I'm Ezra Klein, this is the Ezra Klein Show.
Our society has long treated weight gain as a function of insufficient willpower.
If you're overweight, it's because you chose to be.
You ate too much, or you didn't exercise enough.
You lack the virtue and the discipline of the thin.
This story is great.
It is great for punishing anyone who struggles with weight.
It is great for justifying discrimination and maltreatment.
But it is just nonsense if you take even a cursory look at the data.
And Steph and G&A has looked, and I put this very lightly, a lot deeper than that.
G&A is a neurobiologist by training.
He is obsessive about study interpretation and experimental design and methodology.
And his book, The Hungry Brain, is to me the most convincing model for why obesity is rising year after year, why so many who try so hard to change their way signs fail even after they sometimes first succeed, and why our individualized narratives around this are so cruel and also so wrong.
His argument based on reams of evidence is that weight gain is a product of this fundamental mismatch between our brains, not just our waistlines or something, our brains, our genetics and our social environment.
We live in a world where we are surrounded by endless varieties of cheap, convenient food that is engineered to make us crave it.
And craving is not just about liking something.
It is often a signal the brain is getting that this is calorically dense.
This is the kind of thing that can keep you alive.
We have brains tuned for a world of food scarcity.
You can't understand any of this without understanding that.
G&A's book came out in 2017, and in the past year or so, we've seen the introduction of new weight loss drugs that fit the Hungry Brain model perfectly.
These drugs, they don't work by making your body burn more calories.
They make your brain want less food.
As I wanted to have G&A on, he's looked quite deeply at these drugs and how they work.
To talk through his model, to walk me through these drugs, and to think a bit about the strange and complicated, almost ironic, it's like a Greek myth, world we're in.
One where having solved for many people the central problem of humankind up to this point, how do we get enough to eat?
Many are now searching for drugs and therapies at great cost, at great expense, at great difficulty to change our brains in biology so that we eat less.
As always, my email, azurekindshow, at mytimes.com.
Steph and G&A, welcome to the show.
Thanks for having me, Ezra.
So the core argument of the book is that at the heart of our modern food system is this mismatch between the way our brains are wired and the food and social environment we've built.

Tell me about that mismatch.
So I think there's this common understanding of food intake and body fatness, which is that people make conscious decisions about their eating, and those conscious decisions result in a certain calorie intake, and they have a certain physical activity level, and the output of that determines their body fatness.
And so this is the kind of calories in, calories out, reasoning, and then if you want to lose weight, all you have to do is just stop eating so much, and you lose weight, and it's not a problem.
However, what we see is that it's not quite so easy, because when you just tell people to eat less, they don't lose that much weight, and what we see is that it's not really sustainable.
So they can't lose weight to the extent that they would like to.
And so this suggests that there is kind of this dichotomy happening between a conscious rational brain that wants us to lose weight and be lean and eat less and be healthy, and then this non-conscious, intuitive, impulsive brain that is composed of these regulatory circuits that are responding to our environment and are responding to our genetics and that are causing us to eat more.
And essentially, when you take this non-conscious brain out of the context where it evolved, where all of those impulses that it generates made a lot of sense, and you put it into the modern food environment where we're surrounded by easily accessible, calorie-dense, highly rewarding foods, those same impulses pull us in the wrong direction and cause us to over-consume.
What is the difference between seeing these differences person to person as being about willpower and seeing them as being at least partially about genetic susceptibility?
Yeah, I mean, I think it's pretty hard to attribute something entirely to willpower when there are strong genetic susceptibility factors.
You know, it's like, you look at height, height is highly genetic.
You look at body mass index, body fatness, it's highly genetic.
And this has been studied scientifically and the studies suggest that depending on the method you look at, somewhere between 40 and 80% of differences in body fatness are determined by genetic differences.
And so genetics has a very strong influence on body fatness.
And certainly it relates to behaviors, but you have to consider that our behaviors are also genetically influenced.
Pretty much anything you look at, almost any human trait is genetically influenced.
And even things like willpower to the extent that they may contribute to body fatness are also genetically influenced.
So I think it's a pretty complex conversation when, I mean, I don't think that we should be, you know, drawing moral conclusions based on people's weight.
That's my position.
But I think even if you were to try to do that, it's a pretty complicated conversation because of the fact that all these things are genetically influenced.
But I think this is actually a profound conversation too.
And I want to hold on the height weight analogy there because the reason I think weight feels different to people is it is related to behavior, whether or not you eat a third or fourth or

fifth slice of pizza, whether or not you go to the gym, but your point that behavior is itself often an expression of genetic predisposition is pretty profound.
So talk a bit about this argument that what is happening here is that you have genes expressing yourselves in the brain and the brain is in controlling behavior.
And we shouldn't understand that all as a matter of individual choice.
I think a good entry point into this is to consider where hunger comes from.
So you know, when you get hungry at a certain time of day, let's say, is that because you chose to feel hunger?
Or is that something that arises out of circuits in your non-conscious mind?
Or if you smell the smell of brownies or you walk past a bakery and you smell fresh baked bread and suddenly you feel a desire to eat what you smelled, is that something that you chose?
Did you choose to suddenly develop this motivational response, this craving toward brownies or bread or pizza or whatever it is that you smelled?
No, these are things that arise from non-conscious brain regions.
And I think, you know, because they're non-conscious, it's not really intuitive to think about the fact that our behavior is strongly influenced by these brain regions.
You know, they're non-conscious, so we can't directly observe them.
We can only kind of indirectly observe their outputs.
But it turns out that these regions have a very strong impact on our behavior.
So if you think about someone's appetite, some people just have bigger appetites than others.
Is that something they chose?
Of course not.
But the amount of calories that we eat, it can be influenced in many ways.
It's not just hunger that influences our calorie intake.
But many of these influences on our calorie intake, such as our hunger and how susceptible we are to food cues related to highly rewarding foods, such as smelling a brownie, those are not things that we're choosing.
Those are things that are being generated by non-conscious brain circuits that are influenced both by genetics and by our prior experience, like our upbringing and our environment.
This puts me in mind of a conversation I had years ago with a friend.
We were out at lunch together, and we weren't talking about food, but there were chips on the table.
And he said, as way of an analogy to something else, and I forget what he was actually talking about because the thing he actually said was so astonishing to me, but he said, as way of an analogy to something else, that doing or not doing that thing was as trivial and unthinking for him as not eating all the chips in the bowl.
And I remember saying, well, what do you mean by that?
It's an enormous, constant act of willpower to not eat all the chips in the bowl.
And 55% of my brain, this whole conversation, has been on what is a socially acceptable number of chips and how much of my push the boundary on that.
And I had this moment as we talked about this, that I realized he just had a completely different experience of moving through the world and being around food than I did, that

