

## How Smell, Taste & Pheromone-Like Chemicals Control You | Huberman Lab Podcast #25

This episode I explain how we sense chemicals by way of smell, taste and pheromones. How things smell and taste and bodily chemicals of others have a profound effect on how we feel, what we do and our hormones. I explain the 3 types of responses to smell, the 5 types of tastes, the possible existence of sixth taste sense. I explain how smell and taste reflect brain health and can be used to assess and even promote brain regeneration. Both basic science and protocols are described including how to make sour things taste sweet and how to develop a heightened sense of smell and taste.

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Links:

1. What Is Color? By Arielle & Joann Eckstut

<https://www.amazon.com/What-Color-Questions-Answers-Science/dp/1419734512>

2. The smell of tears lowers testosterone

DOI: 10.1126/science.1198331

3. Inhaling (sniffing) improves non olfactory attention & cognition:

<https://pubmed.ncbi.nlm.nih.gov/31089297/>

#### 4. Smelling Salts & Improved Athletic Performance

<https://pubmed.ncbi.nlm.nih.gov/28922211/>

#### 5. Taste Receptors Are Expressed By Ovaries & Testes

doi:10.1093/molehr/gat009

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- Welcome to the Huberman Lab Podcast, where we discuss science and science-based tools for everyday life. [gentle music] I'm Andrew Huberman, and I'm a Professor of Neurobiology and Ophthalmology at Stanford School of Medicine. This podcast is separate from my teaching and research roles at Stanford. It is however, part of my desire and effort to bring zero cost to consumer information about science and science-related tools to the general public. In keeping with that theme, I'd like to thank the sponsors of today's podcast. Our first sponsor is Roka. Roka makes sunglasses and eyeglasses that in my opinion are the absolute best out there. The sunglasses and eyeglasses that are made by Roka have a number of properties that are really unique. First of all, they're extremely lightweight, you never even notice that they're on your face. Second, the optical clarity is fantastic. One of the things that's really hard to accomplish, but that Roka succeeded in accomplishing is making sunglasses that you can wear in lots of different environments. As you move from bright to shadowed regions for instance, or as the amount of sunlight changes many eyeglasses will make it such that it's hard to see your environment and you need to take the eyeglasses off, or you can't see or detect borders. With Roka sunglasses, all of that is seamless, they clearly understand the adaptation mechanisms and habituation mechanisms, all these fancy details about the human visual system have allowed them to design a sunglass that allows you to be in any environment and to see that environment extremely well. The eyeglasses are terrific, I wear readers at night and again, they just make the whole experience of reading or working on a screen at night very, very easy, very easy on the eyes. The aesthetic of the eyeglasses and sunglasses is also superb. You know, I chuckle sometimes when I see sports frames or sports glasses, a lot of them just look ridiculous frankly, but the Roka eyeglasses and sunglasses have a terrific aesthetic, they have a huge variety to select from. If you'd like to try Roka glasses, you can go to Roka, that's [roka.com](https://roka.com) and enter the code Huberman and you'll get 20% off your first order, that's [roka.com](https://roka.com) and enter the code Huberman to get 20% off your first order. Today's podcast is also brought to us by InsideTracker. InsideTracker is a personalized nutrition platform that analyzes data from your blood and DNA to help you better understand your body and help you reach your health goals. I'm a big believer in getting regular blood

work done for the simple reason that many of the factors that impact your immediate and long-term health can only be detected from a quality blood test. One of the major problems with blood tests however is that oftentimes you'll get information back about levels of metabolic factors, hormones, et cetera, and there won't be any directives about what to do with that information. With InsideTracker, it makes all of that very easy. First of all, they can come to your home to do the blood test and DNA test or you can go to a local clinic, they make that very easy. Second of all, when you get the information back about the levels of hormones, and metabolic factors, and other things in your blood it gives you simple directives. They have a dashboard that allows you to assess for instance, whether or not you ought to make changes in your nutrition, or changes in your exercise, or changes in your sleep regimen, any number of different lifestyle factors that can help bring the markers and the various factors in your blood and DNA to the appropriate levels. So, really they're putting you in the driver's seat for your health. In fact, one of the listeners of this podcast contacted me recently and said I took an InsideTracker test, I felt like I was in great health, but I noticed from the test that I had high CRP, C-reactive protein. C-reactive protein is a marker that if it's too high is a cautionary note about various cardiac and even eye diseases, so it's something that they are now taking actions on as a consequence of getting their blood work done and taking the InsideTracker test. So, I think that's just one of many examples that we hear about. I have examples from my own life for instance of different factors in my blood being off and making adjustments to nutrition and other aspects of my life that have allowed me to bring those into the proper range. So, if you care about your health InsideTracker may very well be right for you. If you'd like to try InsideTracker you can go to [insidetracker.com/huberman](https://insidetracker.com/huberman). And if you do that, you'll get 25% off any of InsideTracker's plans, just use the code Huberman at checkout. Today's episode is also brought to us by Athletic Greens. Athletic Greens is an all-in-one vitamin, mineral probiotic drink. I've been using Athletic Greens since 2012 so I'm delighted that they're sponsoring the podcast. Athletic Greens is terrific because it covers your nutritional bases. If I drink Athletic Greens once and I sometimes drink it twice a day, then I'm sure that all the vitamins I need, I'm getting those. All the minerals I need, I'm getting those, and the probiotics. There's now a ton of data showing that a healthy gut microbiome is vital to brain function, vital to immune function, and vital to all aspects of our health. So with Athletic Greens, you get the vitamins, the minerals, and the probiotics to cover all your bases. In fact, anytime people ask me what should they take or what could they do to

support their health, provided that they already have their sleep and other aspects of their life in order, Athletic Greens is the thing that I recommend because it covers all the foundations, all the bases of what one really wants from a supplement without having to take a ton of different things. It also tastes great, almost everybody that tries it and then reported back to me has told me that they really liked the taste. I mix mine with water, a little bit of lemon and lime juice, and I really like the taste, it's delicious to me. I drink it once or twice a day. It's keto compatible, it's compatible with most fasting regimens, it's compatible with if you're a vegan or if you're not vegan, it's compatible with essentially every nutritional plan out there, so it's just a terrific all around supplement and benefit to one's health and diet. If you'd like to try Athletic Greens, you can go to [athleticgreens.com/huberman](https://athleticgreens.com/huberman). And if you do that, you'll claim a special offer, they'll give you five free travel packs that make it easy to mix up Athletic Greens while you're on the road,

00:06:02 Sensing Chemicals: Smell, Taste & Chemicals That People Make To Control Each Other

and they'll give you a year supply of vitamin D3, K2. Again, go to [athleticgreens.com/huberman](https://athleticgreens.com/huberman) to claim that special offer. This month, we've been talking about the senses, how we detect things in our environment. The last episode was all about vision, how we take light and convert that information into things that we can perceive like colors, and faces, and motion, things of that sort as well as how we use light to change our biology in ways that are subconscious that we don't realize, things like mood, and metabolism, and levels of alertness. Today, we're going to talk about chemical sensing, we're going to talk about the sense of smell, our ability to detect odors in our environment. We're also going to talk about taste, our ability to detect chemicals and make sense of chemicals that are put in our mouth and into our digestive tract. And we are going to talk about chemicals that are made by other human beings that powerfully modulate the way that we feel, our hormones, and our health. Now, that last category are sometimes called pheromones. However, whether or not pheromones exist in humans is rather controversial, there actually hasn't been a clear example of a true human pheromonal effect, but what is absolutely clear, what is undeniable is that there are chemicals that human beings make and release in things like tears onto our skin, and sweat, and even breath that powerfully modulate or control the biology of other

individuals. In fact right now, even if you're completely alone, your chemical environment internally is being controlled by external chemicals, your nervous system, and your hormones, and your metabolism are being modified by things in your environment, so we're going to talk about those. It's an absolutely fascinating aspect to our biology, it's one of our most primordial, meaning primitive aspects of our biology, but it's still very active in all of us today. This episode, believe it or not, will have a lot of tools, a lot of protocols. Even though I'm guessing most of you can probably smell your environment just fine, that you know what you like to eat and what tastes good, and what doesn't taste good to you, today's episode is going to talk about tools that will allow you to actually leverage these chemical sensing mechanisms, including how you smell not how you smell in the qualitative sense, but how you smell in the verb sense, the action of sniffing and smelling to enhance your sense of smell and to enhance your sense of taste as well, believe it or not, to enhance your cognition, your ability to learn and remember things. Everything we're going to talk about as always is grounded in quality peer-reviewed studies from some excellent laboratories, I'll provide some resources along the way, so that means tools and protocols and also basic information. You're going to learn a ton of neuroscience and lot of biology in general. And I think what you'll come to realize by the end is that while we are clearly different from the other animals,

#### 00:09:10 Vision Protocols Recap (Brief) & Correction

there are aspects to our biology that are very similar to that of other animals in very interesting ways. Before we dive into chemical sensing, I want to just briefly touch on a few things from the vision episode. One is a summary of a protocol. So, I covered 13 protocols last episode, if you haven't seen that episode, check it out. Those protocols will allow you to be more alert and to see better over time if you follow them. All of them are zero cost, you can find any and all of them at [hubermanlab.com](http://hubermanlab.com), there's a link to those videos and tools and protocols, everything is timestamped. The two protocols that I just want to remind everybody of are the protocol of near-far viewing that all of us regardless of age, should probably spend about five minutes three times a week, doing some near-far viewing exercises. So, that would be bringing a pen or pencil up close to the point where you're about to cross your eyes, but you don't cross your eyes and then out at some distance. And then look beyond that pen or other object that you're using off as far as you can into the distance. It would be great if you could do this on a balcony or deck

and then look way off in the distance and then bring it back in. This is going to exercise that accommodation reflex, the change in the shape of the lens can help offset a number of things including myopia, near-sightedness. The other one is this incredible study that showed that two hours a day outside, even if you're doing other things while you're outside can help offset myopia, nearsightedness. So, try and get outside, it's really the sunlight and the blue light, right? Everyone's been demonizing blue light out there, but blue light is great provided it's not super, super bright and really close to your eyes. Blue is terrific if it comes from sunlight. Two hours a day outside is going to help offset myopia, nearsightedness. Now, that's a lot of time, I think most of us are not getting that time, but since you can do other things like gardening, or reading, or walking, or running. If you can get that two hours outside your visual system and your brain will benefit. I also would like to make one brief correction to something that I said incorrectly in the previous episode. At the end of the episode, I talked about lutein, and how lutein may help offset some moderate to severe age-related macular degeneration. As well, I talked about how some people are supplementing with lutein even though they don't have age-related macular degeneration with the idea in mind that it might help offset some vision loss as they get older. I said lutein, and lutein was the correct thing to say, but once or twice, when I started speaking fast I said leucine and not lutein. I want to emphasize that leucine, an amino acid, very interesting, important for muscle building covered in previous episodes, but lutein, L-U-T-E-I-N, is the molecule and compound that I was referring to in terms of supplementing for sake of vision. So I apologize, please forgive me I misspoke, a couple of you caught that right away, in listening to the episode after it went up I realized that I had misspoken. So, lutein for vision,

00:12:20 Color Vision: Excellent Resource: What is Color? (The Book)

leucine for muscles, and muscle growth, and strength, et cetera. Before we dive into the content of today's episode, I want to just briefly touch on color vision. Many of you asked questions about color vision and color perception. And indeed color perception is a fascinating aspect of the human visual system, it's one of the things that makes us unique. There are certainly other animals out there that can detect all the colors of the rainbow, some can even detect into the infrared, into the far-red that we can't see, but nonetheless, human color vision, provided that somebody isn't colorblind, is really remarkable. And if you're interested in color vision or you want to answer questions

about art or about for instance why that dress that showed up online a few years ago looks blue to you and yellow to somebody else. All the answers to that are in this terrific book which is "What Is Color?: 50 Questions and Answers on the Science of Color". I did not write this book, I wish I had, the book is by Arielle and Joann Eckstut, that E-C-K-S-T-U-T. So, it's "What Is Color?: 50 Questions and Answers on the Science of Color". It's an absolutely fabulous book, I've no business relationship to them. I did help them get in contact with some color vision scientists when they reached out to me. And you can know that all the information in the book was vetted by excellent color vision scientists. It's a really wonderful and beautiful book, the illustrations are beautiful. If you're somebody who's interested in design or art, or you're just curious about the science of color, it's a terrific book, I highly recommend it.

