Why Do We Crave Sugar? | Dr. Charles Zuker & Dr. Andrew Huberman

Let me tell you it about the gut brain axis and our insatiable appetite for sugar and fat insatiable for sugar and quenchable for fat And this is a story about the fundamental difference between liking and wanting like in sugar is the function of the taste system And it's not really liking sugar It's liking sweet one tin sugar our never ending appetite for sugar It's the story of the God brain access liking versus wanting And this work is work of my own laboratory You know that began long ago when we discovered the sweet receptors and you can now engineer mice that lack these receptors So in essence these animals will be unable to taste sweet a life without sweetness How horrible And if you give a normal mouse a bottle containing sweet and we're gonna put either sugar or an artificial sweetener All right they both are sweet they have slightly different tastes But that's simply because artificial sweeteners have some off tastes But as far as the sweet receptor is concerned they both activate the same receptor trigger the same signal And if you give an animal an option of a bottle containing sugar or sweetener versus water This animal will drink 10 to 1 from the bottle containing sweet That's the taste system Animal goes samples each one licks a couple of licks and then uh uh that's the one I want because it's appetitive and because I love it So it prefers sugar to artificial sweetener No no no no no This experiment this experiment I'm gonna put only sweet in one bottle and it could be either sugar or artificial sweetener It doesn't matter which one OK We're gonna do the next experiment where we separate those two For now it's sweet versus water And sweet means sweet not sugar sweet means anything that tastes sweet All right And sugar is one example And splendor is another example Aspartame monk fruit doesn't matter I mean there's some that only humans can taste mice cannot taste because their receptors between humans and mice are different But we have put the human receptor into mice We engineer mice and we completely humanize this mouse's taste world All right But for the purpose of this conversation we're only comparing sweet versus water an option My goodness they will leak to know in you know from the sweet side 10 to 1 at least versus the water makes sense All right Now we're gonna take the mice and we're going to genetically engineer it to remove the sweet receptors So these mice no longer have in their oral cavity any sensors that can detect sweetness be that sugar molecule be it an artificial sweetener Be it

anything else that tastes sweet And if you give this mice an option between sweet versus water sugar versus water artificial tuna versus water it will drink equally well from both because he cannot tell them apart because it doesn't have the receptor for sweet So that sweet bottle tastes just like water makes sense makes sense Very good Now we're gonna do the experiment with sugar from now on let's focus on sugar So I'm gonna give a mouse Now sugar versus water Normal mouse would drink from the sugar sugar sugar sugar very little from the water knock out the sweet receptors eliminate them Mouse can no longer tell them apart and they will drink from both But if I keep the mouse in that cage for the next 48 hours something extraordinary happens when I come 48 hours later and I see what the mouse is leaking or drinking from The mouse is drinking almost exclusively from the sugar bottle How could this be He can taste It doesn't have sweet receptors during those 48 hours The mouse learn that there is something in that bottle that makes me feel good and that is the bottle I want to consume Now how does the mouse identify that bottle It does So by using other sensory features the smell of the bottle the texture of the solution inside sugar the high concentrations is kind of goopy the sides in which the bottle is in the cage It doesn't matter what but the mouse realized there is something there that makes me feel good and that's what I want And that is the fundamental basis of our unquenchable desire and our craving for sugar and is mediated by the gut brain axis The first clue is that it takes a long time to develop immediately suggesting a post ingested effect So we reason if this is true and is the gut brain axis that's driving sugar preference then there should be a group of neurons in the brain that are responding to post ingested sugar And lo and behold we identify a group of neurons in the brain that does this and these neurons receive their input directly from the gut brain axis from other neurons You got it And so what's happening is that sugar is recognized normally by the ton activates an appetitive response Now you ingest it and now it activates a selective group of cells in your intestines that now send a signal to the brain via the vagal ganglia that says I got what I need The tongue doesn't know that you got what you need It only knows that you tasted it This knows that it got to the point that it's going to be used which is the gu and now it sends the signal to now reinforce the consumption of this thing because this is the one that I needed sugar source of energy And these are these neurons in the gut So these are not neurons in the gut So these are gut cells that recognize the sugar molecule say send the signal and that signal is received by the vagal neuron directly got it and it sends a signal through

the gut brain axis to the cell bodies of these neurons in the vagal ganglia and from there to the brain stem to now trigger the preference for sugar Two questions one you mentioned that these cells that detect sugar within the gut are actually within the intestine You didn't say stomach which surprised me I always think gut as stomach but of course in intestine because that's where all the absorption happens So you want the signal you see you want the brain to know that you had successful injection and breakdown of whatever you consume into the building blocks of life and you know glucose amino acids fat And so you want to make sure that once they are in the form that intestines can now absorb them is where you get the signal back saying this is what I want OK Now let me just take it one step further and this now sugar molecules activate this unique gut brain circuit that now drives the development of our preference for sugar Now a key element of this circuit is that the sensors in the gut that recognize the sugar do not recognize artificial sweeteners at all Not because of their nutrient value is uncoupled from the taste Generically speaking one can make that by this because it's a very different type of receptor I see it turns out that it's not the tongue receptors being used in the gut is a completely different molecule that only recognizes the glucose molecule not artificial sweeteners This has a profound impact on the effect of ultimately artificial sweeteners in curbing our appetite Our craving our insatiable desire for sugar since they don't activate the gut brain axis they'll never satisfy the craving for sugar like sugar That and the reason I believe that artificial sweeteners have failed in the market to curb our appetite Our need our desire for sugar is because they beautifully work on the tongue The liking to recognize sweet versus non sweet but they failed to activate the key sensors in the cat that now inform the brain you get sugar No need to crave more So the uh the issue of wanting can we relate that to a particular set of neurochemicals upstream of So the pathway is so glucose is activating the cells in the gut that through the vagus that's communicated through the presumably the nodose gangland and up into the brain stem very good And from there where does it go Yeah where is it going What is the substrate of wanting I uh you know of course I think molecules like dopamine craving there's a book even called the molecule of more et cetera et cetera Dopamine is a very diabolical molecule as you know because it evokes both a sense of pleasure ish but also a sense of desiring more of craving So um if I understand you correctly artificial sweeteners are and I agree are failing as a means to satisfy sugar craving at the level of nutrient sensing And yet if we trigger this true sugar evoked wanting pathway too

much And we've all experienced this then we eat sugar and we find ourselves wanting more and more sugar Now that could also be insulin disregulation But uh can we uncouple those Yeah I mean look if we have a mega problem with over consumption of sugar and fat you know we're facing a unique time in our evolution where diseases of malnutrition are due to over nutrition I mean how nuts is that e I mean historically diseases of malnutrition have always been linked to under nutrition And so we need to come up with strategies that can meaningfully change the activation of these circuits that control our wanting certainly in the populations at risk and this gut brain circuit that ultimately you know it's the lines of communication that are informing the brain the presence of intestinal sugar In this example it's a very important target in the way we think about Is there a way that we can meaningfully modulate the circuits So I make your brain think that you get satisfied with sugar even though I'm not giving you sugar So that immediately raised the question are the receptors for glucose in these gut cells susceptible to other things that are healthier for us That's very good excellent idea And I think an important goal will be to come up with a strategy and identify those very means that allow us to modulate the circuits in a way that certainly for all of those where this is a big issue he can really have a you know dramatic impact in improving human health