it just wasn't this kind of thinking and obsessing and pushing and troubled control.
And so I want to hold on this for a minute because I think it's important both to your book and a lot of what we're going to talk about here.
When you say a lot affects how people act beyond just hunger cues, what do we actually know about that?
What is the difference in the subjective experience of somebody susceptible to eating a lot, overeating,
weight gain, whatever it might be when they're sitting near foods that appeal to them versus somebody who does not have some of these same genetic proclivities?
I would say that we don't have a lot of great, really concrete information that gives us the whole causal chain from the common genetic variants all the way through to behavior.
However, there are things that have been identified that differ between people who are more susceptible
to overconsumption and weight gain and people who are not.
And one of the things that has been identified is that certain people just have a much stronger motivational response to seductive food.
So if you have chips sitting in front of you on the table, that's one example of it.
Leonard Epstein has done a lot of this research where they can actually quantify how hard people are willing to work for food.
So they'll give people a snack so they're not really hungry, and then they'll have them play these video games where you have to give a certain number of responses, and the number of responses you have to give goes up and up and up each time you receive a reward, which is like a little piece of candy bar or some soda or something like that.
And then you can compare that to non-food reward like a magazine or a little video game or something.
You can see how motivated our people for this seductive food relative to a non-food reward.
And that is an individual trait that varies greatly between individuals.
And so you will see that some people will work really hard for a little piece of candy bar or for a sip of soda, whereas some people really will not work very hard.
Once the response requirement starts to increase, they just kind of give up.
They don't care anymore.
And so there's this trait of food reward responsiveness, you could say, or the technical term is relative
reinforcing value of food.
And that describes exactly the scenario that you're talking about with the difference between you and your friend.
We've been talking here about the differences between individuals.
But I want to talk about something that's going to your book, which is the similarities and in particular the sort of evolutionary environment in which our brain's response to different kinds of food emerged, which was an environment in much more food scarcity.
So tell me a bit about the world our minds believe we are living in and are prepared for.
So the human brain is very flexible, so it can adapt to a variety of different environments,

of course.
But at the same time, we do have hardwired inclinations.
The human brain is not infinitely flexible.
And the situation we're in right now is radically different than the range of situations that humans evolved in in terms of our relationship with food.
So if you look at hunter-gatherers, humans were hunter-gatherers for something like 99.5% of our evolutionary history since the development of the genus Homo.
And if you look at cultures today, historic and current cultures that are living a hunter-gatherer lifestyle, what you see is they're having to work really hard to get their food.
And there are periods where they don't necessarily get the quantity or the quality of food that they would like.
And so I think it's radically different in terms of the convenience of the food.
If you think about if people had to walk five miles in climate tree to get the food that they eat every time they wanted to eat, that would be a pretty powerful disincentive for people to be eating as much as we typically do, even if the food was the same.
But at the same time, their food was also quite different.
The food, of course, that hunter-gatherers eat is basically whatever they can get from the environment.
And usually that's a mix of plant and animal foods.
Usually they have very little ability to process and refine those foods.
Now humans process food, that's one of our characteristics.
So it's not like they didn't process food at all.
So they cooked things, that's the main processing method.
They would cut things up, cuts of meat and pound things to soften them and stuff like that.
But there was not this ability to refine and recombine ingredients like we do in the modern world.
And particularly, I think a thing that's really key is over the course of human history, we've gained through technology and affluence, we've gained the ability to separate out and purify the active ingredients in food that mediate their seductiveness, the ingredients in food that cause dopamine release in the brain.
And so we basically have these purified, almost drug-like ingredients that we can concentrate and recombine to create things that are more motivating for our brains than a hunter-gatherer would typically experience.
Well, we'll talk through what makes a food particularly motivating to the brain.
What are the signals and what is the brain taking from those signals?
So the main ones that have been identified so far, either identified or strongly suspected, are carbohydrate, both starch and sugar, fat, protein, and salt, and umami, or glutamate, that kind of meaty flavor that's in cooked meat and bone broth and soy sauce and fish sauce.
Those are food properties that are reinforcing, which means that they stimulate and strengthen behavior.
They stimulate repeat behavior and strengthen behavior.

The brain basically learns, brain wants them and learns how to acquire them and how to generate motivational responses around them.
And particularly, the more those are concentrated and combined, concentrated up to a point, there's kind of what's called a bliss point of maximum seductiveness.
And to the extent that they are concentrated and combined, they stimulate our motivational drive, which is mediated by dopamine release in the brain.
So essentially, you eat foods that contain these substances, dopamine spikes in your brain, that generates a motivational response, and it generates learning that makes you more motivated in the future.
And it's a natural, healthy process normally.
Like this is what's supposed to happen when you eat food.
This is the process that guided our ancestors to the foods that supported them and allowed them to survive and reproduce.
However, when you purify out the ingredients that spike dopamine, you purify it away from the water and the fiber and maybe some of the less desirable flavors that would be in a unrefined food, then suddenly you are concentrating the dopamine stimulating properties of that food and accentuating the seductiveness of it far beyond the foods that our ancestors, our distant ancestors, would have experienced.
And just to draw this out, the basic thing that the brain is trying to pick up on here is that these flavors are signals of caloric density.
Yeah, yeah, I appreciate you mentioning that.
So that is one of the main points here, is that aside from the salt, all of those other properties I mentioned are properties that correlate with the energy content of the food.
So if we look at how the brain is set up, the signals that it responds to, the signals that trigger motivational response, they revolve quite a bit around calories, around acquiring calories.
So that is how we are wired and that suggests that calorie intake, like learning which foods are the most calorie dense was a very important thing for the survival and reproduction of our ancestors.
So it was good for them to have a high level of motivation for calorie dense foods.
That's how our brain is wired.
But unfortunately, today it's just a little too easy to get those foods.
And so that for many of us becomes counterproductive.
You give this interesting analogy in the book between the way we refine cocaine from the cocoa leaf and the way we refine chocolate out of the cocoa bean that I just find to be provocative as an analogy.
But also interesting is a way to think about the process here.
Can you talk through that?
Yeah, absolutely.
So the cocoa plant is a plant that contains a low concentration of this substance, cocaine, and it's been chewed by indigenous South American cultures for thousands of years as a mild stimulant.
It's kind of like drinking a cup of coffee, you chew cocoa leaves.

