is that, essentially, when a brain is in an environment where it can get a lot of this food that it finds valuable, that instinctively it finds extremely valuable because it's really calorie dense and high in these properties at once, it basically facilitates the consumption of this awesome food by affecting these circuits that are regulating your

appetite and body fatness and shifting it all upward to allow you to consume more of this awesome food while it's around.

Julia Galef: Let's say my weight fluctuates throughout my life -- whatever the highest weight is, that's the weight my body is going to want to stay at the rest of my life? No, wait, because that implies that the set point is based on weight. It's not, it's based on the kind of food I'm eating.

Stephan Guyenet: It's both. This is another thing that I think is really important: the set point, the level of body fatness which is your brain is going to defend, is context dependent. I think this is the part that makes the conversation go from seemingly hopeless to hopeful, for people who carry excess weight.

Let's go back to the experiment I was describing. We had these animals that their "preferred weight" or defended body weight is dependent on which diet they were on, not how many calories they're currently eating. If you take those animals that have gained a bunch of weight from eating these really awesome, calorie dense, delicious food and you switch them back to a healthy diet, a lower calorie density, unrefined diet, they will spontaneously lose weight even if you let them eat as much as they want. Their set point actually changes. It can actually go back down even if it had gone up.

And I think you see the same thing in people. Not everyone who diets does so by forcing themselves to eat smaller portions. Sometimes, when people change their diets in ways that are qualitatively better, like going from a refined calorie dense, junk food diet to a lower calorie density, healthy diet that's fresh vegetables and meats and fruits and whole grains and potatoes and things, you will see that people will spontaneously lose weight. Their appetite will spontaneously decrease, and they, without trying to restrict their calorie intake even if they're eating to fullness -- you'll see that, typically, people will be able to lose a certain amount of weight comfortably without having to fight themselves.

I think it's probably the same phenomenon that you see in the animal experiments. There are controlled experiments in humans that have suggested similar things. There was one that I think is interesting on this topic where they gave people this bland liquid shake, basically. They said, "This is all you have to eat for the next two weeks," and they lost I think ...

Julia Galef: Were they allowed to eat as much as they wanted of this?

Stephan Guyenet: Yeah, yeah, as much as they wanted. They lost seven pounds. They just weren't eating that many calories of it. And they were told, "Eat to fullness. You're not depriving yourself, just eat to fullness." They lost about seven pounds. That's what people tend to do when they go on really bland, repetitive diets, they don't feel as hungry, they don't eat as much.

Julia Galef: Did they gain it back when they stopped?

Stephan Guyenet: I don't know, the study didn't report that.

Julia Galef: But your model would predict that they wouldn't, because their set point was lowered by eating bland food?

Stephan Guyenet: My model would predict that they wouldn't as long as they stayed on the bland diet. As soon as they go back to their normal diet, my model predicts that they would bounce back up. Yeah, so that's the catch.

To finish my thought, they had another group of people that they asked to lose the same amount of weight over the same period of time by just applying portion control to their habitual diet. It's like, you're going to eat the same foods you always eat, you're just going to eat less of it to match this weight loss curve of this other group.

What they found is that the group that lost weight by portion control was ravenous. They had very, very different responses. They reported in the study that the people were very uncomfortable, they were dreaming of food. I'm not going to go into it because it would take a long time to explain, but they had some more physiological measures of hunger drive.

Basically, what they found was that people who lost weight on the bland diet weren't any more hungry at the end. People who lost weight by portion control were super hungry, and their food motivation kicked in so that starvation response was activated in one case but not the other, presumably because the set point had changed.

Julia Galef: Well, I know this is just one study in the context of many studies, but if I was just looking at this study, the way that I would interpret it would be to say: Presumably the diet they're eating normally is more calorie dense and less filling. I would expect them to be less full eating the same number of calories as the boring shake group, because their food is less filling than the shake would be. Also, the tastiness of food is more salient, and so, of course, your cravings are going to kick in when you were just eating a donut and now, you want more donuts -- as opposed to if you haven't looked at a donut in weeks.

` That model doesn't rely on set points at all. Would say that that is consistent with the data, and the reason you're interpreting it differently is just because of other evidence you have about set points? Or am I wrong about it being consistent?

Stephan Guyenet: I'm trying to think this through here. Potentially, I would have to go back and look at the study design to see if it would be possible to exclude that interpretation.

Julia Galef: To leave out set points to explain it?

Stephan Guyenet: No.

Julia Galef: To rule out my interpretation.

Stephan Guyenet: Yeah, yeah. Again, some of the measures that they used are a little bit too complicated for me to explain efficiently right now. I think it would depend on when those were done. If those were done right after a meal, when there could, potentially, be differences in satiety, then perhaps. If they were done first thing in the morning, like these types of tests often are where you hadn't eaten in a long time, I wouldn't think it would be influenced by a recent meal.

Julia Galef: Yeah. I mean, still think about my breakfast for hours after I eat it, if it was good! But no, that's a fair distinction.

Stephan Guyenet: Yeah, it definitely integrates information from other lines of evidence as well, my belief.