00:13:54 How We Sense Chemicals: Enter Our Nose, Mouth, Eyes, Skin

If you just look it up online, there are a variety of places that will allow you to access the book. So, let's talk about sensing chemicals and how chemicals control us. In our environment, there are a lot of different physical stimuli. There is light, photons, which are light energy and those land on your retinas and your retinas tell your brain about them, and your brain creates this thing we call vision. There are sound waves, literally particles moving through the air and reverberations that create what we call sound and hearing. And of course there are mechanical stimuli, pressure, light touch, scratch, tickle, et cetera, that lands on our skin or the blowing of a breeze that deflects the hairs on our skin, and we can sense mechanical touch, mechanical sensation. And there are chemicals, there are things floating around in the environment which we call volatile chemicals. So, volatile sounds oftentimes like emotionally volatile, but it just means that they're floating around out there. So, when you actually smell something like let's say you smell a wonderfully smelling rose or cake. Yes, you are inhaling the particles into your nose, they're literally little particles of those chemicals are going up into your nose and being detected by your brain. Also, if you smell something putrid, disgusting, or awful, use your imagination, those particles are going up into your nose and being detected by neurons that are part of your brain. Other ways of getting chemicals into our system is by putting them in our mouth, by literally taking foods and chewing them, or sucking on them and breaking them down into their component parts, and that's one way that we sense chemicals with this thing, our tongue. And there are chemicals that can

enter through other mucosal linings and other kind of just think damp, sticky linings of your body. And the main ones would be the eyes, so you've got your nose, your eyes and your mouth. But mainly when we have chemicals coming into our system it's through our nose or through our mouth. Although, sometimes through our skin certain things can go transdermal, not many, and through our eyes. So these chemicals, we sometimes bring into our body, into our biology, through deliberate action. We select a food, we chew that food, and we do it intentionally. Sometimes they're coming into our body through non-deliberate action. We enter an environment, and there's smoke and we smell the smoke, and as a consequence we take action. Sometimes we are forced to eat something because somebody tells us we should eat it or we do it to be polite. So, there are all these ways that chemicals can make it into our body. Sometimes however, other people are actively making chemicals with their body, typically this would be with their breath, with their tears, or possibly, I want to underscore possibly, by making what are called pheromones, molecules that they release into the environment typically through the breath that enter our system through our nose, or our eyes, or our mouth that fundamentally change our biology. I will explain how smell and taste and these pheromone effects work, but I'll just give an example,

00:17:28 The Chemicals From Other People's Tears Lower Testosterone & Libido

which is a very salient and interesting one that was published about 10 years ago in the Journal Science. Science Magazine is one of the three what we call apex journals. There are a lot of journals out there, but for those of you that want to know, Science Magazine, Nature Magazine, and Cell are considered the three top kind of apex journals, they are the most stringent in terms of getting papers accepted, they're even reviewed there. They have about a 95% rejection rate at the front gate, meaning they don't even review 95% of what gets sent to them. Of the things that they do decide to review then get sent out, a very small percentage of those get published, it's very stringent. This paper came out in Science showing that humans, men in particular in this study, have a strong biological response and hormonal response to the tears of women. What they did is they had women, and in this case it was only women for whatever reason, cry and they collected their tears. Then those tears were smelled by male subjects, or male subjects got what was essentially the control, which was the saline. Men that smelled these tears that were evoked by sadness had a reduction in their testosterone levels that was

significant. They also had a reduction in brain areas that were associated with sexual arousal. Now, before you run off with your interpretations about what this means and criticize the study for any variety of reasons, let's just take a step back. I will criticize the study for a variety of reasons too. One is that they only used female tears and male subjects, so it would have been nice for them to also use female tears and female subjects smelling those, male tears and male subjects smelling those, male tears and female subjects smelling those, and so on. They didn't do that, they did have a large number of subjects, so that's good, that adds power to the study. And they did have to collect these tears by having the women watch what was essentially a sad scene from a movie. They actually recruited subjects that had a high propensity for crying at sad movies, which was not all women. It turns out that the people that they recruited for the study were people who said, "Yes, I tend to cry when I see sad things in movies." What they're really trying to do is get just get tears that were authentically cried in response to sadness, as opposed to putting some irritant in the eye and collecting tears that were evoked by something else like just having the eyes irritated. Nonetheless, what this study illustrates is that there are chemicals in tears that are evoking or changing the biology of other individuals. Now, most of us don't think about sniffing or smelling other people's tears, but you can imagine how in close couples, or in family members, or even close friendships, et cetera, that we are often in close proximity to other people's tears. Now, I didn't select this study as an example because I want to focus on the effects of tears on hormones, per se, although I do find the results really interesting. I chose it because I wanted to just emphasize or underscore the fact that chemicals that are made by other individuals are powerfully modulating our internal state, and that's something that most of us don't appreciate. I think most of us can appreciate the fact that if we smell something putrid, we tend to retract, or if we smell something delicious, we tend to lean into it. But there are all these ways in which chemicals are affecting our biology,

00:21:16 SMELL: Sniffing, A Piece of Your Brain In Your Nose, 3 Responses To Smells

and interpersonal communication using chemicals is not something that we hear that often about, but it's super interesting. So, let's talk about smell and what smell is and how it works. I'm going to make this very basic, but I am going to touch on some of the core elements of the neurobiology. So, here's how smell works. Smell starts with sniffing. Now, that may come as no surprise, but no volatile chemicals can enter our nose unless

we inhale them. If our nose is occluded, or if we're actively exhaling it's much more difficult for smells to enter our nose, which is why people cover their nose when something smells bad. Now, the way that these volatile odors come into the nose is interesting. The nose has a mucosal lining, mucus that is designed to trap things, to actually bring things in and get stuck there. At the base of your brain, so you could actually imagine this or if you wanted, you could touch the roof of your mouth. So, right above the roof of the mouth, about two centimeters is your olfactory bulb. The olfactory bulb is a collection of neurons and those neurons actually extend out of the skull, out of your skull into your nose into the mucosal lining. So, what this means in kind of a literal sense is that you have neurons that extend their little dendrites and axon-like things, they're little processes as we call them, out into the mucus, and they respond to different odorant compounds. Now, the olfactory neurons also send a branch deeper into the brain and they split off into three different paths. So, one path is for what we call innate odor responses, so you have some hard wired aspects to the way that you smell the world that were there from the day you were born and that will be there until the day you die. These are the pathways and the neurons that respond to things like smoke, which as you can imagine there's a highly adaptive function to being able to detect burning things because burning things generally means lack of safety or impending threat of some kind. It calls for action, and indeed these neurons project to the central area of the brain called the amygdala, which is often discussed in terms of fear, but it's really fear and threat detection. So some compounds, some chemicals in your environment when you smell them, unless you're trained to overcome them because you're a firefighter you will naturally have a heightened level of alertness, you will sense threat, and if you're in sleep, even it will wake you up. All right, so that's a good thing, it's kind of an emergency system. You also have neurons in your nose that respond to odorants or combinations of odorants that evoke a sense of desire and what we call appetitive behaviors, approach behaviors, that make you want to move toward something. So, when you smell a delicious cookie, or some dish that's really savory that you really like, or a wonderful orange, and you say, "Mmm," or it feels delicious, or it smells delicious that's because of these innate pathway, these pathways that require no learning whatsoever. Now, some of the pathways from the nose,

00:24:40 Smells & Memory: Why They Are So Powerfully Associated

these olfactory neurons into the brain are involved in learned associations with odors. Many people have this experience that they can remember the smell of their grandmother's home, or their grandmother's hands even, or the smell of particular items baking, or on the stove in a particular environment. Typically, these memories tend to be of a kind of nurturing sort of feeling safe and protected. But one of the reasons why olfaction smell is so closely tied to memory is because olfaction is the most ancient sense that we have, or I should say chemical sensing is among the most primitive and ancient senses that we have, probably almost certainly evolved before vision and before hearing. But when we come into the world because we're still learning about the statistics of life about who's friendly and who's not friendly, and where's a fun place to be and where's a boring place to be, that all takes a long time to learn. But the olfactory system seems to imprint, seems to lay down memories very early and create these very powerful associations. And if you think about it long enough and hard enough many of you can probably realize that there are certain smells that evoke a memory of a particular place, or person, or context. And that's because you also have pathways out of the nose that are not for innate behaviors like cringing, or repulsion, or gagging, or for that appetitive mmm sensation, but that just remind you of a place, or a thing, or a context, could be flowers in spring, could be grandmother's home and cookies. This is a very common occurrence, and it's a very common occurrence because this generally exists in all of us. So, we have pathway for innate responses and a pathway for learned responses. And then we have this other pathway,

00:26:40 Pheromone Effects: Spontaneous Miscarriage, Males & Timing Female Puberty

and in humans it's a little bit controversial as to whether or not it sits truly separate from the standard olfactory system or whether or not it's its own system embedded in there, but that they call the accessory olfactory pathway. Accessory olfactory pathway is what in other animals is responsible for true pheromone effects. We will talk about true pheromone effects, but for example in rodents and in some primates, including mandrills. If you've ever seen a mandrill, they have these like big beak noses things, you may have seen them at the zoo, look them up if you haven't seen them already, M-A-N-D-R-I-L-S mandrills, there are strong pheromone effects. Some of those include things like if you take a pregnant female rodent or mandrill, you take away the father that

created those fetuses or fetus, and you introduce the scent of the urine or the fur of a novel male, she will spontaneously abort or miscarry those fetuses, it's a very powerful effect. In humans, it's still controversial whether or not anything like that can happen, but it's a very powerful pheromonal effect in other animals. Another example of a pheromone effect is called the Vandenberg effect named after the person who discovered this effect, where you take a female of a given species that has not entered puberty, you expose her to the scent or the urine from a sexually competent, meaning post-pubertal male, and she spontaneously goes into puberty earlier. So, something about the scent triggers something through this accessory olfactory system, this is a true pheromonal effect and creates ovulation, right and menstruation. Or in rodents it's an estrous cycle, not a menstrual cycle. So, this is not to say that the exact same things happen in humans. In humans, as I mentioned earlier, there are chemical sensing between individuals that may be independent of the nose. And we will talk about those, but those are basically the three paths