And in that context, it is a perfectly constructive habit to have, just like drinking coffee.
It's a pretty benign indulgence.
And however, if you then take that leaf and you refine out the cocaine, you're taking the active ingredient out of that leaf.
And by the way, cocaine is an inhibitor of dopamine reuptake at the synapse in the brain, which means that it increases dopamine levels.
That's how cocaine works.
And so you're taking out the active dopamine stimulating ingredient and you're concentrating it many fold.
And now you've taken something that was a mild stimulant and you've turned it into a strong stimulant that's highly reinforcing that spikes dopamine to very high levels and can create addiction because of that.
You're purifying out the dopamine stimulating element and the more you spike dopamine, the closer we get to addiction.
And if we then take that cocaine and we free base it, which basically means that now it can freely cross lipid membranes and get into the brain really easily.
Now it has faster kinetics when you take it and that's crack cocaine.
And that's even more addictive.
So essentially each processing step has enhanced the active ingredient, concentrated and enhanced the active ingredient in the coca leaf, cocaine, and turned it from a benign indulgence and a useful substance into a life destroying, potentially life destroying drug, addictive drug.
And so over the course of human history, the analogy here is that we have developed the ability to identify and purify the dopamine stimulating nutrients in food as well.
And so there's a lot of debate over whether we can call food addictive or not per se, use that word per se.
So I think, you know, I just want to acknowledge that not everyone in the research community agrees that we can really call food addictive.
However, it remains true whether we call it addictive or not, that we have concentrated the dopamine stimulating properties and made that food a lot more seductive than what our ancestors would have experienced and what our brains are accustomed to.
And so if we look at chocolate, chocolate has properties that stimulate a lot of dopamine.
So first of all, it's very high in fat, very high in calorie density.
Once you add sugar to it, it also has carbohydrate and that combination of fat and carbohydrate is particularly stimulating to our reward circuits.
And you know, that alone would make a highly rewarding food, but chocolate has something else in it that really takes it to the next level.
And that is a habit forming drug called theobromine.
Theobromine is pretty much like caffeine, very similar to caffeine.
So on its own, it's not highly habit forming, you know, it's like caffeine.
But when you combine that ability to stimulate that dopamine signaling pathway with the concentrated
nutrients that are in the chocolate, you get a really powerful response.

And what we see is that chocolate is actually the most craved food.
If you just do surveys of what foods people crave the most, what foods people lose control around the most, chocolate is number one, particularly for women, but it's very high on the list for men as well.
Well to further the, I don't exactly want to say the addiction analogy, but I always think of addiction as a pretty broad spectrum of human behavior, and it's at least useful as a sort of cognitive label because it connects to something important in this conversation, which is not only that I don't think we want to admit it being a widespread problem, but that it has then implications which we very much don't want to face up to.
So with things we have classified as problematically addicting, to varying extents, we have quite a bit of prohibition on at least the legal acquisition of more and more purified experimental versions of them.
So we have, I mean, people argue about whether or not we have enough rules on alcohol, but you're not in most states supposed to drink until 21, and you can't drive after you drink and so on and so forth, we have become extremely prohibitionist around cigarettes in terms of the social consequences of smoking, in terms of where you can smoke.
I remember being in D.C. when the smoking ban was passed, you'd be in bars before that and it would be like being inside somebody's lung, and all of a sudden you couldn't and you'd have to be outside in the cold.
A lot of drugs that are extremely rewarding, cocaine we talked about, they are illegal to use, except in very, very unusual circumstances.
But with food, it's not just that obviously it's illegal, but it's a multi-multi-multi-billion-dollar industry to figure out how to make it even and ever more distilled such that it is that much more rewarding.
I mean, you think of the money and branding efforts it went into making tacos made out of Doritos a couple of years ago when that was a big deal, or the amount that goes into perfecting a McDonald's meal or whatever it might be, that we really do, I think, keep getting better at this.
I have extremely, extremely low patience for people who want to pretend that all this food research doesn't work to make things that are tasty, if it really quite clearly does.
And as such, you really have this, again, maybe a mismatch is right, language for it between brains and particularly for individuals who are susceptible to this, between how palatable we find these foods and then a gigantic industry that has a lot of really remarkable brainpower and money to say nothing of marketing, going in to trying to find the exact food that we will find most palatable and habit-forming and getting us to buy it really quite often all the way down to when we're little kids and are seeing Paw Patrol on cereal boxes as we walk through the aisle, that there's just a tremendous corporate world here that is trying to work with us part of our psychology, physiology, and I think that is sustained, that is only safe so long as it doesn't get categorized in this place where when we've categorized other things that way, the regulatory hammer has come down.
Yeah, it's a striking contrast, I agree.
And I think at the same time, I want to acknowledge that having strong motivational drives to work food or perhaps we could call it addiction in some people is not the same as alcoholism,

it's not the same as being addicted to crack cocaine or meth, I mean, I think, or even cigarettes, you know, it's important to acknowledge that these habits are not equivalent in terms of their impacts on people's lives and on society, so I think that's part of it.
Obesity is something that accumulates over many years and yes, it's bad for your health, but it's not as bad as doing meth, and the other thing is it's a much bigger, more amorphous problem, you know, like targeting meth, like there's a real clear target there.
With food, it's just a lot murkier.
Hi I'm Josh Hainer and I'm a staff photographer at the New York Times covering climate change.
For years, we've sort of imagined this picture of a polar bear floating on a piece of ice.
Those have been the images associated with climate change.
My challenge is to find stories that show you how climate change is affecting our world right now.
If you want to support the kind of journalism that we're working on here on the climate environment desk at the New York Times, please subscribe on our website or our app.
Some of the most interesting studies in the book to me were the ones that put people on different kinds of either cafeteria diets or bland diets or liquid diets and saw what happened not to weight but to appetite, because I really understand what you're saying here as being that we've had this very dominant calories in, calories out model, or it's about what we eat in and the fat that comes out model, and that the missing piece in a lot of this is appetite, how much our brain tells us to eat, and then sort of all these subsidiary ways that it convinces us to do so.
Tell me a bit about some of those studies where in manipulating the environment manipulates the hunger queues.
So the first thing I'll say is that appetite is a regulated quantity regulated by the brain.
Body fatness is also a regulated quantity by the brain.
And appetite is the primary factor arm of the body fat regulating system.
So appetite is the primary thing that goes up or down in order to regulate your body fatness.
It's a primary lever you can think of for influencing body fatness in humans.
So in the 1970s, a researcher named Anthony Sclafani had a sort of chance observation.
He was trying to develop obesity models in rats.
There was obesity in the 1970s, researchers were trying to study it.
And it was kind of the early days of figuring out how do you fatten a rat and how do you do so quickly and efficiently so that you can have a graduate student study obesity in your lab.
And at the time they were adding fat to rat chow and that was effective to some extent but took too long and it wasn't reliable enough.
But one day Anthony Sclafani saw a rat that was placed on his lab bench, saw it walk over to a bowl of fruit loops and start eating them and just kind of gorged on these fruit loops.
And first of all, a rat these days would never be on a lab bench like that because we have these really sophisticated facilities that exclude pathogens.
So this was really the old days.