Julia Galef: Right. Yeah, that makes sense.

I'm sure listeners will be curious about how your model explains the fact that specific diets, like low carb diets, for example, seem to be pretty effective in causing people to lose weight. Would you just explain that success by those diets being less rewarding?

Stephan Guyenet: I think that's part of it. By the way, I want to clarify something, we're calling this “my model” but this is really a model that is not something that I came up with, for the most part. This is something that is taken from the scientific community, including me, that I'm trying to communicate. Not to say that every scientist believes everything that I say -- but yeah, I can't take full credit for this. I want to say that within my field, most of what I'm saying is pretty commonly accepted.

Julia Galef: Sorry, then, before you answer my most recent question -- what would you say is the distribution of views? Would it be like 90% of people researching obesity basically just agree with everything that you said and 10% think it's… insulin, or…?

Stephan Guyenet: I wouldn't want to claim that 90% agree with everything I say. I think in broad strokes, almost everyone in the research community would agree that food reward plays an important role in obesity. I would put that, at least at 90%. Just that big idea.

Julia Galef: What are the main disagreements then?

Stephan Guyenet: I don't think there is a huge amount of disagreement, to be honest with you, within the scientific community.

Julia Galef: All this controversy that I encounter is just among outsiders?

Stephan Guyenet: For the most part, yeah. I think in the scientific community, people are siloed. They may not have strong beliefs about what somebody else thinks is causing obesity, and they tend to say, "Well, it's probably a lot of things coming together that's causing obesity." With all those things converging through thermodynamics.

Julia Galef: Right. Okay, so then back to the question that you were trying to answer for me a few minutes ago, about explaining the success of, say, low carb diets.

Stephan Guyenet: Yeah, yeah. I personally -- and I don't want to suggest that this hypothesis has been tested, this is just my belief based on other evidence -- I think personally that the reward concept can, at least, partially explain the success of low carb diets.

Again, the human brain is wired to seek certain properties in food. Things like starch and fat and sugar and salt. And those are things that basically the brain wants as much as possible of all those things, all the time, on a certain non-conscious, impulsive level.

Restricting any one of those things -- saying, "Well, I'm going to completely cut out carbohydrate," or "I'm going to completely cut out fat" -- you're basically providing a diet to the brain. You're providing a palette of foods that is less desirable to the brain, in terms of your brain's intrinsic motivation to eat.

I think that's part of it. And it offers, at least, a partial explanation for why you see people losing weight on diametrically opposed diets.

Julia Galef: Like low carb and low fat?

Stephan Guyenet: Low fat, for example.

Julia Galef: Really?

Stephan Guyenet: Yeah.

Julia Galef: People lose similar amounts of weight?

Stephan Guyenet: Well, that is an interesting question, and it depends on how you look at it. First of all, I will note that people, whether or not the amounts are similar, people do lose weight on both. Which implies that it's not as simple as saying carbs are fattening and the more you eat, the fatter you get.

Julia Galef: I suppose, for some people, carbs could be more rewarding than fat, and for others, it's the other way around. If so, that would explain that.

Stephan Guyenet: I think that's right. I think there is a huge amount of variability and people clearly do respond differently to different types of diets.

The other point I want to make is there are a lot of randomized controlled trials that have compared low carbohydrate to low fat diets. Generally, the low carbohydrate diets cause more weight loss, although they both cause weight loss.

But when you really start to dig in to those studies, the answer becomes less obvious than it seems on the surface. The reason is that if you really look at the low fat diets that are typically used as a comparator, they're really, really wimpy low fat diets.

Julia Galef: How so?

Stephan Guyenet: They're not very low in fat, first of all. They're usually not as low in fat as the low carb diet is low in carbs. Second of all, they tend to be based on this antiquated concept of low fat diets, where only the low fat matters and you don't care about any other aspects of quality.

Julia Galef: People often replace the fat with sugar to make it taste good.

Stephan Guyenet: Yeah, it's like the SnackWell Cookie Effect.

Julia Galef: Yeah, that's exactly what I was thinking of when I said that.

Stephan Guyenet: So what does it mean for low carb to be more effective than that?

Now, increasingly, you have more studies that are coming out where people are starting to care more about diet quality, and about matching diet quality between the arms.

Julia Galef: Here's how I would do it. The right comparison, in my view, would be to pick a certain calorie threshold -- and then, let people design the most palatable diet possible, under the constraint of that calorie limit and a certain carb limit. Then similarly, the same calorie limit and the same fat limit, design the most palatable diet you can. And then, compare those head-to-head.

Of course, it would be different for different people, so it's hard to do a nice clean study, so it wouldn't work so well but ...

Stephan Guyenet: Yeah, yeah. There are really complex hypotheses to test sometimes. What you see in these more modern studies, that are paying more attention to matching the conditions and focusing on diet quality, is: first of all, improving diet quality gives you better effectiveness. Focusing on diet quality, I should say, gives you better effectiveness to not caring. You get better weight loss and ...

Julia Galef: Caring just in any way?

Stephan Guyenet: What I mean is the quality aspect matters independently of the macro-nutrient aspect.