00:28:56 Sniffing Creates Alertness & If Done Properly Can Help You Focus & Learn Better

by which smells, odors impact us. So, I want to talk about the act of smelling, and if you are not somebody who is very interested in smell, but you are somebody who is interested in making your brain work better, learning faster, remembering more things, this next little segment is for you because it turns out that how you smell, meaning the act of smelling, not how good or bad you smell, but the act of smelling, sniffing, and inhalation powerfully impacts how your brain functions and what you can learn and what you can't learn. Breathing generally consists of two actions, inhaling and exhaling, and we have the option of course to do that through our nose or our mouth. I've talked on previous episodes about the fact that there are great advantages to being a nasal breather, and there are a great disadvantages to being a mouth breather. There are excellent books and data on this, there's the recent book "Breath" by James Nestor, which is an excellent book that describes some of the positive effects of nasal breathing as well as other breathing practices. There's also the book "Jaws" by my colleagues, Paul Ehrlich and Sandra Kahn, with a foreword by Jared Diamond and an introduction by Robert Sapolsky from Stanford. So, that's a book chockablock with heavy hitter authors that describes how being a nasal breather is beneficial for jaw structure, for immune

system function, et cetera Breathing in through your nose, sniffing actually has positive effects on the way that you can acquire and remember information. Noam Sobel's group originally at UC Berkeley and then at the Weizmann Institute has published a number of papers that I'd like to discuss today. One of them, Human Non-Olfactory Cognition Phase-Locked with Inhalation, this was published in Nature Human Behavior, an excellent journal. Showed that the act of inhaling [Andrew inhales deeply] has a couple of interesting and powerful consequences. First of all, as we inhale the brain increases in arousal, our level of alertness and attention increases when we inhale as compared to when we exhale. Now, of course with every inhale, there's an exhale, you could probably double up on your inhales if you're doing size or something, physiological size I've talked about these before, so double inhales [inhales twice] followed by an exhale [exhales], something like that. Or if you're speaking, you're going to change your cadence and ratio of inhales and exhales, but typically we inhale, then we exhale. As we inhale, what this paper shows is that the level of alertness goes up in the brain, and this makes sense because as the most primitive and primordial sense by which we interact with our environment and bring chemicals into our system and detect our environment, inhaling is a cue for the rest of the brain to essentially to pay attention to what's happening, not just to the odors as the name of this paper suggests, Human Non-Olfactory Cognition Phase-Locked with Inhalation. What that means is that the act of inhaling itself wakes up the brain, it's not about what you're perceiving or what you're smelling. And indeed sniffing as an action, inhaling as an action has a powerful effect on your ability to be alert, your ability to attend, to focus, and your ability to remember information. When we exhale, the brain goes through a subtle, but nonetheless significant dip in level of arousal and ability to learn. So, what does this mean? How should you use this knowledge? Well, you could imagine, and I think this will be beneficial for most people to focus on nasal breathing while doing any kind of focused work that doesn't require that you speak, or eat, or ingest something. There's a separate paper published in the journal of neuroscience that showed that indeed if subjects, human subjects, are restricted to breathing through their nose, they learn better than if they have the option of breathing through their mouth, or a combination of their nose and mouth. These are significant effects in humans using modern techniques from excellent groups. So, sniffing itself is a powerful modulator of our cognition and our ability to learn. You can imagine all sorts of ways that you might apply that as a tool. And I suggest that you play with it a bit that if you're having a hard time staying awake and alert, you're having a hard time

remembering information, you feel like you have a kind of attention deficit, nonclinical of course, nasal breathing ought to help, extending or making your inhales more intense ought to help. Now, this isn't really about chemical sensing per se, but here's where it gets interesting and exciting. If you are somebody who doesn't have a very good sense of smell, or you're somebody who simply wants to get better

#### 00:34:00 Protocol 1: Sniffing (Nothing) 10-15X Enhances Your Ability to Smell & Taste

at smelling and tasting things, you can actually practice sniffing. I know that sounds ridiculous, but it turns out that simply sniffing nothing. So, doing something like this. [Andrew sniffs deeply] I guess the microphone sort of has a smell [sniffs], I guess my pen doesn't have a smell. [Andrew sniffs deeply] It turns out that doing a series of inhales, and of course each one is followed by an exhale, 10 or 15 times and then smelling an object like an orange or another item of food, or even the skin of somebody else will lead to an increase in your ability to perceive those odors. Now, there are probably two reasons for that. One reason is that the brain systems of detecting things are waking up as a mere consequence of inhaling. Okay, so this is sort of the olfactory equivalent of opening your eyes wider in order to see, more or less. Okay, last episode I talked about how opening your eyes wider actually increases your level of alertness, it's not just that your level of alertness causes your eyes to be open wider. Opening your eyes wider can actually increase your level of alertness. Well, it turns out that breathing more deeply through the nose, wakes up your brain and it creates a heightened sensitivity of the neurons that relate to smell. And there's a close crossover, I'm sure you know this, between smell and taste. If any of you have ever had a cold or you have for whatever reason you've lost your sense of smell, you become what they call anosmic, your sense of taste suffers also. We'll talk a little bit more about why that is in a few minutes, but as a first protocol, I'd really like all of you to consider becoming nasal breathers while you're trying to learn, while you're trying to listen, while you're trying to wake up your brain in any way and learn and retain information, this is a powerful tool. Now, there are other ways

#### 00:35:50 Smelling Salts, Ammonia & Adrenaline

to wake up your brain more as well. For instance, the use of smelling salts. I'm not

recommending that you do this necessarily, but there are excellent peer reviewed data showing that indeed, if you use smelling salts, which are mostly of the sort that include ammonia, ammonia is a very toxic scent, but it's toxic in a way that triggers this innate pathway, the pathway from the nose to the amygdala, and wakes up the brain and body in a major way. This is why they use smelling salts when people pass out, this is why fighters used to use or maybe sometimes still use smelling salts in order to heighten their level of alertness, this is why powerlifters will inhale smelling salts. They work because they trigger the fear and kind of overall arousal systems of the brain, this is why I think most people probably shouldn't use ammonia or smelling salts to try and wake up, but they really do work. If you've ever smelled smelling salts and I have, I tried this, they give you a serious jolt, it's like six espresso infused into your bloodstream all at once, you are wide awake immediately and you feel a heightened sense of kind of desire to move because you release adrenaline into your body. Now, inhaling through your nose and doing nasal breathing is not going to do that, it's going to be a more subtle version of waking up your system of alerting your brain overall. And for those of you that are interested in having a richer, a more deep connection to the things that you smell and taste, including other individuals perhaps not just food, practicing or enhancing your sense of sniffing, your ability to sniff might sound like a kind of ridiculous protocol, but it's actually a kind of fun and cool experiment that you can do. You just do the simple experiment of taking for instance an orange, you smell it, try and gauge your level of perception of how orange-ish it smells, or lemony, lemonish, lemony, I don't know is it lemonish or lemony? Lemony it smells, then set it away, do 10 or 15 inhales [Andrew inhales and exhales] followed by exhales of course, or just through the nose. [Andrew breaths rapidly] I'm not going to do all 10 or 15. And then smell it again, and you'll notice that your perception of that smell, the kind of richness of that smell will be significantly increased. And that's again, for two reasons, one, the brain is in a position to respond to it better, your brain has been aroused by the mere act of sniffing, but also the neurons that respond to that lemon odor, that lemony or odor are going to respond better.

00:38:25 How You Can Become A Human Scent Hound, Detecting Cancer, & Tasting Better

So, you can actually have a heightened experience of something, and that of course will also be true for the taste system. You also can really train your sense of smell to get

much, much better. When Noam Sobel's group was at Berkeley I happened to be a graduate student around that time, and every once in a while I'd look outside and there would be people crawling around on the grass with goggles on, gloves on, and these hoods on with earmuffs. And they looked ridiculous, but what they were doing is they were actually learning to follow scent trails. So, in the world of dogs you have sight hounds that use their eyes in order to navigate and find things, and you have scent hounds that use their nose. And the scent hounds are remarkable, they can be trained to detect a scent. These are the sniffing, you know, the bomb sniffing and the drug sniffing dogs in airports. There are now dogs actually that can sniff out COVID infections with a very high degree of accuracy, they can be trained to do that. There's something about the COVID and similar infections that the body produces probably in the immune response, some odors and the dogs are I think as high as 90% in some cases, maybe even 95% accuracy, just remarkable. There are theories that dogs can sniff out cancer, this stuff all exceeds statistical significance. It's still a little bit mysterious in some ways, but you may not ever achieve the olfactory capabilities of a scent hound, but what Noam Sobel's lab did is they had people completely eliminate their visual experience by having them wear dark glasses or goggles, so they couldn't see, and they couldn't hear, they couldn't sense anything with their sense of touch, they had thick gloves on. But they had these masks on where just their nasal passages were open and people could in a fairly short amount of time learn to follow a chocolate scent trail on the ground, which is not something that most people want to do, but what they showed using brain imaging, et cetera in subsequent studies is that the human brain, you can learn to really enhance your sense of smell and become very astute in distinguishing whether or not one particular odor or combinations of odors is such that it's less than, or more than a different odor for instance. Now, why would you want to do this? Well, if you like to eat as much as I do, one of the things that can really enhance your sense of pleasure from the experience of ingesting food is to enhance your sense of smell. And if you don't have a great sense of smell, or if you have a sense of smell that's really so good that it's always picking up bad odors, we'll talk about that in a minute. Well, then you might want to tune up your sense of smell by doing this practice of 10 or 15 breaths, excuse me, sniffs, not breaths, sniffs and then interacting with some food item or thing that you're interested in smelling more of. So, these could be the ingredients that you're cooking with, I really encourage you to try and really smell them. You sometimes hear this as kind of a mindfulness practice like ooh, really smell the food, really taste the food. And

we always hear about that as kind of a mindfulness and presence thing, but you actually can increase the sensitivity of your olfactory and your taste system by doing this. And it has long-term effects, that's what's so interesting. This isn't the kind of thing that you have to do every time you eat. You don't have to be the weirdo in the restaurant that's like picking up the radish and like jamming it up your nostrils, please don't do that. You don't have to necessarily smell everything, although it's nice sometimes to smell the food that you're about to eat and as you eat it, but it has long-term effects in terms of your ability to distinguish and discriminate different types of odors. And these don't even have to be very pungent foods it turns out, the studies show that doesn't have to be some really stinky cheese, you know, there are cheese shops that I've walked into where like I just basically gag, I can't handle it, I just can't be in there, it just overwhelms me. Other people, they love that smell. So, you have to tune it to your interest and experience, but I think even for you fasters out there, everybody eats at some point, everybody ingests chemicals through their mouth. And one of the ways that you can powerfully increase your relationship to that experience and make it much more positive is through just the occasional practice of 10 or 15 sniffs of nothing, which almost sounds ridiculous like how could that be? But now, you understand why, it's because of the way that the sniffing action increases the alertness of the brain as well as increasing the sensitivity of the system. No other system that I'm aware of in our body is as amenable to these kinds of behavioral training shifts and allow them to happen so quickly. I would love to be able to tell you that just doing 10 or 15 near-far exercises with a pen or going outside for 10 or 15 seconds each morning is going to completely change the way that you see the world. But it actually isn't the case, you actually, it requires more training, a little bit more effort in the visual system. In the olfactory system, and your smell system, and in your taste system just the tiniest bit of training and attention, and sniffing, inhaling can radically change your relationship to food such that you actually start to feel very different as a consequence of ingesting those foods as well as becoming more discerning about which foods you like and which ones you don't like. And we're going to talk about that because there's a really wonderful thing that happens when you start developing a sensitive palate