But second of all, rats, they have something called neophobia where they usually are very cautious about new foods.
But this rat, as soon as it tasted the fruit loops, it just kind of went crazy on him.
So he saw this and said, well, maybe we should try something else to make these rats fat.
Instead of just manipulating the macronutrients instead of just adding fat, let's feed them tasty human foods.
And so he went to the grocery store and he bought a variety of tasty human foods like sausages and cookies and fries and things like that and put them in the rat's cage.
And what happened was that the rats over consumed dramatically.
Their calorie intake went way up.
Their body weight went way up.
And there was not really anything you could do to stop this.
So first of all, they continued to have access to the healthy lower calorie food, but they basically ignored it.
You know, if you have access to salami and chocolate chip cookies, you're probably not going to be worried about this bowl of whole grains over here.
And so physical activity attenuated the fat gain, but did not prevent it.
An enriched environment, so giving the animals lots of stuff to do, didn't have any impact on it.
So basically he discovered this method of fattening rats that was much more effective than any nutritional intervention that you could do to its pellets, any way of modifying the nutrient content, way more effective than that, and it happened to be tasty human food.
And it turns out that basically any animal that can develop obesity will develop obesity when they are exposed to a wide variety, easy access, unlimited amount of tasty human food.
And this same phenomenon has been observed in humans.
So Eric Raveson's, by the way, this was called the cafeteria diet.
That's kind of what they named it in the rodent research world.
And Eric Raveson back in the 90s did a series of experiments that were basically the equivalent in humans.
He locked people up in a research facility with a wide variety of tasty human foods in, you know, very easy access.
And in this situation, people dramatically over consumed calories.
And nobody was being asked to do so.
The rats weren't being asked to over consume.
The humans were not being asked to over consume.
This was just a natural outflow of the environment that they were placed in, the environment and the foods.
And then we have more recent studies that have been done by Kevin Hall's group where they give people access to in a very controlled environment, in a laboratory environment.
They give people a diet of unrefined foods or a diet of ultra processed foods.
These are the kind of industrially processed, highly processed foods that, you know, many people might call junk foods.
And what you see is a dramatic divergence in calorie intake in these experiments.

People will eat 500 more calories a day, roughly, of ultra processed food than of unrefined food.
And again, nobody was being instructed to eat any particular amount of calories.
This is purely the brain's intuitive, instinctive response to the food that is being provided.
Tell me about what researchers call sensory specific satiety.
So sensory specific satiety is the observation that we can basically get full on a particular type of food, like a food with a particular sensory quality, like savory or sweet, and not necessarily be full for different foods with different sensory qualities.
And so you can give people a particular food, let them eat as much as they want.
They might be full on that food, they have no desire to eat any more of that particular food, but you give them a different type of food and they'll be prepared to eat possibly several hundred calories of additional food from that or other foods.
And so this explains why we tend to eat so much at buffets because we have so many different sensory experiences to choose from and people tend to over consume dramatically in that situation.
And you can see the same thing in rodent studies.
If you give rodents one tasty food like chocolate chip cookies, in addition to their normal food, they will eat more and gain weight.
If you give them three tasty foods at the same time, they will gain even more weight.
And so the variety of food seems to have a pretty substantial impact on our intake and ultimately possibly on our weight.
I think another thing that is interesting to note is that this also goes a long way toward explaining why we eat dessert because you can have a savory meal, let's say you have fish and potatoes and a salad, you can be completely done with those savory foods, not interested in eating any more of those savory foods.
Somebody brought another potato out, you're not going to eat it, but as soon as there's ice cream or cake or a brownie or something like that, you might be prepared to eat hundreds of extra calories.
Part of that is due to sensory specific satiety, part of it is due to the high reward value of those dessert items.
One just stat from the book that speaks to this variety, I think in a kind of astonishing way, was you cited a report from the Food Marketing Institute that found the average US grocery store contained around 15,000 items in 1980, which is great, a lot of items, and has about 44,000 in the present.
And this is a couple of years old, so it might be higher than that now.
It really, I mean, I know people know this on some level, we all know this, but the variety is totally astonishing that we have access to, not just the variety, but the convenience.
I mean, I remember a study that influenced me a lot, back when I used to cover food and health policy more closely, is by, I want to say it was David Cutler and some co-authors, and they really found that people weren't eating that much more in meals, what they were doing was eating much more during snacking periods, that accounted for a lot of weight gain over time, and that in part, that was just because it had become easy to have a variety of foods around you in between meals.

Nobody had to put any effort into cooking them or changing them.
We had preservation, we had refrigeration, we had vending machines in the modern era, and as such, it's not just that variety exists, but variety exists across time now.
There might have been variety at dinner in 1950 or 1930, but it was harder to get that same variety at 3 p.m. or at 11 a.m.
But now, it's not just a lot of foods, but a lot of foods that are available to you at all times.
You know, your workplace maybe, if you work in the tech company or some kinds of companies now has a kitchen with all kinds of stuff around for you all the time, that it's really, the food environment is unbelievably dramatically different.
Absolutely, and I wish I had highlighted that stat about increases in snacking in my book, because I think that's actually one of the most compelling correlates of the so-called obesity epidemic, which is in the U.S. the increase in obesity prevalence since about 1980.
What you see is that the number of snacking occasions has increased quite a bit, and it really correlates with that period where obesity rates started to rise rapidly.
And by the way, I'm using the word snacking loosely, because this includes between meals, sugar, sweetened beverages.
So, you know, solid foods as well as beverages, both of those things increased.
And if you look at the number of calories that's supplied by these additional snacking occasions that we didn't have in the 1970s, it's actually single-handedly able to explain our increase in calorie intake over the course of the obesity epidemic.
So then let me ask about a study all the way on the other side of the spectrum, which is from the 1960s in which participants were only given bland liquid food from a straw.
What happened there?
Yeah, so this was an interesting experiment with, I think, for the investigators, really unexpected results.
So there was a research team that was trying to understand what happens when you eliminate basically all of the normal food cues that we would experience at a meal.
You know, eating, it's complicated, and it's influenced by many different variables, number of people who are there, the types of food, all of your habits, the time of day.
And they were trying to say, like, if we strip all of that away, and we, you know, what does food intake going to look like?
And so they had people in this hospitalized setting where they could control their food intake completely, and they gave them access to this bland liquid diet.
And essentially what people had to do was press a button on this machine that dispensed 7.4 milliliters of this bland liquid diet directly into their mouth every time they pressed the button.
And you could press the button as many times as you wanted per day.
And you were not instructed on how much you should be eating, and they just left people to their own devices to see, you know, what their eating behavior would be like.
And what they saw was that in lean people, lean people basically maintained their normal calorie intake on this setup.