Julia Galef: Sorry. By quality here, you mean like ... ?

Stephan Guyenet: By quality, I'm talking about the degree to which a diet is refined junkie food.

Julia Galef: I see. I got it.

Stephan Guyenet: Yeah, yeah. When you focus on that quality, you get better results.

And what you also see is that there's often very little or no difference in the weight loss response you see between low fat and low carbohydrate diets. In fact, there was a recent study that came out from Chris Gardener's group that was actually funded by The Nutrition Science Initiative, which is this organization headed by Gary Taubes, who is a big proponent of the idea that carbs are bad and fat is good. This one showed exactly what I just described, that there was no difference when diet quality was high in both the low fat and the low carb arm. Both arms lost a pretty good amount of weight, and there was no difference.

I think there's this received wisdom that we have that low carb is more effective than low fat for weight loss. But I think that emerging evidence is suggesting that that might not be quite as straightforward as we thought it was -- as I thought it was, as well. I think it's very individual. There are big error bars on these results. You put people on any kind of diet, you're going to see a range of responses that ranges from really, really impressive weight loss all the way to weight gain. All you have to do is look at the standard deviation of these measures and you can see that there's a huge range of responses. It's very individual. Whether one diet is superior to another in an average sense, may not be exceptionally informative with respect to how an individual will respond to a diet.

Julia Galef: Yeah. I know that your book goes into this in much greater depth than we're going to be able to in the last, oh Lord, two minutes that we have left. We're already actually way over the time that I had expected to spend, but that's fine. The other elephant in the room is the, like, "Great, what do I do about this?" question. I imagine many people are thinking, "Okay, so is the answer is I just have to stick to a completely bland and unrewarding diet. And when I go off of it, even briefly, then suddenly I've increased my set point and now, my body is going to try to make me obese?"

Maybe these low carb, low fat diets that we were just talking about are a compromise?

Stephan Guyenet: Yeah, yeah. I think I've probably given people the impression that I'm a little bit more of a drill sergeant about food reward than I really am. What food reward is, it's a tool that you can use to achieve whatever your body weight goals are. Among other tools. It's not the only tool that's available to us.

Julia Galef: "You" being your brain, or you being ... ?

Stephan Guyenet: An individual.

Julia Galef: Okay, but I feel like food reward is the thing that I'm fighting against. I have goals and food reward is getting in the way of those goals. It doesn't feel like a tool to me.

Stephan Guyenet: Well, what I mean is it's a tool in the sense that understanding how it works can ...

Julia Galef: Okay, yeah.

Stephan Guyenet: Yeah, you can lower it in order to lower your food intake. There are other tools that can work. Eating a diet that's lower in calorie density is something that is, at least, partially independent of that reward factor. Then, there's physical activity, there's stress management, there's sleep management. You could, theoretically, put together a slimming diet and lifestyle that doesn't have reduced food reward. That said, you are leaving a tool on the table that you could be using.

I think one thing to keep in mind is that you don't necessarily have to eat a completely bland, uninteresting diet to achieve your goals. Personally, the balance that I like to strike is I like to focus on the natural flavors of high-quality, unrefined foods. A really nice fruit, a really nice vegetable, a really nice piece of meat, really nice eggs, a potato with nothing on it.

Julia Galef: You're not really selling me…

Stephan Guyenet: Do you see what I'm trying to say though?

Julia Galef: It sounds like, for you, unrewarding food is less frustrating than it is for many people.

Stephan Guyenet: Well, that is possible. That is possible. We have our expectations set by living in a society where we're used to having our palates constantly entertained. That's part of the problem. What I'm trying to get at is there's a difference between getting reward from eating french fries or fried chicken or something, ice cream -- and having an enjoyable meal that is a piece of fish with some herbs on it or something like that, that tastes good, but is a more simple, unrefined flavor, rather than having all these highly palatable accoutrements. Does that make sense?

Julia Galef: Yeah, that does make sense. I'll try to keep that in mind next time I'm picking a restaurant. Well, we really should wrap up at this point unfortunately. There's a lot more detail in *The Hungry Brain* so we'll put a link to that in the website.

Before I let you go, Stephan, do you want to give the Rationally Speaking pick of the episode? For this episode, I'd love you to suggest a book or some other resource that, if you had to pick one additional book to recommend to

people, to flesh out their understanding of this topic, that you didn't cover and isn't in your book. What would that be?

Stephan Guyenet: I think Michael Moss's book, *Salt, Sugar, Fat* is a really nice one. My book is a lot about the science and especially, the neuroscience of overeating and eating behavior. I think what Michael Moss does is he really fleshes out the changes that occurred in the food industry, and our food culture, that were some of the triggers of this modern relationship that we have with food that's driving us to overeat. I think that's a really nice compliment to my book. Even independent of my book, it's something that I learned a lot from.

Julia Galef: Great. Well, we'll link to that on the podcast website as well. Stephan, thank you so much for joining us on Rationally Speaking.

Stephan Guyenet: My pleasure.

Julia Galef: This concludes another episode of Rationally Speaking. Join us next time for more explorations on the borderlands between reason and nonsense.