00:43:45 Smell As A Readout Of Brain Health & Longevity; Regaining Lost Sense Of Smell

and a sensitive sense of smell in a way that allows you to guide your eating and smelling decisions, and maybe even interpersonal decisions about who you spend time with, or mate with, or whatever, in a way that is really in line with your biology. In fact, how well we can smell and taste things is actually a very strong indication of our brain health. Now, that's not to say that if you have a poor sense of smell or a poor sense of taste, that you're somehow brain damaged or you're going to have dementia, although sometimes early signs of dementia or loss of neurons in other regions of the brain related to say Parkinson's can show up first as a loss of sense of smell. Again, it's not causal, and it's certainly not the case that every time you have a sudden loss of smell that there's necessarily brain damage, I want to be very about that, but they are often correlated. There's also a lot of interest right now in loss of sense of smell because one of the early detection signs of COVID-19 was a loss of sense of smell. So, I just briefly want to talk about loss of sense of smell and regaining sense of smell and taste because these have powerful implications for overall health. And in fact can indicate something about brain damage and can even inform how quickly we might be recovering from something like a concussion. So, our olfactory neurons, these neurons in our nose that detect odors are really unique among other brain neurons because they get replenished throughout life, they don't just regenerate, but they get replenished. So regeneration is when something is damaged and it regrows, these neurons are constantly turning over throughout our lifespan, they're constantly being replenished, they're dying off and they're being replaced by new ones. This is an amazing aspect of our brain that's basically unique to these neurons, there's one other region of the brain where there's a little bit of this maybe, but these olfactory neurons about every three or four weeks they die. And when they die, they're replaced by new ones that come from a different region of the brain, a region called the subventricular zone. The name isn't as important, but as the phenomenon, but these neurons are born in the ventricle, the area of your brain that's a hole that contains... It's not an empty hole, it's a hole basically that contains cerebral spinal fluid. Well, there's a little subventricular zone, there's a little zone below, sub ventricles. And that zone, if you are exercising regularly, if your dopamine levels are high enough, those little cells there are like stem cells. They are stem cells and they spit out what are called little neuroblasts, those little neuroblasts migrate into the front of your brain and then shimmy, they kind of move through what's called the rostral migratory stream. They kind of shimmy along and land back in your olfactory bulb, settle down and extend little wires into your olfactory mucosa. This is an ongoing process of what we call

neurogenesis or the birth of new neurons. Now, this is really interesting because other neurons in your cortex, in your retina, in your cerebellum, they do not do this, they are not continually replenished throughout life. But these neurons, these olfactory neurons are, they are special. And there are a number of things that seem to increase the amount of olfactory neuron neurogenesis. There is evidence that exercise, blood flow, can increase olfactory neuron neurogenesis. Although, those data are fewer in comparison to things like social interactions, or actually interacting with odorants of different kinds. So, if you're somebody who doesn't smell things well, you have a poor sense of smell, your olfactory system doesn't seem very sensitive, more sniffing, more smelling is going to be good. And then the molecule dopamine, this neuromodulator, that is associated with motivation and drive. And in some cases, if it's very, very high with mania, or if it's very, very low with depression or Parkinson's, but for most people where dopamine is in essentially normal ranges dopamine is also a powerful trigger of the establishment of these new neurons and their migration into the olfactory bulb and your ability to smell. Now, you don't want to confuse correlation with causation, so if you're not good at smelling does that mean you have low dopamine? No, not necessarily. If you have low dopamine, does that mean that you have a poor sense of smell? No, not necessarily. Some people who take antidepressants of the sort

00:48:30 Dopamine, Sense Of Smell, New Neurons & New Relationships

that impact the dopamine system strongly like Wellbutrin will report a sudden, meaning within a couple of days, increase in their ability to smell particular odors, and it's a very striking effect. Some people when they are in a new relationship because dopamine and the hormones, testosterone and estrogen are associated with novelty and the sorts of behaviors that often are associated with new relationships those three molecules; dopamine, testosterone, and estrogen kind of work together. And oftentimes people will say or report when they're newly in love or in a new relationship that they're just obsessed with, or they just so enjoy the scent of another person so much so that they like to borrow the other person's clothing or they'll sniff the other person's clothing or they can even just in the absence of the person they can imagine their smell and feel a biological response, something that we'll talk more about. So, these neurons turnover throughout the lifespan and as we age, we actually can lose our sense of smell. And it's likely, I want to underscore likely, that that loss of sense of smell as we age is correlated

with a loss of other neurons in the retina, in the ears, a loss of vision, loss of hearing, loss of smell, loss of the sense apparatus which our neurons is correlated with aging. So, what we've been talking about today is the ability to sense these odors, but what I'd like to do is empower you with tools that will allow you to keep these systems tuned up. Last time, we talked about tuning up and keeping your visual system tuned up and healthy regardless of age. Here, we're talking about really enhancing your olfactory abilities, your taste abilities as well by interacting a lot with odors, preferably positive odors, and sniffing more, inhaling more, which almost sounds crazy, but now you understand why. Even though it might sound crazy

00:50:20 Why Brain Injury Causes Loss Of Smell; Using Smell To Gauge & Speed Recovery

it's grounded in real mechanistic biology of how the brain wakes up and responds to these chemicals. Now, speaking of brain injury, olfactory dysfunction is a common theme in traumatic brain injury for the following reason, these olfactory neurons as I mention extend wires into the mucosa of the nose, but they also extend a wire up into the skull. And they extend up into the skull through what's called the cribriform plate, it's like a Swiss cheese type plate where they're going through. And if you get a head hit, that bone, the cribriform plate, shears those little wires off and those neurons die. Now, eventually they'll be replaced, but there's a phenomenon by which concussion and the severity of concussion and the recovery from a head injury can actually be gauged in part, in part, not in whole, but in part by how well or fully one recovers their sense of smell. So, if you're somebody that unfortunately has suffered a concussion, your sense of smell is one readout by which you might evaluate whether or not you're regaining some of your sensory performance. Of course, there will be others like balance, and cognition, and sleep, et cetera. But I'd like to refer you to a really nice paper which is entitled Olfactory Dysfunction in Traumatic Brain Injury: the Role of Neurogenesis the first author is Marin, M-A-R-I-N. The paper was published in Current Allergy and Asthma Report, this is 2020. I spent some time with this paper, it's quite good, it's a review article, I like reviews if they're peer-reviewed reviews and in quality journals. And what they discuss is and I'll just read here briefly 'cause they said it better than I could, "Olfactory functioning disturbances are common following traumatic brain injury, TBI, and can have a significant impact on the quality of life. Although there is no standard

treatment for patients with the loss of smell." Now I'm paraphrasing, "Post-injury olfactory training has shown promise for beneficial effects. Some of this involves," they go on to tell us the role of dopamine, dopaminergic signaling, as I mentioned before, but what does this mean? This means that if you've had a head injury or repeated head injuries that enhancing your sense of smell is one way by which you can create new neurons. And now, you know how to enhance your sense of smell by interacting with things that have an odor very closely, and by essentially inhaling more, focusing on the inhale to wake up the brain and to really focus on some of the nuance of those smells. So, you might do for instance a smell test by which you smell something like a lemon, put it down, do 10 inhales or so, smell again, et cetera. You might also just take a more active role in trying to taste and smell your food, and taste and smell various things. I mean, please don't ingest anything that's poisonous that you're not supposed to be ingesting, but you know what I mean, really tuning up this system, I think is an excellent review, we're going to do an entire episode all about the use of the visual system in particular, but also the olfactory system for treatment of traumatic brain injury, as well as other methods. But I wanted to just mention it here because a number of people asked me about TBI. And here again, we're in this place where the senses and our ability to sense these chemicals through these two holes in the front of our face, our nostrils is a powerful readout

#### 00:53:33 Using Smell To Immediately Becoming Physically Stronger

and way to control brain function and nervous system function generally. Just a quick note about the use of smelling salts, I have a feeling that some of you may be interested in that and its application. If you are interested in that, I recommend you go to the scientific literature first rather than straight to some vendor or to the what do they call it these days? Costello bro science, he says, bro science, the bro science. You can go to this paper, which is excellent and is real science, which is Acute Effects of Ammonia Inhalants on Strength and Power Performance in Trained Men. It's a randomized controlled trial, it was published in the Journal of Strength and Conditioning Research in 2018, and it should be very easy to find. I will provide a link to the so-called PubMed ID, which is a string of numbers, and we'll put that in the caption if you want to go straight to that article, does show a significant what they call, this is what the words they use literally in quotes, "psyching up effect through the use of these ammonia inhalants and a

significant increase in maximal force in force development in a variety of different movements."

00:54:40 Smelling In Our Dreams, Active Sniffing In Sleep, Sniffing As a Sign Of Consciousness

So, for those of you that are interested in ammonia inhalants, so-called smelling salts, that might be a good reference. The other thing I wanted to talk about with reference to odors is this myth which is that we don't actually smell things in our dreams, that we don't have a sense of smell. That's pure fiction, I don't know who came up with that, it's very clear that we are capable of smelling things in our sleep. However, when we are in REM sleep, rapid eye movement sleep, which is the sleep that predominates toward the second half of the night our ability to wake up in response to odors is diminished. It's not absent, but it's diminished. If smoke comes into the room, we will likely wake up if the concentration of smoke is high enough regardless of the stage of sleep we're in, but in REM sleep we tend to be less likely to smell, to sniff. And that actually was measured in a number of studies that sniffing in sleep is possible. So, if you put an odor like a lemon underneath someone's nostrils in the early portion of the night, they will smell, and they will later... They will sniff, excuse me, whether or not they smell or not, I guess depends on them and when they showered last, but they will definitely sniff and they will report later, especially if you wake them up soon after that, they had a dream or a percept of the scent of a lemon for instance. Later in the night, it's harder for that relationship to be established, it's likely that because of some of the paralysis associated with rapid eye movement sleep, which is a healthy paralysis, so-called sleep atonia, you don't want to act out your dreams in REM sleep that there is a less active tendency to sniff. And actually this has real clinical implications, the ability to sniff in response to the introduction of an odor is actually one way in which clinicians assess whether or not somebody's brain is so-called brain dead. That's not a nice term, but brain dead, or whether or not they have the capacity to recover from things like coma and other states of deep unconsciousness, or I guess you'd call it subconsciousness. So, what will happen is if someone has an injury and they're essentially out cold, the production of a sniffing reflex, or a sniffing response to say a lemon or some other odor presented below the nostrils is considered a sign that the brain is capable of waking up. Now, that's not always the case, but it's one indication. So just like you could use mechano sensation,

so, a toe pinch for instance, you know, or scraping the bottom of somebody's barefoot to see if they're conscious, or shining light in their eyes, these are all things that you've seen in movies and television, or maybe if you've seen in real life as well. Well, odors and chemical sensing is another way by which you can assess whether or not the brain is capable of arousal. And actually olfactory stimulation