So their calorie intake really didn't change at all, and their weight didn't change.
However, when they did the same thing in people with obesity, what they saw is that their calorie intake plummeted.
So they went from eating, you know, probably 27, 3000 calories per day down to like a few hundred calories a day.
And again, they were not asked to restrict their food intake.
This was the instinctive, intuitive output of their own brain.
This was how much their brain was driving them to eat.
And it was a strikingly small amount.
Once you strip away all of the food cues, all of the food reward, all of the food cues.
And they had people on this regimen for weeks, and they were maintaining this very low calorie intake and losing weight at a rapid rate.
There was one person who actually maintained it for a year and lost, if I'm recalling correctly, half his body weight.
So yeah, it's just an interesting illustration of the impact that all of these food properties have on these non-conscious circuits that impact our calorie intake.
So it's interesting and weird, I think it's kind of intuitive and also misleading.
And this gets then to the other side of this, because I think you could listen to some of the studies we just spoke about and say, okay, we've solved it.
Just put people on a bland diet for six or eight or 12 or 24 weeks, lose a bunch of weight, and we'll be good here.
But then there was these other regulatory systems.
So tell me a bit about the body's set point.
So the first concept to understand is that there is a regulatory system for body fat in the brain.
And it's in a part of the brain called the hypothalamus that specializes in what's called homeostatic regulation.
And so that means keeping certain quantities in the body within a particular desired range.
So for example, there is a thermostat in your brain that regulates your body temperature.
So that's one of the things that is regulated homeostatically in a manner that's analogous to how your home thermostat regulates the temperature in your home.
And similarly, there is a system for regulating body fatness that some, including me, call the lipo stat.
So lipo is fat and stat is the same.
And this system responds to a variety of signals.
Some of the signals it responds to have actually been uncovered since I wrote my book.
But the main one, the most powerful one that it responds to is a hormone called leptin that is secreted by fat tissue.
And the way leptin works is that it is secreted by fat tissue in proportion to its mass.
So the more fat you have, the more leptin you have in circulation.
And that is a key signal that the brain uses to measure the amount of fat your body has and to determine whether that is an appropriate amount of fat.
So essentially, your hypothalamus has an idea of how much fat it wants you to have, and

it compares your circulating leptin level to that idea.
So that idea is the set point, that term that you mentioned, or a defended level of body fat, just like we have a defended level of body temperature.
We have a defended level of body fat that the hypothalamus prefers not to depart from.
And this system, I want to note that it's asymmetric in that it's a lot better at protecting against weight loss.
I guess I should put protecting in air quotes.
It's a lot better at protecting against weight loss than it is at protecting against weight gain.
Obviously, people tend to gain weight over the course of their lives.
So what we see is that the set point tends to creep up as people gain weight.
So it's not just that people are gaining weight.
It's that the heavier weight is the new normal, the new defended level for the brain.
It's the new set point.
And the way we know that is that when you put people on a weight loss diet, you tend to see rebound.
So a person, just to give you an example to highlight this, if you have two people at the same body mass index, the same body fatness, let's say BMI of 25, one of them used to have obesity and dieted down through calorie restriction to that level.
The other person has always been at that level and that's their comfortable weight.
Then if you follow those two people up for the next few years, you're going to see that the person who previously lost weight is much more susceptible to weight gain than the person who has always been at that weight.
So those two people are not the same physiologically.
One of them is below their set point and their brain is fighting to regain that fat.
And so this is a key reason why weight loss is difficult.
Your brain, once the body fat starts to decline and the leptin starts to decline, your brain detects that and initiates what I call a starvation response, which I believe that phrase is literally accurate and that engages a suite of behavioral and physiological responses that are intended to increase your calorie intake and sometimes curtail your metabolic rate in order to get fat back into that fat tissue and bring you back to the set point, the place where your brain instinctively prefers you to be.
Yeah, you have a nice analogy on this where you say, imagine someone turning up the temperature on the thermostat in your house by 10 degrees and you try to cool the house down by opening the windows, but the thermostat reacts by turning on the furnace.
So even with the windows open, you're still hotter than you'd rather be or you're struggling against regulatory system.
And then my colleague, Roger Carmba, I thought had a nice addition to this.
It's really like a thermostat with a broken AC system because on the one hand, if you go low, it'll turn on the heat to try to get you higher again.
If you lose 15 or 20 or 25 or 30 pounds or in this analogy, go down that many degrees, the heat turns on and you really, really have to fight it.
Whereas if you go up by that much, the AC doesn't turn on.

Nothing happens or much less happens, maybe I should say, to bring you back down.
Yeah.
And so it's a very frustrating reality.
Yes, absolutely.
And you know, I think that highlights this evolutionary mismatch that this system was not designed for the modern environment.
It wasn't designed for the challenges that we face today.
I do want to say though that the AC does work for some people.
So you can see this in overfeeding trials where they have people in a controlled environment eating a specific number of excess calories.
Some people gain a lot more fat than others in that scenario.
And that resistance to fat gain is something that has a tremendous amount of individual variability.
And so I think some people do have good AC.
Maybe people's AC gets weaker and weaker with age.
I think that would be a compelling hypothesis to test.
But I think also how good your AC is is one of the things that determines whether a person is susceptible to obesity or not.
That's a very good addition to that.
Tell me about the biggest loser study.
Yeah.
So this is a really interesting one.
So I think probably listeners will be familiar with the show, The Biggest Loser.
They are going through this extreme diet and physical activity intervention in order to try to lose a large amount of weight very quickly.
And it's, you know, a high pressure competitive environment.
And people do lose a lot of weight.
So, you know, it's not uncommon for people to lose more than 100 pounds.
But what you see is that if you follow up with those people after the show, they tend to regain a lot of that weight.
And this is typical, you know, this is what we see in weight loss trials as well.
But to take the big picture on it, this study, like many, many other studies, all those, this was a very extreme version because of The Biggest Loser's extreme nature as a project.
It shows that even when people do do this hard thing of successfully losing weight, the proportion to keep it off over five years, let's call it, is fairly low.
And yet sometimes I'll read or listen to work on this and hear people describe it.
And there does have a tendency to be a, like, who are you going to believe?
All these studies are your lying eyes because we all do know people who have lost weight and kept it off for long periods of time, who have changed their bodies quite dramatically.
And so how do you think about the sort of unbelievable pessimism that I think has begun to be dominant in the way we talk about this?
And in some of these studies, you know, you hear things like 95% of all diets fail, that kind of thing.

And also the reality that the people do lose weight, they do in many cases or in some cases keep that weight off.
What's going on there for them?
I think there is a lot of pessimism and I think some of that is justified.
You know, we have these randomized controlled trials, which is a gold standard for determining cause and effect in domains of health and nutrition.
And these trials are suggesting that if you put people on a diet and lifestyle weight loss program, you know, if your program is good, maybe they'll lose something like five to 7% of body weight.
And then over the next few years, on average, even if they're trying to maintain that loss, they will tend to regain most of that weight.
And so, you know, that's the reality of the situation, but it's absolutely true that there are people who can lose a lot of weight and maintain that.
But the problem is, you know, when we look around us and we see individual examples of people who are losing a lot of weight and maintaining it, you know, that's very susceptible to bias because we don't see all the people who tried to lose weight and weren't able to do it successfully.
And I think there are a lot of those people.
In fact, if you look at the statistics from the Centers for Disease Control, they do surveys on obesity prevalence and what kind of weight loss behaviors people are engaging in.
And you can see that two-thirds of people with obesity each year engage in some sort of weight loss effort in the United States.
So people with obesity, most of them are actively trying to lose weight every year and not succeeding.
So I think it's really easy to get confirmation bias, and I think that is something that makes us think that weight loss approaches are better than they are.
Like when you're looking at, you know, whatever the diet is you're interested in, you go on their website.
They're going to be highlighting the success stories of Suzy who lost 100 pounds and kept it off for a million years, but that's not typical results.
That's just the best results.
So before we talk about some of the new treatments, given that I agree with you, the data is extremely
clear that diet and exercise are not reliable for the vast majority of people in over any kind of significant period of time.
There's a question of should we worry about this at all, right?
There are arguments about whether or not obesity really does have that much of an effect on health, whether or not some of that is simply bias or improperly understood studies.
How do you understand at this point the relationship between obesity and health?
Yeah, I think there is a very strong relationship between body fatness and health, and I think that relationship is causal.
I think if you have a large amount of excess body fat that is going to contribute to an adverse metabolic milieu in your body that is going to increase the risk of type 2 diabetes