#### 00:57:35 Mint Scents Create Alertness By Activating Broad Wake-Up Pathways

is one of the more prominent ones that's being used in various clinics. As a last point about specific odors and compounds that can increase arousal and alertness, and this was simply through sniffing them not through ingesting them. There are data, believe it or not, there are good data on peppermint and the smell of peppermint, minty type sense, whether you like them or not will increase attention, and they can create the same sort of arousal response although not as intensely or as dramatically as ammonia salts can for instance. By the way, please don't go sniff real ammonia, you could actually damage your olfactory epithelium if you do that too close to the ammonia. If you're going to use smelling salts be sure you work with someone or you know what you're getting and how you're using this. You can damage your olfactory pathway in ways that are pretty severe, you can also damage your vision. If you've ever teared up because you inhaled something that was really noxious, that is not a good thing, it doesn't mean you necessarily cause damage, but it means that you have irritated the mucosal lining and possibly even the surfaces of your eyes, so please be very, very careful. Scents like peppermint, like these ammonia smelling salts, the reason they wake you up is because they trigger specific olfactory neurons that communicate with the specific centers of the brain, namely the amygdala and associated neurocircuitry and pathways that trigger alertness of the same sort that a cold shower or an ice bath, or a sudden surprise, or a stressful text message would evoke. Remember, the systems of your body that produce arousal, and alertness, and attention, and that cue you for optimal learning, aka focus. Those are very general mechanisms, they involve very basic molecules like adrenaline and epinephrin same thing actually, adrenaline and epinephrin. The number of stimuli, whether it's peppermint or ammonia, or a loud blast, the number of stimuli that can evoke that adrenaline response and that wake up response are near infinite. And that's the beauty of your nervous system, it was designed to take any variety of different stimuli placed them into categories, and then evoke different categories of very general

responses. Now, you know a lot about olfaction

00:59:48 Protocol 2 Pleasant Or Putrid: The Microwave Popcorn Test, Cilantro, Asparagus, Musk

and how the sense of smell works, here's another experiment that you can do. I'll ask you right now. Do you like, hate, or are you indifferent to the smell of microwave popcorn? Some people, including one member of my podcast staff says it's absolutely disgusting to them, they feel like it's completely nauseating. I don't mind it at all, in fact, I kind of like it. I think the smell of a microwave popcorn is kind of pleasant. I don't particularly like it, but it's certainly not unpleasant. Some people have a gene that makes them sensitive to the smell of things like microwave popcorn such that it smells like vomit. I probably don't have that gene because I find the smell of microwaved popcorn pretty pleasant. Some people hate the smell of cilantro, some people ingest asparagus, and when they urinate they can smell the asparagus in a very pungent way, other people can't smell it at all. These are variants in genes that encode for what are called olfactory receptors. Each olfactory sensory neuron expresses one odorant gene, one gene that codes for a receptor that responds to a particular odor. If you don't have that gene you will not respond to that odor. So, the reason why some people find the smell of microwave popcorn to be very noxious, putrid in fact, is because they have a gene that allows them to smell the kind of putrid odor within that. Other people who lack that gene just simply can't smell it, so we are not all the same with respect to our sensory experience. What one person finds delicious, another person might find disgusting. I'll give a good example which is that I absolutely despise Gorgonzola and blue cheese, absolutely despise it, it smells and tastes like dirty moldy socks to me. Some people love it, they crave it, actually, some people get a visceral response to it, and we will talk about how certain tastes can actually evoke very deep biological responses, even hormonal responses when we talk about taste in a few minutes. But there are these odors, for instance in popcorn it's the molecule 2-acetyl-1-pyrroline, not proline but pyrroline, that gives off to some people like me a toasted smell as the sugars in the kernels heat, but the compound is also found in things like white bread and jasmine rice, which don't have as pungent an odor, but some people smell that and it smells like cat urine. Now, there are scents like musky scents and musty scents that are secreted by animals like skunks and other animals of the so-called Mustelidae family. So, these would be ferrets and

other animals that can spray in response to fear, or if they just want to mark a territory because they want to say that's mine. Dogs incidentally have scent glands that they rub on things, cats have them too. This musty odor, some people find actually quite pleasant,

01:03:00 Skunks, Costello, All Quiet On The Western Front

some people find it to be very noxious and that will depend of course on the concentration, right? I'll never forget the first time Costello got sprayed by a skunk and it was awful. I actually don't mind the smell of skunk at a distance, it's actually a little bit pleasant, I admit it's a little bit pleasant to me. I don't think that makes me too weird because if you ever read the book "All Quiet on the Western Front" about World War I, there's a description in there about the smell of skunk at a distance being mildly pleasant, so the author of that book probably shared a similar olfactory profile to me, or I to them rather, but some people find even the tiniest bit of the smell of skunk or musk to be noxious or awful. Now, of course in high concentrations, it's really awful. And unfortunately, poor Costello, he was like literally red-eyed and just snorting, and it was awful. There's a joke about dogs that says that dogs either get skunked one time and never again or 50 or a hundred times. Costello has been skunked no fewer, I'm not making this up, has been skunked no fewer than 103 times. And that's because if he sees something or hears something in the bushes, he just goes straight in, he does not learn. But if you like this, that musty scent or musky scent, well that says something about the genes that you express in your olfactory neurons, it is completely inherited. And if you don't like that scent, if it's really noxious or you have this response to microwave popcorn, well, that means you have a different compliment, a different constellation if you will of genes that make up for these olfactory sensory neurons

01:04:32 TASTE: Sweet, Salty, Bitter, Umami, Sour; Your Tongue, Gustatory Nerve, NST, Cortex

and the receptors that they express. Let's talk about taste. Not whether or not you have taste or you don't have taste, there's no way for me to assess that, but rather how we taste things, meaning how we sense chemicals in food and in drink. There are essentially five, but scientists now believe there may be six things that we taste alone or

in combination, they are sweet tastes, salty tastes, bitter tastes, sour tastes, and umami taste. Most of you probably heard of umami by now, it's U-M-A-M-I. Umami is actually the name for a particular receptor that you express on your tongue that detects savory tastes, so it's the kind of thing in braised meats. Sometimes people can even get the activation of umami by tomatoes or tomato sauces. What are each of these tastes and taste receptors responsible for? And then we'll talk about the sixth, maybe you can guess what it is, I don't know if you can guess it now. I couldn't guess it, but of the five tastes each one has a specific utility or function. Each one has a particular group of neurons in your mouth, in your tongue, believe it or not, that responds to particular chemicals and particular chemical structures. It is a total myth, complete fiction, that different parts of your tongue harbor different taste receptors. You know, that high school textbook diagram that you know sweet is in one part of the tongue and sour is in another, and bitters in another, complete fiction, just total fiction related to very old studies that were performed in a very poorly controlled way, no serious biologists and certainly no one that works on tastes would contend that that's the way that the taste receptors are organized, they are completely intermixed along your tongue. If you have heightened or decreased sensitivity to one of those five things I mentioned; sweet, salty, bitter, umami, or sour at one location in your tongue, it likely reflects the density of overall receptors or something going on in your brain, but not the differential distribution of those receptors. So, the sweet receptors are neurons that express a receptor that respond to sugars, in the same way that you have cones, photoreceptors, in your eye that respond to short, medium, or long wavelength light, meaning blueish, greenish, or reddish light. You have a neuron, or neurons plural, in your tongue that respond to sugars. And then those neurons, they don't say sweet, they don't actually send any sugar into the brain, they send what we call a volley, a barrage of action potentials of electrical signals off into the brain. It's an amazing system. So, all these receptors in your tongue make up what are called the neurons that give rise to a nerve, a collection of wires, nerve bundles of what's called the gustatory nerve, it goes from the tongue to the so-called nucleus of the solitary tract. And some of you requested names, I usually don't like to include too many names for sake of clarity, but the gustatory nerve from the tongue goes to the nucleus of the solitary tract and then to the thalamus and to insular cortex. You don't have to remember any of those names if you don't want to, but if you want mechanism, you want neural circuits, that's the circuit, gustatory nerve from the tongue, nucleus of the solitary tract in the brainstem, then the thalamus, and then insular

cortex. And it is in insular cortex, this regenerate cortex that we sort out and make sense of and perceive the various tastes. Now, it's amazing because just taking a little bit of sugar or something sour like a little bit of lemon juice and touching it to the tongue within 100 milliseconds, right? Just 100 milliseconds, far less than one second, you can immediately distinguish ah, that's sour, that's sweet, that's bitter, that's umami,

01:08:45 Energy, Electrolytes, Poisons, Gagging, Amino Acid & Fatty Acid Sensing, Fermentation

and that's an assessment that's made by the cortex. Now, what do these different five receptors encode for? Well, sweet, salty, bitter, umami, sour, but what are they really looking for? What are they sensing? Well, sweet stuff signals the presence of energy, of sugars. And while we're all trying or we're told that we should eat less sugar for a variety of reasons, the ability to sense whether or not a food has rapid energy source or could give rise to glucose is essential so we have sweet receptors. The salty receptors, these neurons are trying to sense whether or not there are electrolytes in a given food or drink. Electrolytes are vitally important for the function of our nervous system, and for our entire body, sodium is what allows neurons to fire. What allows them to be electrically active. We also need potassium and magnesium, those are the ions that allow the neurons to be active. So the salty receptors, the reason that they are there is to make sure that we are getting enough, but not too much salt, we don't want to ingest things that are far too salty. Bitter receptors are there to make sure we don't ingest things that are poisonous. How do I know this? How can I say that? Even though I was definitely not consulted at the design phase, how can I say that? Well, the bitter receptors create a what we call labeled line, a unique trajectory to the neurons of the brainstem that control the [gags], the gag reflex. If we taste something very bitter it automatically triggers the gag reflex. Now, some people like bitter taste, I actually liked the taste of bitter coffee, children generally like sweet tastes more than bitter tastes, but even babies if they taste something bitter, they'll just immediately spit it up, it's like the gag reflex. Putrid smells will also evoke the same neurons, so some people are very sensitive, they have a very sensitive or low threshold vomit reflex, you're going to and there was somebody in my lab early on. And we never did this intentionally, and we're just laughing 'cause it was so dramatic. How we would have a discussion, someone would say something about something kind of gross, appropriate for the workplace, but nonetheless gross, we are

biologists, would say something and they would say, "Stop, stop stop, I'm going to throw up." You know and some people have a very low threshold quick gag reflex. Other people don't, other people have a very stable stomach, they don't, you know, they rarely, if ever vomit. The umami receptor isn't sensing savory because the body loves savory, it's because savory is a signal for the presence of amino acids. And we'll talk more about this, but the presence of amino acids in our gut and in our digestive system, and the presence of fatty acids is essential, there is in fact, no essential carbohydrate or sugar. Now, I'm not a huge proponent of ketogenic diets nor am I against them, I think it's highly individual, you have to decide what's right for you, but everybody needs amino acids to survive, the brain needs them and we need fatty acids, especially to build a healthy brain during development, you need amino acids and fatty acids. And the sour receptor, why would we have a sour receptor? So, that we could have those really like sour candies? I think they've gotten more and more sour over the years. I admit I don't eat candy much, but I do have a particular weakness for like a really good really sour like gummy peach or they if the gummy cherries are dipped in whatever that sour powder, so I was a kid who I admit it, I liked the LIK-M-AID thing, I'd like drink the powder. Please don't do this, don't give this garbage to your kids, but I liked it, it was tasty, but sour receptors are not there so that you can ingest gummy sour gummy peaches or something like that, that's not why the system evolved, it's there and we know it's there to detect the presence of spoiled or fermented food. Fermented fruit has a sour element to it, and fermented things while certainly some fermented foods like sauerkraut, and kimchi, and things of that sort can be very healthy for us and are very healthy in reducing inflammation, there's great data on that, pro quality microbiome, et cetera. Fermented fruit can be poisonous, right? Alcohols are poisonous in many forms to our system and the sour receptor bearing neurons communicate to an area of the brainstem that evokes the pucker response, closing of the eyes and essentially shutting of the mouth, and cringing away. I think cringe is like a thing now, my niece, whenever I seem to say something or do something it's either an eye-roll, a cringe, or both in combination. So the sour, the sweet, the salty, the bitter, and the umami system, were not there so that we could have this wonderful pallet of foods that we enjoy so much, they'll allow us to do that, but they're there to make sure that we bring in certain things

01:13:48 Our 6th Sense of Taste: FAT Sensing

to our system and that we don't ingest other things. Now, what's the sixth sense within the taste system? Not sixth sense generally, but within the taste system. What's this putative possible sixth receptor? I already kind of hinted at it when I talked about fatty acids, there are now data to support the idea although there's still more work that needs to be done that we also have receptors on our tongue that sense fat. And that because fat is so vital for the function of our nervous system and the other organs of our body that we are sensing the fat content in food, maybe this is why I can only eat half, but no less than half of a jar of almond butter or peanut butter in one sitting. I just can't, unless it's not salted, in which case, it makes no sense to me. But it's remarkable how that texture, and also the flavor, but that texture of fat. I love butter, I am guilty, and Costello is definitely guilty of eating pats of butter from time to time, I have no guilt about this. People eat pats of cheese, why shouldn't we eat a pat of butter? If you think that's gross then maybe I have a greater abundance of the fat receptors in my tongue, maybe I have a fat tongue than you do. But nonetheless, the ability to sense fat here in our mouth