and cardiovascular disease, certain types of cancers, and a wide variety of other conditions that we don't want to have.
In fact, I think that now that cigarette smoking is receding in the United States and infectious diseases are not as much of a problem as they were 100 years ago.
I think physiological energy excess, having too much energy in the body, I would say is probably the number one cause of health problems in the United States at this time.
Too much energy in the body being too much excess stored fat?
Yeah, I think it's a little bit more complicated than that.
Really, what it is is excess energy exposure to lean tissues, and that is related to the amount of body fat you have, but a lot of it relates to your body fat's capacity as well.
If you have the ability to store and sequester, because fat tissue is the body's professional fat storage organ, that's where fat is supposed to be in your body, but once you get too much fat in your fat cells and they lose the ability to effectively sequester it, now you've got a lot of spillover going on to tissues that can't handle it constructively.
That's really where you're going to start getting insulin resistance, the type 2 diabetes, the cardiovascular disease.
You're going to get fat in your liver, you're going to get in your muscle and your pancreas.
That's where you're going to start seeing the more serious metabolic consequences.
Depending on the individual that can happen at different amounts of body fat doesn't necessarily take a lot.
There's been a lot of debate about this, and I want to acknowledge that there's a spectrum of opinions in the scientific community about the relationship between body fatness and health, but I think it seems pretty clear to me that there is a strong relationship.
We could get into the methodological details of why I think that.
I don't want to get too...
Well, let me get into one dimension of it just because I want to make sure this perspective is heard, which is that we have a lot of observational studies here.
There's often a sense that it's very hard to untangle obesity from other things like lack of exercise, discrimination in medical care, poverty.
There's a lot of correlation between socioeconomic conditions and obesity, but that also then correlates to bad sleep, it correlates distress, it correlates to a bunch of other things.
There's one argument I have heard made quite a bit, is that there's an over attribution of negative health consequences to obesity, which frames fat itself or excess fat storage or exposure to lean tissue or whatever, as the causal mechanism when it's actually downstream of the causal mechanisms.
How do you think about that?
Yeah, I mean, I'm sure that that's true to a certain extent.
Observational studies, there's a million things that could potentially confound them, and I'm certain that what you said is part of the story.
However, we have intervention studies.
We don't have to just rely on observational studies.
We have intervention studies in humans, we have intervention studies in animals.

These are best developed in the case of type 2 diabetes.
Type 2 diabetes risk is exquisitely sensitive to body fatness.
We have a number of huge randomized controlled trials in humans showing that if you take people with pre-diabetes, so they have metabolic disturbances suggesting that they're at a high risk of developing type 2 diabetes, you put them on a weight loss diet, you can dramatically reduce their risk of progressing to type 2 diabetes.
You can even take people who have type 2 diabetes, and if you get them to lose enough weight, what you will see is that their lean tissues, the fat in their lean tissues will start to clear out, and their type 2 diabetes will go into remission.
You can literally reverse people's type 2 diabetes just by restricting their calorie intake and causing them to lose fat.
At the same time, you see improvements in other risk factors like blood pressure, blood lipids, things that are known to contribute to cardiovascular disease.
You see the same thing with bariatric surgery.
Major weight loss via bariatric surgery is associated with stunning improvements in health outcomes.
You reduce your risk of developing diabetes by 80-some percent.
You reduce your risk of cardiovascular disease by something like 50 percent.
You reduce your risk of developing certain cancers of all cause mortality.
The effects are huge.
If you look at the intervention studies, there's really, in my mind, there's very little room for different interpretations other than that body fat has a major impact on our health.
So I think if you back up five years, our conversation is pretty current right then.
And where this then goes is the problem is we don't have a good intervention.
Individual willpower, diet and exercise, kinds of interventions, they don't really work.
Not for most people, not for very long.
You can imagine very heavy-handed regulation that would change the environment.
The light things like caloric labeling and trying to address food deserts, that hasn't really worked.
Heavy things like you saw in Denmark, attacks on saturated fat-rich foods, they had to scrap it because it was so politically unpopular, New York City banned large sodas in 2013.
That was repealed by a court.
So the idea that you're going to radically change the food environment through legislation, that's not really there either.
It's a bariatric surgery, that's a pretty intense kind of medical intervention.
And then, I mean, I know it's not truly indirect development all of a sudden, but it really feels like all of a sudden you now have this new class of drugs, semi-glutides, that are seeing a totally different kind of effect.
So tell me a bit about these new drugs and how their effects compare to what we've seen before and how they work, how they create those effects.
Yeah, so just to give you a basis for comparison, as I said before, an effective, best in class behavioral weight loss program.
So that means diet and lifestyle for the average person is going to produce something

like five to seven percent weight loss, and that will gradually diminish over the years.
So they'll have a tendency to regain over the years.
So that's not nothing, but it's not as much as most people would prefer, not as much as their doctors would prefer.
We've talked about some of the reasons why that's the case.
We have these brain systems that push back against weight loss and tend to cause us to regain.
And so there are a lot of people who have been doing research on these brain systems, trying to understand how they work and trying to find ways to target them.
And, you know, my book is about trying to understand these brain systems, but at the time I wrote it, we didn't have these new GLP-1 receptor agonists like somagelotide.
And so I think it's really interesting that that is exactly what these drugs do.
They target these brain circuits that regulate food intake and body fatness.
So somagelotide, just to give you first the percentages, somagelotide in randomized controlled trials, which again is that rigorous way of measuring biological effects, causes typically 15 to 18 percent loss of body weight.
So it's much more effective for weight loss than your typical behavioral weight loss program.
And it's based on a hormone called GLP-1 that is secreted in the gut when we eat food.
The distal small intestine and signals from the gut to the brain.
It's also a neurotransmitter that's used in the brain stem as part of satiety processing.
So that process that we talked about earlier, how the brain accumulates information about what we've eaten and eventually generates the satiation or satiety response that causes us to terminate a meal.
So basically this drug goes into the brain and it stimulates these satiety circuits in the brain.
And what you see is people's calorie intake drops by quite a lot.
They lose weight and they gain better control over their eating behavior.
And what is the experience of being on a drug like this?
What would I feel if I were on it?
How do I administer it?
What are some of the side effects?
Just subjectively, what is it like to try one of these therapies?
Yeah, so I've never been on them and I'm also not a doctor.
I don't work with patients who have been on them.
So what I know about it is just from hearing people describe it, hearing patients describe it, hearing doctors describe it.
It is an injection, it's a very small injection that you do once a week.
And typically what would happen is you would start on a very low dose and frequently people will start off experiencing some gastrointestinal side effects.
So things like nausea or diarrhea or constipation.
Typically those are things that happen in the beginning during the dose escalation phase.
So you would gradually escalate the amount that you're taking over a period of a couple of months.

And usually by the time people are done escalating, they aren't experiencing those side effects anymore.
What they are continuing to experience is that they're not as hungry anymore.
They're not experiencing the same type of cravings for food.
So cravings are greatly reduced.
You're not, you know, food is not as seductive to you as it used to be.
You're not losing control over your eating behavior like you used to.
And that's actually one of the most marked and durable effects of semaglotide.
So it's really targeting both these circuits that drive us to eat energy as well as the circuits that determine the seductiveness of food, the reward value of food.
And interestingly along those lines, people report that they also often experience a reduced drive to engage in other reward driven behaviors like drinking alcohol and online shopping.
So that's additional evidence that it targets reward circuits.
And in fact, there's research happening right now in the drug addiction field, looking at the ability of these drugs to target addiction.
And in fact, that's common for a lot of obesity drugs.
So a lot of the weight loss drugs that we have target pathways in the brain that are related to food reward and addiction.
And one of the things that, at least I've read about this, is the thermostatic set point the effect is not wiped out here.
So one concern people have is that these therapies are functionally forever therapies, that in the cases where people have used them and use them successfully and then gone off them.
I mean, they are expensive.
They're about $15,000 a year right now.
That there's the kind of same snapback effect you see on other things that your body turns up the heat again and you have a lot more appetite and it wants to get you back to where you were.
Is that a fair description of what you've seen in the research and in the studies?
Yes, when you stop taking the drug.
I think it's important to contextualize this though.
And by the way, I think the cost of these drugs is a really huge barrier.
And I think that is an important one to acknowledge.
But it's important to contextualize that any weight loss intervention that you're doing, if you stop doing it, you're going to regain the weight.
So that's not something that's unique to somagotide.
That's something that happens for any kind of weight loss method.
In a perfect world, we would be able to drop the weight and then stop doing whatever we're doing and just cruise at the new weight.
But that's not how the hypothalamus works.
The hypothalamus and the rest of the brain is determining your weight based on the signals that you're feeding it.
And if you stop feeding it, those slimming signals, it's going to go back to the weight where you were.

So there's that context.
And then there's also the context of other drugs like antihypertensive medications, so blood pressure drugs and drugs for cholesterol.
Those drugs, the benefits only last for as long as you're taking the drugs.
You don't expect your cholesterol to stay low if you go off of the cholesterol-lowering drug.
So as much as we would love to have a drug that permanently resets the set point, take it temporarily and permanently reset it, that unfortunately is not what we have currently.
I want to talk about some of the other things we've seen in the studies here.
So you have a great piece on this.
And you write that in two of these major trials, somaglutide reduces major cardiovascular events by 21% to 24% and people type 2 diabetes and high cardiovascular risk respectively.
That's comparable to commonly used cholesterol-lowering drugs.
So it seems that we're not just seeing a reduction in weight, but we're also seeing a reduction in the sort of dangerous events that have been at least associated with high weight.
Is that fair?
Absolutely.
And I think this is consistent with other weight loss methods like bariatric surgery.
There's also a meta-analysis of voluntary diet weight loss trials showing that it reduces all cause mortality.
So I think this is pretty consistent with at least some other weight loss methods.
That said, it is absolutely not a given that a weight loss drug will improve your health.
And in fact, in that piece that you mentioned, I discussed several examples of weight loss drugs that were actually catastrophic for people's health.
One of them that I think I didn't include in that piece, but one of the best examples is FENFEN, which is a combination of two drugs that cause massive cardiovascular harm.
So at the time that people were taking FENFEN, it was relatively effective weight loss drug relative to the other options that were available, but it damaged the heart.
So it wasn't the weight loss itself that was unhealthy, it was the side effects of this drug on the cardiovascular system.
So if you can get a drug that causes weight loss without causing catastrophic side effects for health, then I would very much expect it to benefit health.
Now, of course, that needs to be directly demonstrated with any intervention like this.
But thus far, the evidence we have for somagelotide and that drug class suggests that that does apply.
And are we confident in the duration of that evidence?
I mean, we're talking here about drugs people might be on functionally for their entire lives.
They at least seem to many to be quite new in the market.
I mean, they certainly are new in terms of being widely prescribed.
Are we confident that five years from now, 15 years from now, it's not going to be another one of these, oh, yeah, that definitely seemed good at the time, but it turns out it causes total like taking a wrecking ball to your lungs or something.

I don't think that we have enough evidence to completely exclude long term adverse effects.
That said, we actually have a lot of data on this drug class.
So not somagelotide, but other related drugs stretching back for 18 years.
And as far as we can tell, it's a very safe drug class.
The other thing, so we have evidence suggesting that cardiovascular risk is lower that in people with type two diabetes, all cause mortality is reduced by somagelotide.
And we have thousands and thousands of people who have gone through randomized controlled trials at this point, they're relatively short term.
I think the longest one has been maybe two years.
And so I would say, somagelotide has been in use for a while for diabetes.
And there are people who have been using it off label for obesity at the current dosage that is now FDA approved and is called WIGAV.
And so we do have data, we have years of data, we don't have two decades of data on somagelotide per se.
So is there some uncertainty remaining?
Yes, absolutely.
But I think you have to consider that a person who has obesity and is not being treated for that is already at substantial risk of health problems.
And so the question is based on what we know right now of the demonstrated benefits of no real signal of harm and of the harm of not doing anything, where is the cost-benefit balance for this?
And to me, I think it's an absolute win, but I cannot completely exclude the possibility that we'll learn something bad at some point in the future about it.
I just think it's very unlikely.
One of the weird reports that is being seen a lot that you read up is that these aren't just reducing food cravings, we're also seeing sort of a wide spectrum of dopamine-backed behaviors go down, including drinking alcohol, including late night Amazon shopping.
Tell me a bit about that and the theory around it.
I think these kinds of effects are a little bit surprising to some people, including me, because if you look at the site of action of these drugs, the primary site of action is in these satiety centers in the brainstem.
And so why would affecting satiety and hunger, why would that impact things like drug use and shopping, other reward-driven behaviors?
And there are some suggestions in the scientific literature that this drug might target some reward-related regions directly, but it's really not clear how that happens.
What we do know is that downstream of these initial cells that actually have the GLP1 receptors, you do get activation of, you get changes in activity in reward-related regions.
And so it's not really clear to me whether it's like this drug has two effects.
One is specifically on reward in general.
One is on appetite, and those both converge on the weight loss effect or whether the effects on reward are downstream of the effects in these satiety circuits, and all of what we're seeing is ultimately coming from these satiety circuits.
So I think it's really not clear, but I think it is an interesting observation that if you