#### 01:15:05 Gut-Brain: Your Mouth As An Extension Of Your Gut; Burned Mouth & Regeneration

seems to be critical, you can imagine why that is. I want to talk about the tongue and the mouth as an extension of your digestive tract. I know that might not be pleasant to think about, but when you look at it through the lens that I'm about to provide, it will completely change the way you think about the gut brain and about all the stuff that you've heard in these recent years about oh, we have this second brain, it's all these neurons in our gut, I've been chuckling through these last few years as people have gotten so excited about the gut brain, not because of their excitement, I think that excitement is wonderful, but we always knew that the nervous system extended out of the brain and into the body, and people seem kind of overwhelmed and surprised by the idea that we have neurons in our gut that can sense things like sugars and fatty acids. And I think those are beautiful discoveries, don't get me wrong. Diego Bohorquez's lab out of Duke University has done beautiful studies showing that within the mucosal lining of our gut we have neurons that sense fatty acids, sugars, and amino acids, and that when we ingest something that contains one or two or three of those things, there's a signal sent via the vagus nerve up into what's called the nodose ganglion, N-O-D-O-S-E, and then into the brain where it secretes dopamine which makes us want more of that thing, it makes us

more motivated to pursue and eat more of that thing, that's either fatty, or umami, savory, or has a sweet taste, any one or two or three of those qualities, independent of the taste. Now, I think those are beautiful data, but we know that this thing, the mouth. And for those of you listening I've just got my couple of fingers in my mouth, that's why I sound like I've got something in my mouth. This thing in the front of our face, we use it for speaking, but it is the front of our digestive tract. We are essentially a series of tubes and that tube starts with your mouth and heads down into your stomach. And so, that you would sense so much of the chemical constituents of the stuff that you might bring into your body or that you might want to expel and not swallow or not interact with by being able to smell is it putrid? Does it smell good? Does it taste good? Is this safe? Is it salty? Is it so sour that it's fermented and it's going to poison me? Is it so bitter that it could poison me? Is it so savory that, mmm, yes. I want more and more of this. Well, then you'd want to trigger dopamine, that's all starting in the mouth. So, you have to understand that you were equipped with this amazing chemical sensing apparatus, we call your mouth and your tongue. And those little bumps on your tongue that they call the papillae, those are not your taste buds. Surrounding those little papillae like little rivers are these little dents and indentations. And what dents and indentations do in a tissue is they allow more surface area, they allow you to pack more receptors. So, down in those grooves are where all these little neurons and their little processes are with these little receptors for sweet, salty, bitter, umami, sour, and maybe fat as well. And so, it's this incredible device that you've been equipped with, that you can use to interact with various components of the outside world and decide whether or not you want to bring them in or not. Just as you can lose those olfactory neurons, if you happen to get hit on the head or you have some other thing, maybe it was an infection that caused loss of those olfactory sensory neurons, you can also lose taste receptors in your mouth. If you've ever eaten something that's too hot, not spicy hot, but too hot, you burn your tongue, you burn receptors. It takes about a week to recover those receptors. For some people it's a little bit more quickly, but if you burn your tongue badly by ingesting a soup that's too hot or a beverage that's too hot, you will greatly reduce your sense of taste for essentially all tastes. And that's because those neurons sit very shallow beneath the tongue's surface, and so that if you put something too hot on, you literally just burn those neurons away. Luckily those neurons also can replenish themselves. Those neurons are of the peripheral nervous system, and like all peripheral system neurons they can replenish or regenerate. So, if you burn your mouth in about a week or so hopefully

sooner you'll be able to taste again.

01:19:30 Protocol 3: Learn To Be A Super-Taster By Top-Down Behavioral Plasticity

In fact, everybody's ability to taste is highly subject to training. You can really enhance your ability to taste and taste the different component parts of different foods simply by paying attention to what you're trying to taste, this is an amazing aspect of the taste system. I think more than any other system, the taste system and perhaps the smell system as well can be trained so that you can learn to pick out the tones, if you will of different ice cream, or different beverages. I'm somebody who, you know, I don't drink much alcohol, I'll occasionally have a drink or something, but a while ago I got to taste a bunch of different white tequilas, these are different kinds of tequilas that are, they're not brown, they're white. And I sort of assumed that all tequila was disgusting, that was my assumption before doing this. And then I tasted a couple of white tequilas and I realized oh, those aren't aren't too bad. I tasted a few more, and then pretty soon I could really start to detect the nuance and the difference. Now, I haven't had a tequilas in a long time, now I sort of tend to not drink at all these days, but in a very short period of time like a couple of days I got very good at detecting which things I liked and I could start to pick out tones. So, I'm not a wine drinker, but for those of you that are, you know, you hear about oh, it has floral tones, or berry tones, or chocolate tones. You know, some of that is just kind of menu-based and kind of marketing-based silliness designed to get you excited about what you're about to ingest. But some of it is real, and for people that are skilled in assessing wines or assessing foods. I'm much more of an eater than a drinker, you can really start to develop a sensitive palate, a nuanced palette through what we call top-down mechanisms. This olfactory cortex that takes these five, maybe the sixth fat receptor too, information and tries to make sense of what's out there in the world. And what its utility is, is it good? Is it bad? Do I want more of it or less than it? That neural circuitry is unlike other neural circuitry in that it seems very amenable to behavioral plasticity for whatever reason, and we could talk about what those reasons might be. You know, it's interesting sometimes to think about how your taste literally, chemical taste, is probably very different than that of other people, how a food tastes to you is probably very different than how it tastes to somebody else. The same probably cannot be said of something like vision or hearing, unless you're somebody who has perfect pitch or your color vision is disrupted, or you're a mantis shrimp, chances are when we

look at the same object two people are seeing more or less the same object or perceiving it in a very similar way. There are experiments that essentially establish that. Now we, have taste receptors and a lot of those tastes receptors, their chemical structures are known,

#### 01:22:20 The Umami-Sweet Distinction: Tigers Versus Pandas

they come with fancy names like the T1R1 or the T1R2, which were identified as the sweet and umami receptors. So, what's interesting is that this umami flavor is the savory flavor rather than that's sensed by umami receptors is very close to the receptor that detects sweet things. Similarly, bitter is sensed by a whole other set of receptors. Now, there's a fun naturally occurring experiment that will forever change the way that you look at animals, and the way certainly that I think about dogs and Costello in particular. Carnivorous large animals like tigers and some grizzly bears for instance, we know that they have no ability to detect sweet, they don't actually have the receptors for sweet on their tongue, but their concentration of umami receptors or their ability to detect savory is at least 5,000 times that which it is in humans. In other words, if I eat a little piece of steak, or Costello eats a little piece of steak, that steak probably tastes much, much more savory than it does to me. So dogs, and tigers, and bears, et cetera, they're going to taste savory things and smell savory things with a much higher degree of sensitivity, but they can't taste sweet things. Other large animals, which are mostly herbivores like the panda bear for instance. It's hard to believe that thing is even a bear, I got nothing against pandas, I just think that they get a little bit too much of the limelight frankly. So, no vendetta against Panda, save the pandas, I hope they replenish all the pandas, but pandas in all their whatever have no umami receptors, they can't taste savory, but they have greatly heightened density of sweet receptors. So, there they are eating these whatever bamboos all day or not bamboozle, but bamboos all day and they can taste things that are very sweet with a much higher degree of intensity. And in general, animals that are more gentle that are herbivores, excuse me. Or animals that have the propensity for aggression, that's where you really see the divergence of the umami receptor because it's associated with meat and amino acids. And where you see the enhancement of the sweet receptors for animals that eat a lot of plants and fruits, and they probably taste very different to them than they do to you and me. And, so it's interesting to note that animals that eat meat, that eat other organisms can actually

extract more savory experience from that.

#### 01:25:05 Eating More Plants Versus Eating More Meat, Cravings & Desire

What does this mean for you? All right, do you associate yourself as a tiger, or a grizzly bear, or a panda, or a combination of both? Most people are omnivores. However, you may find it interesting that people that for instance eat a pure carnivore type diet or a keto diet where they are ingesting a lot of meat, so therefore are sensing a lot of umami flavors. And I realized not everyone who's keto eats meat, but those who do that will develop a more sensitive palate and likely there are some data, although early data, craving for umami-like foods. Whereas people that eat a more plant-based diet are likely developing a heightened sensitivity and desire for, and maybe even dopamine response to sugars and plant-based foods. Now, this is my partial attempt to reconcile the kind of online battle that seems to exist between plant-based versus animal-based, purely plant-based or purely animal-based diets. I think most people are omnivores, but it's kind of interesting to think that the systems are plastic such that people might want more meat if they eat more meat, people might want more plants if they eat enough plants for a long period of time. And this might explain some of the chasm that exists between these two groups. Now, this is not to say anything about the ethical or the environmental impacts of different things, I don't even want to get into that because the meat people say that the plant-based diets have as much a negative impact as the plant people say that the meat based diets, that's a totally different discussion. What I'm talking about here is food craving and food seeking and one's ability to detect these umami, savory flavors is going to be enhanced by ingesting more meat and less activation of the sweet receptors. So in other words, the more meat you eat the more you're going to become like a tiger, so to speak. And the more that you avoid these umami flavors and meats and the more that you would eat plant-based foods and in particular sweet foods, the more you will likely suppress that umami system and that you will have a heightened desire for, appetite for and sensing of sweet foods

#### 01:27:15 Food That Makes You Feel Good Or Bad: Taste Receptors On Our Testes Or Ovaries

or foods that contain sugars. What I'm about to tell you is going to seem crazy, but is

extremely interesting with respect to taste and taste receptors. Remember, even though we can enjoy food and we can evolve our sense of what's tasty or not tasty, depending on life decisions, environmental changes, et cetera, the taste system just like the olfactory system and the visual system was laid down for the purpose of moving towards things that are good for us and moving away from things that are bad for us, that's the kind of core function of the nervous system. Well, taste receptors are not just expressed on the tongue, they are expressed in other cells and other tissues as well. Some of you may be able to imagine foods that are so delicious to you that they make your entire body feel good. Or foods that are so horrifically awful to think about let alone taste, that they create a whole body shuddering or kind of repellent-type response where you just either cringe or turn your face away even in the absence of that food. That's sort of how I feel about pungent, Gorgonzola cheese. If you like Gorgonzola cheese, I don't judge you, I just, that's an individual difference. I happen to love certain foods, I do like savory foods very much. I, when I think about them, they just they make me feel good. And I'm oftentimes not even associating with the taste of those foods, it feels almost like a visceral thing. Well, it turns out that some of the taste receptors extend beyond the tongue, that they actually can extend into portions of the gut and digestive system. And if that's not strange enough, turns out that some of the taste receptors are actually expressed on the ovaries and the testes. So, what that means is that the gonads, the very cells, and tissues, and organs in our body that make up the reproductive axis are expressing taste receptors. Okay, so how do we interpret this? Does this mean that when you eat something that's very savory or very sweet for instance, that it's triggering activation of the ovaries or of the testes? Well, it's possible. Now, how those molecules, those chemical molecules would actually get there isn't clear, the digestive track does not run directly to the testes or to the ovaries. But nonetheless, what this means is that chemical sensing of the very things that we detect on our tongue and that we call taste in quotes in food is also evoking cellular responses within the reproductive gonads. Now, whether or not this underlies the positive association