look at the most effective obesity drugs that we have, pretty much all of them target both of those things, the reward and the appetite.
Tell me a bit about what looks to be the next generation of these drugs or combination drugs or therapeutic approaches.
So I mean, it's a great time for this research field, and it's a great time for the pharmaceutical industry in this area.
Let me just say, first of all, I have no conflicts of interest with the pharmaceutical industry, just to make that clear.
But there are lots of drugs in the pipeline right now that are very exciting for weight loss and obesity management.
So the one that I'll start with is called Terzepotide, and that is from Eli Lilly.
And that is also a similar type of drug to Somagelotide.
It's based on the GLP1 hormone.
It's kind of interesting.
It's a combination.
It also has another hormone, GIP.
It's both of those fused together.
And that one, that drug appears to be even more effective than Somagelotide.
So if you look at the amount of weight loss that's produced by it, it's more in the kind of 18 to 22% range rather than the 15 to 18% range of Somagelotide.
So it's a little bit more effective.
It's also a little bit more effective for treating diabetes, which is where both of these drugs came from initially.
And then we just have other drugs that are being developed that are kind of in a similar class based on the GLP1 signaling pathway.
And it's really interesting.
This kind of gut to brain communication highway is really the thing that's been the most productive in the development of weight loss therapy.
So if you look at bariatric surgery, you're modifying the digestive tract in order to alter eating behaviors and eating drive.
And with these drugs, you're modifying gut brain communication as well.
So it's been really a very productive pathway.
One of the things that I'm really interested in is a drug that Pfizer is developing that is a small molecule GLP1 receptor agonist.
And the advantage of that is you can make it into a pill that you can just eat and possibly longer shelf life, possibly lower production costs.
And that solves a lot of the kind of technical problems with these GLP1 receptor agonists.
So that's currently in the clinical trial pipeline.
I don't know whether it will eventually become an FDA approved weight loss drug, but right now it looks really promising.
I want to, as we kind of end here, zoom out to what seems like a slightly weird picture, at least a picture to fully appreciate.
We've talked about sort of the way the brain evolved.

We've talked sort of negatively, but you can really see it, I think, as a remarkable achievement of human civilization that at least for many of us, not everybody in the world, of course, the problem is this food abundance and this technological creation of foods that are unbelievably tasty and sugary and salty and palatable.
It's just a joy to eat a lot of this food and we have the ability to do it all the time.
And that we've done this and now we're having to create very expensive injectable drugs to rework our brains so we can survive in this food environment that we have created by choice.
Such that it doesn't make us sick over time.
There's just a strangeness to it that I'm curious if you have any thoughts or reflections on.
Yeah, it is very strange.
I think if we zoom out and take the bigger picture, essentially, with the progress of technology and affluence, we have gotten increasingly good at satisfying our own innate preferences.
We see that with food, we see it with information like social media and other media.
We see it with pornography, et cetera, et cetera, et cetera.
And I think, essentially, we're just fulfilling our own preferences so hard that we're creating problems for ourselves.
And now through this same affluence in technology, we're trying to create technological solutions for these problems that are created by this evolutionary mismatch.
And I don't think this is the world that any of us want.
I don't think we want to be in a situation where we are creating massive problems for ourselves and then having to solve them through technology.
I think all of us would rather live in a world where those problems were not there in the first place, but that's not the world we live in.
And this is the world we've created, too, like you said.
We created this through consumer demand, our food environment, our media environment, et cetera.
And it's not all a bad thing, of course.
There are many good things about it.
But at this point, it's hard to see a solution that is not technological, in my opinion.
Is this just the condition of modernity on some level?
When I look at this issue, it feels, actually, in many ways, very similar to things like climate change.
We have had this amazing success in creating energy abundance that energy abundance has created, energy abundance for some, maybe is what I should say there, but that abundance of energy compared to the history of our species has created terrible effects.
And now we are coming up with a lot of technological solutions that I think are actually the most realistic solutions.
I'm not somebody who believes we're going to get people to stop using energy, but we're going to have a lot of lithium mining, and maybe eventually we're going to have geoengineering, and we've got to put solar panels everywhere, and wind turbines everywhere, and run electric

transmission everywhere.
And sometimes I feel like it's all the same story playing out again and again in a ways what Elizabeth Colbert's Under a White Sky is about.
But these problems of control, like we have had amazing successes controlling our world, that then creates difficulties, sometimes really profound ones.
And then we have to control those problems, and then we have to deal with the problems of the controls we put in place.
And it can sometimes feel like wildly coyote, just like always running a little bit ahead of the realization of what we've done.
But on the other hand, on the other side of it, these are really amazing human achievements.
And I kind of can't quite tell what to do with the feeling of weirdness, it inspires.
But on the other hand, I think as you're saying here, we're not going back to the days of food scarcity, or we don't want to anyway, and I don't think we're going back to days of not having enough energy and not having cars and so on.
And so maybe it's something to embrace rather than feel strange about.
Yeah, I think that's a great analogy.
I would say that one place where our food environment diverges from that analogy is that climate change is a collective problem, whereas obesity is an individual problem.
I mean, it has societal influences, of course.
But the one person having obesity doesn't affect other people having obesity.
And so I think, and where I'm going with this is that as an individual, you can make a difference for yourself.
So I think that on a societal level, it's hard to imagine a solution that is not technological, in my opinion, because I just don't see us regulating our food environment to such an extent that it reverses the obesity epidemic.
However, on an individual level, we can absolutely improve our own food environment and reduce our own risk of obesity.
So I think that's a place where, at contrast with climate change, where with climate change, you can control your own carbon dioxide production, but it's a drop in the bucket in terms of global CO2 levels.
I think that's a fair point.
I think it's all a good place to end.
So always our final question.
What are the three books you'd recommend to the audience?
So the first one I want to recommend is Herman Ponser's book, Burn.
It's a really great book on several levels.
First of all, it's really well-written, really entertaining, and second of all, as opposed to a lot of nutrition books or nutrition and physiology-related books that make big claims about having some kind of incredible discovery about the human body, this book actually does have an incredible discovery about the human body, and it relates to the relationship between our energy expenditure and our physical activity level, which we were discussing earlier.
Just a really great book.

Second one I want to recommend is Michael Moss's Salt Sugar Fat, also a really entertaining book, and it really details the kind of path that the food industry took that brought us to where we are today in terms of our current processed food environment in the United States. It's really interesting behind the scenes look at that.
And the third book I want to recommend is The Secret of Our Success by Joe Henrich. Joe Henrich is an anthropologist who has some really interesting ideas about what it means to be human and what is special about the human species that made us so successful relative to other species.
Jeff in DNA, thank you very much.
The Ezra Clanj is produced by Emma Fagawu, Annie Galvin, Jeff Geld, Rochette Karma and Kristen Lin.
Fact-checking by Michelle Harris and Kate Sinclair, mixing by Sonja Herrero, original music by Isaac Jones, an audience strategy by Shannon Busta.
The executive producer of New York Times opinion audio is Annie Rose Strasser, and special thanks to Pat Bacusker and Christina Semiluski.