01:30:05 Biological Basis For The Sensuality of Umami and Sweet Foods

that we have with certain foods isn't clear, but I'd be remiss if I didn't point out the obvious, which is that the relationship between the sensual nature of particular foods and sensuality generally and the reproductive axis is something that's been covered in

many movies, there are entire movies that are focused on the relationship between for instance, chocolate and love and reproductive behaviors, or certain feasts of meat and their wonderful tastes and the kind of sensuality around feasts of different types of foods, but in general, it's the sweet and the savory, rarely is it the sour or the bitter, the salty or the fat. And not surprisingly perhaps, it is the T2Rs and the T1Rs, the receptors that are associated with the sweet and with the umami, the savory flavors that are expressed not just on the tongue and in portions of the digestive tract, but on the gonads themselves. So, what does this mean? Does this mean that eating certain foods can stimulate the gonads? Maybe, there's no data that immediately support that right now, but this is an emerging area. If you'd like to read more about this there's a great review, entitled Taste perception: From the tongue to the testis, although they do also talk about the ovaries. Why they didn't include that in the title is I think a reflection of the bias of the author. The author indeed not incidentally is Feng Li, last name L-I. It's a very interesting paper published in Molecular Human Reproduction. You can find it easily online, it's downloadable, I'll also provide a link to it. I just think it's fascinating that these taste receptors are expressed in other tissues. And I should mention that they're expressed in tissues of other areas of the body as well, including the respiratory system, but the richest aggregation or concentration of these receptors for umami and sweet of course is on the tongue, but also on the gonads. And I think it does speak to the possible bridge between what we think of as a sensory or a sensual experience of food and the deeper kind of visceral sense within the gut, and maybe even within the gonads as well of something that we find extremely pleasurable,

01:32:28 Appetitive & Aversive Sensing: Touching Certain Surfaces, Tasting Certain Foods

or even appetitive that we want to move toward it. We are actually going to return to that general theme in the discussion about touch sensation. Some people for instance, when they touch certain surfaces like furs, or sheep skins, or velvet, or soft, smooth surfaces it feels good elsewhere in their body, not just at the point of contact with that surface. And similarly, if there's the... How about this one? The screech of chalk on a chalkboard, it's a sound, but it has a very strong visceral component, or sandpaper, like fingernails on a chalkboard, not the sound, but the feeling, right? Exactly, so our whole nervous system is tuned to either be drawn toward appetitive, or repelled by aversive behaviors, right?

So there's this push-pull that exists, and what I'm referring to in terms of these receptors on the tongue that are also expressed on the gonads is yet another example of what at least in this case seems to be an appetitive thing, a desire to move toward certain foods and maybe even the experiences

01:33:35 Amino Acids Are Key To Life, The Maillard Reaction, Smell-Taste Merge, Food Texture

that are associated with those foods. I want to talk about a particular aspect of food and a chemical reaction in cooking called the Maillard reaction. Some of you have probably heard of the Maillard reaction, it's spelled M-A-I-L-L-A-R-D. The D is silent, so don't call it the Maillard reaction, and it's not the Maillard reaction, it is the Maillard reaction. And the Maillard reaction is a reaction that for the aficionados is a non-enzymatic browning. The other form of non-enzymatic browning is caramelization, although when you hear caramel, carmel, I think it's caramel. You think sweet, and indeed caramelization is a sugar-sugar chemical interaction that leads to a kind of nicely toasted not burnt, but nicely toasted sweet taste. Whereas the Maillard reaction is that really savory reaction that occurs when you have a sugar amino acid reaction. Remember, we have neurons in our gut, but also neurons in our tongue and neurons deep in the brain that are comparing the amount of sugar to savory. Okay, and the Maillard reaction is very interesting for you chemists out there, this is going to be way too elementary. And for you non-chemists it's probably going to be a little bit of a reach, but just bear with me, all these chemicals that we sense have a different structure, it's like hydrogens, and oxygens, and aldehyde groups, and all these things. And basically the Maillard reaction involves what's called a free aldehyde. If you didn't like chemistry, don't worry about it, it's basically got a group there that kind of sits open that allows it to interact with other things and actually through the use of heat and the process that we call braising, which I'll talk about in a moment you create a what's called a ketone group. Now, most people now have heard of ketones 'cause they think about the ketogenic diet, but a ketone group is actually a chemical compound that can be used for energy, and that's why people say you can use ketones for energy, but if you've ever actually encountered ketones, if you for instance, get liquid ketones, a ketone ester, and you smell it, what does it smell like? It smells a little bit like an alcohol, but it has a kind of savory taste, even when you smell it. Okay, there are other smells that have these tastes too, but for

the Maillard reaction which could be created for instance like if you took a piece of meat, or if you're not a meat eater if you took tomatoes and you cook them in a pan and you cooked it nice and slow till it's simmered and almost started to brown and burn a little bit. Usually if I do it burns, I'm not a good cook as Costello points out a lot, but it gets that like almost tangy, very umami-like flavor. And sometimes it will even stick to the pan, if you scrape it off and actually you can taste it in your mouth as you're cooking it. That's the Maillard reaction, that's that free aldehyde group, and that's the production of a ketone group. When you smell ketones, it smells very much like that. Okay, some people talk about the ketones will produce like fruity breath. And that's true if people are really far into ketosis, their breath has a kind of fruity odor, that's a little bit of a different thing. So, the relationship between smell and taste is a very, very close one. And this is why when people drink wine they often will inhale and then sip, some of that is just kind of like pomp and circumstance frankly, they make a big deal of it, but they can sense things with their mouth. The combination of odor receptors being activated in a particular way, and taste receptors in the mouth being activated in a particular way, triggers the activation of multiple brain areas that are associated with taste, and circuitry within the body that's associated with the behaviors that relate to that taste like leaning toward it, or leaning away from it depending on whether or not it's appetitive or aversive. So the Maillard reaction is a very interesting reaction involving this sugar amino acid thing, but really it's what it's doing is heating up food such that the amino acids are more available literally in their chemical form for detection by the neurons. This is a phenomenon that occurs in other domains of the taste system. For instance, a lot of what's happened with highly processed foods is that manufacturers have figured out how to trigger more dopamine response by ingestion of these sugary foods and created textures, and created essentially design of foods for two purposes. I'm not out to completely demonize processed food, I did that in a previous episode, but processed foods are really designed to take foods that ordinarily would spoil, that would have a shelf life and extend their shelf life to turn foods which are not a commodity into a commodity. Something could be stored and used essentially as a tradable purchasable, sellable resource. In doing that they change, they've also decided to change the texture so that you want to chew more of them. Like I have this thing I don't know what it is for those Triscuit crackers. I don't know why are those things so good? It's probably the texture, got those layers, they're just kind of perfectly salty. I haven't had one in a long time, so I bet if I had one now it wouldn't taste as good as I'm imagining it. But those combinations of texture, smell, and

taste are what combine to activate these different brain areas that make you really want to desire something. And the people who make foods, processed foods in particular, are phenomenally good at figuring out what drives the dopamine system and makes you want more

#### 01:39:00 How Processed Food Make You Crave More Processed Foods

of these things either because of the way they taste and/or because of the way they trigger neurons in your gut that have nothing to do with taste that simply make you desire more of the food. In other words, many of the foods that are processed foods make you desire more of them, it's impossible to eat one chip kind of thing. Not because they taste good, but because in your gut they're activating the neurons that activate dopamine which make you seek more of those foods independent of blood sugar or anything else. So, you may actually be eating more particular foods not because they taste good, but because they feel good on your tongue and mouth, and because the neurons in your gut which are totally independent of conscious taste are triggering the release of dopamine which is a molecule that makes you seek more of,

#### 01:39:44 Protocol 4: Invert Your Sense of Sweet & Sour: Miracle Fruit; Swapping Bitter & Sweet

and do more of anything that led to the ingestion of that food. There's a fun experiment that you can do, which is to completely invert your sense of sweet and sour, there's actually a way to do this readily. When I was a post-doc, I used to have a journal club at my house, people would come over in the evening once a month, and we would read a paper, typically the weirdest paper we could find and we would eat food and hang out, that's what nerds did and do for fun, so that's what we did. And one time someone brought what's called miracle berry. Okay, so this isn't some psychedelic plant medicine thing, miracle berry, you can purchase online, it's relatively inexpensive. It actually causes a change in the configuration of taste receptors such that when you eat something sour, it tastes sweet. And so what's really wild is you ingest miracle berry, and then you bite into a lemon, maybe even the lemon and peel and it tastes as sweet as a peach. And this effect lasts several hours. Definitely, you know, check any warnings, I don't know what sort of warnings these, a miracle berry carries, but I'm sure there's

always something, you can imagine. There are a number of papers on miracle berry or miracle fruit it's called, but it changes your perception of sour at a perceptual level, but it does that by changing the activity of the receptors in the mouth and tongue. Now, this is important as a principle and it's underscored by experiments that have been done by for instance Charles Zuker's lab at Columbia University, where they've essentially genetically engineered animals such that the bitter receptor is swapped with the sweet receptor, or the sweet receptor is swapped with the bitter receptor. And what they show is that the actual food, the experience on the tongue drives different pathways in the brain. Here's what they did, they essentially took mice and swapped out the sweet receptor and put in a bitter receptor. And then what they found is that whereas normally mice would actively seek out and even work for sugar water, sucrose, they really like that. If they replace the sweet receptor with the bitter receptor, the mice would avoid sugar water. And the reverse was also true, that mice would drink a bitter solution avidly, they liked a bitter solution if they swapped out the bitter receptor for sweet receptor. What this means is that our entire experience of what we taste is dependent on how we experience that taste the level of the tongue. And so, you're hopefully not going to do genetic engineering of your taste receptors, but if you'd like to do this sort of experiment you actually can do it very easily using miracle fruit, the instructions of how much to ingest, et cetera, any safety concerns are usually on the package and should be easy to find. And there's a lot of science to support how this works, it's kind of a fun experiment that anyone can do and will completely change your perception of any food that you're accustomed to eating. In fact, you can figure out how much sweet or the sense of sweetness is contributing to your experience of a food, even if you don't think of it as a sweet food through this miracle fruit experiment. You could take miracle fruit, you could eat a slice of pepperoni pizza or cheese pizza, which perhaps normally to you would taste just like pizza, and you'll notice it tastes very different.

01:43:03 Pheromones, Desire To Continue Mating: Coolidge Effect Occurs In Males & Females

What you are detecting is how much the sense of sweet was contributing to that particular flavor. Now, I'd like to return to pheromones. As I mentioned earlier, true pheromonal effects are well-established in animals. And one of the most remarkable pheromone effects that's ever been described is one that actually I've mentioned before

on this podcast, but I'll mention again just briefly, which is the Coolidge effect. The Coolidge effect is the effect of a male of a given species, in most cases, it tended to be a rodent or a rooster mating. And at some point reaching exhaustion or the inability to mate again because they just simply couldn't for whatever reason. The Coolidge effect establishes that if you swap out the hen with a new hen, or the female rat or mouse with a new one then the rat or the rooster spontaneously regains their ability to mate, somehow their vigor is returned, the refractory period after mating that normally occurs is abolished and they can mate again. It turns out that the Coolidge effect runs in the opposite direction too. I did not know this, but I recently learned of a study, it was actually done in hamsters, not in mice, but it turns out that females also will, female rodents will mate to exhaustion. And at some point... At some point, excuse me, they will refuse to mate any longer unless you swap in a new male. And then because mating in rodents involves the female being receptive, there are certain number of behaviors that mean that tell you that she's willing and wanting to mate, so-called lordosis reflex. Then if there's a new male, she will spontaneously regain the lordosis reflex and the desire to mate. And how do you know this? How do we know it's a pheromonal effect? Well, this recovery of the desire and ability to mate both in males and in females can be evoked completely by the odor of a new male or female, it doesn't even have to be the presentation of the actual animal. And that's how you know that it's not some visual interaction or some other interaction, it's a pheromonal interaction. Now, as I mentioned earlier, pheromonal effects in humans have been debated for a long period of time. We are thought to have a vestigial, meaning a kind of shrunken down miniature accessory olfactory bulb called Jacobson's organ, or the vomeronasal organ. Some people don't believe that Jacobson's organ exists, some people do, there is anatomical evidence for it in some cadavers. It sits not very high up in the brain or where your olfactory bulb is, but it's actually in the nasal passages, so there's like little dents as you go up through your nasal passages, and there is evidence of something that's vomeronasal-like.

Vomeronasal is the pheromonal organ, they call it Jacobson's organ if it's present in humans, kind of tucked into some of the divots in the nasal passage. Even if that organ, Jacobson's organ isn't there or is not responsible for the chemical signaling between individuals, there is chemical signaling between human beings. As I mentioned earlier, the effect of tears in suppressing the areas of the brain that are involved in sexual desire and testosterone of males, that's a concrete result, that's a very good result published by an excellent group with no pre-existing bias going in, that's just what they found. There is

also evidence

#### 01:46:40 Do Women Influence Each Others Menstrual Cycles?

both for and against chemical signaling between females in terms of synchronization of menstrual cycles. Now, the original paper on this was published in the 1970s by McClintock, and it essentially said that when women live together in group housing, dormitories, and similar that their menstrual cycles were synchronized and that was due to what was hypothesized to be pheromonal effects. Over the years, that study has been challenged many, many times. The more recent data point to the idea that there is chemical-chemical signaling between women in ways that impact the timing of the menstrual cycle, but that depending on whether or not some of the women are in the ovulation phase, the ovulatory phase of that cycle or whether or not they are in the follicular phase, the phase when the follicle is maturing before the egg actually ovulates. So two separate phases of the 28 day menstrual cycle will either lengthen or shorten the menstrual cycle of the person that smells those women. Translated into English what that means is that it is very likely it seems that something, maybe pheromones, but maybe some other chemical that is independent of pheromones is being conveyed between women that are housed together or spend a lot of time together to shift their menstrual cycle, but it doesn't necessarily mean that they synchronize. So for instance, if one woman is in the follicular phase of the menstrual cycle, it might shorten or delay ovulation. Excuse me, it might accelerate ovulation in another woman, whereas if somebody is in the ovulatory phase of their cycle, it might lengthen the menstrual cycle out so that they, the woman who smells that person's scent or who smells her sweat, we still don't know the origin of the chemical would ovulate later. So, all of this is to say is that chemical-chemical signaling is happening from females to males through tears, we know that. Is that a pheromonal effect? Well, by the strict definition of a pheromone, a molecule that's released from one individual that impacts the biology of another individual, yes. But in terms of identifying what the pheromone is in tears, that's still unknown, it's not clear what the chemical compound is. So, we're reluctant as scientists to call it a true pheromonal effect. The menstrual cycle and the synchronization of the menstrual cycle effect seems to hold up under some conditions. But in some cases, there's a kind of clash of menstrual cycles that's created by chemicals that are emitted from one female to another.

### 01:49:19 Recognizing the Smell Of Your Romantic Partner

So, there are many examples of this in humans, for instance, people can recognize the t-shirt of their mate. If you give... This experiment has been done many times, I know it's been challenged a number of times, but the data are pretty good by now that if you offer, you take a collection of women who are in stable relationships with somebody, you offer them the smell of a hundred different shirts and they can very readily pick out their significant others scent. Okay, that's pure olfaction, that's not pheromonal, but nonetheless is a remarkable degree of discrimination, olfactory discrimination. You can dilute their partner's scent down to the point where they themselves can't consciously detect the difference between the sweat or the t-shirt of a hundred different t-shirts or so, they might say, "I don't really smell the difference, but I think it's this one. Yeah, this one belongs to the person that I've been with." And they are much greater than chance at detecting the t-shirt or identifying the t-shirt correctly. So, there's no question really that there is chemical-chemical signaling between humans, the question is whether or not it's truly pheromonal in basis. Now, you'll notice that a lot of the examples I gave

### 01:50:30 Differences In Odor Detection Ability, Effects Of Hormones

aside from the one of tears is women detecting the scents of men or of other women. And it turns out that there are a number of papers, the best one I think that I could find is published in *Physiology and Behavior* in 2009, it's a review entitled *Sex Differences and Reproductive Hormone Influences on Human Odor Perception* by Doty, D-O-T-Y, and Cameron. I encourage you to check out this review it's available free as a download, we'll provide a link to it, you can get the full PDF if you want. But it does seem that women are better at detecting odors in these odor discrimination tasks than are men. And yes, that it does vary according to where they are in their menstrual cycle. And yes, they also looked at people who had received gonadectomy, they had their ovaries removed, a number of different important controls. None of this surprises me, none of this should surprise you, it's very clear that hormones have a profound effect on enlarge number of systems in our biology and that smell, and taste, and the ability to sense the chemical states of others, either consciously or subconsciously have a profound influence on whether or not we might want to spend time with them, whether or not this

is somebody that we're pair bonded with, whether or not this is somebody that we just met and don't trust yet, things of this sort. And given what's at stake in terms of reproductive biology, not just offspring, but given the possibility of transmission of diseases, et cetera, you know, the risks of childbirth, et cetera. It makes so much sense that much of our biology is wired toward detecting and sensing whether or not things and people are things that we should approach or avoid, whether or not reproduction with that person is the appropriate response or suppression of the reproductive response is the appropriate response, right? As in that's the case with the tears. So, I think these are fascinating studies, it's an area that still needs a lot of work, but there are some really wonderful papers on this. And the one that I mentioned a few minutes ago, Sex Differences and Reproductive Hormone Influences on Human Odor Perception is one of the better reviews that are out there. There are also a number of other reviews for instance that talk about pheromone effects and their impact on mood, and sexual responses, and things of that sort, and we will also provide some links to those. A lot of this is still speculative, but I want to say I know I said it three times, what I really want to underscore because it is vitally important, and people seem to get a little triggered by the notion of pheromones.

01:53:00 We Rub The Chemicals Of Others On Our Eyes and Skin, Bunting Behavior

Just because we haven't identified the actual chemical compound that's acting as a pheromone or putative pheromone does not mean that chemical-chemical signaling between individuals doesn't exist, clearly it does. Actually, you and every other human from the time you're born until the time you die are actively seeking out and sensing and evaluating the chemicals that come from other individuals. There's a really nice study that was done by the Weizmann Institute, a group there, I think it was also Noam Sobel's group, but another group as well as I recall looking at human-human interactions when they meet for the first time. It's a remarkable study because what they found was people would reach out and shake hands. It's is a typical response, you know pre-pandemic, people would meet, they'd reach out and they would shake hands. And what they observed was almost every time within just a few seconds of having shaken hands with this new individual, people will touch their eyes almost without fail. Occasionally, they would touch their eyebrow, occasionally someone would touch their hair. We always associate that with people having some sort of... Or us having some sort of self-

conscious response like oh, we want to make sure shirt tucked in and all prim and proper, whatever it is, or looking right, is there something you're like teeth? This kind of thing, but actually people are doing that even if the person they just met left the room. So, someone's sitting there, someone comes in, they shake hands, and the person inevitably subconsciously touches their eyes. They are taking chemicals from the skin contact and they are placing it on a mucosal membrane of some sort, typically not up to their nose or in their mouth, typically on their eyes. Now, animals do this all the time, there's a phenomenon in animals called bunting. If you have a overeager dog that when you meet them or you see them again after you've been away for the day they'll rub their head against you, right? Cats will do this too, it's called bunting, they're rubbing their scent glands on you, they're marking you. And believe it or not, you're marking other people when you shake their hand, and they are then taking your mark and rubbing it on themselves subconsciously. So, we all do these kinds of behaviors, and now that you're aware of it you can watch for it in your environment, you can pay attention to people. Some of this has probably changed in light of the events of 2020, et cetera, but nonetheless, we are evaluating the molecules on people's breath, we are evaluating the molecules on people's skin by actively rubbing it on ourselves. And we are actively involved in sensing not just their facial expressions, the size of their pupils, and things like that, but the chemicals that they are emitting, their hormone status, how they smell. We're detecting the pheromones possibly, but certainly the odors in their breath. You might say, "Well, I don't actually go around sniffing people's breath. I don't, you know, unless if it's bad," in which case it's aversive, but breath is communicating a lot of signals. And this handshake eye rub experiment shows that we are actively going through behaviors reflexively to wipe ourselves or smear ourselves with other people's chemicals. Now, that might seem odd or even gross to you, but I think it's beautiful, I think that it illustrates the extent to which we as human beings are in some ways among the other animals in our subconscious, sometimes conscious, but certainly subconscious tendency to try and evaluate our chemical environment through what we inhale through our nose, what we ingest through our mouth, and what we actively take off other people's skin and rub on ourselves to evaluate it and what we should do about it,

01:56:40 Summary

and perhaps that person as well. So today, we talked a lot about olfaction taste and

chemical sensing between individuals. I'd like to think that you now know a lot about how your smell system works and why inhaling is a really good thing to do in general for waking up your brain, and for cognitive function, and for enhancing your sense of smell. We talked about how to enhance your sense of taste, and we talked about chemical signaling between individuals as a way of communicating some important aspects about biology. People are shaping each other's biology all the time by way of these chemicals that are being traded from one body to the next through air, and skin to skin contact, and tears. If you're enjoying this podcast and you're finding the information useful please subscribe on YouTube, that's one of the best ways to support us. You can also put any questions you have and feedback in the comment section on YouTube. If you don't already subscribe on Apple and Spotify, you can support us by subscribing on Apple and Spotify. And on apple, you get the opportunity to leave us a review up to five stars, If you think we deserve five stars please give us a five star review. In any case, you can leave us comments there. And we are also very active on Instagram, @hubermanlab on Instagram is where I post yes, clips from the podcast, but also additional new and original content, and you have the opportunity to put your questions in the comment section below those posts as well. I do read all the comments on YouTube, on Apple, and also on Instagram. We have a website [hubermanlab.com](http://hubermanlab.com) where all the podcasts are housed with links to YouTube, Apple, and Spotify as well as downloadable links, everything's zero cost of course. And there, you can also find any links to additional resources that we might post. As well, please check out our sponsors that we mentioned at the beginning of each podcast episode, those sponsors are the way that we are able to bring zero cost to consumer information about all these topics to you each week. And we also have a Patreon, it's [patreon.com/andrewhuberman](https://patreon.com/andrewhuberman), and there you can support us at any level that you like. Today, we didn't really talk about supplements, but previous episodes and in future episodes we'll talk about supplements and things that you can take to modify your biology and nervous system if you like. We've partnered with Thorne, T-H-O-R-N-E, because Thorne has the highest levels of stringency with respect to the amounts of given compounds that are in their supplements, and the quality and purity of those compounds. If you go to Thorne, [thorne.com/u/huberman](https://thorne.com/u/huberman), you can see all the supplements that I take and get 20% off any of those supplements as well as any of the other supplements that Thorne makes, you just go to [thorne.com/u/huberman](https://thorne.com/u/huberman). And if you enter their website through that portal you get 20% off any of their things at checkout. Last but not least, I want to thank you for your time and attention, and your willingness to

embrace new concepts and terms, and to learn about science and biology, and protocols that hopefully can benefit you and the people that you know, and of course thank you for your interest in science. [gentle music]