

Dr. Robert Sapolsky: Science of Stress, Testosterone & Free Will | Huberman Lab Podcast #35

In this episode, I interview Dr. Robert Sapolsky, Ph.D., Professor of Biology, Neurology & Neurosurgery at Stanford University. We discuss stress, what defines short-term versus long-term stress, and how stress can be beneficial or detrimental, depending on the context. We also discuss stress mitigation and how our sense of control over stress mitigation techniques, including exercise, determine health outcomes. Dr. Sapolsky explains some of the key effects of the hormone testosterone — how it can amplify pre-existing tendencies for aggression or sexual behavior, but that it does not produce those behaviors per se. He also explains how testosterone impacts our social hierarchies, sense of confidence, and willingness to embrace challenges of different kinds. He also explains how our behaviors and perceptions shape testosterone levels. And we discuss estrogen and the powerful role it plays in brain development, health and longevity. Finally, we discuss free will, what it means to have free will, and if we have any free will, including how knowledge alone might allow us to make better decisions for ourselves and society.

#HubermanLab #Testosterone #Stress

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Dr. Sapolsky's most recent book, "Behave: The Biology of Humans At Our Best & Worst": <https://amzn.to/3yrZ6k7>

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- [Andrew Huberman] Welcome to the Huberman Lab Podcast where we discuss science and science-based tools for everyday life. - I'm Andrew Huberman, and I'm a Professor of Neurobiology and Ophthalmology at Stanford School of Medicine. Today I have the pleasure of introducing Dr. Robert Sapolsky. Dr. Sapolsky is a Professor of Biology and Neurosurgery at Stanford University. His laboratory has worked on a large variety of topics, including stress, hormones, including testosterone and estrogen, and how the different members of a given species interact according to factors like hormones, hierarchy within primate troops, and how things like stress, reproduction and competition impact behavior. One of the things that makes Dr. Sapolsky's work so unique is that it combines elements from primatology, including field studies with human behavior, in essence trying to unveil how humans as old world primates are controlled by different elements of our biology as well as our psychology. Dr. Sapolsky is also a prolific author of popular books, such as "Why Zebras Don't Get Ulcers", "The Trouble with Testosterone", and "Behave: The Biology of Humans at Our Best and Worst". During the course of our discussion today, Robert also revealed to me that he is close to completing a new book entitled, "Determined: The Science of Life Without Freewill." And indeed we discuss the science of life without freewill during this episode. We also discuss stress and how best to control stress and how stress controls us at both, conscious and subconscious levels. We talk about testosterone and estrogen and hormone replacement therapy and how those impact our mind, our psychology and our interactions with others. As with any discussion with Dr. Sapolsky, we learn about scientific mechanisms that make us who we are. And today we also discuss tools and how we can leverage those scientific mechanisms in order to be better versions of ourselves. I should mention that unlike most guest interviews on the Huberman Lab podcast, this one had to be carried out remotely due to various constraints, so you may hear the occasional audio artifact, please excuse that. We felt that the value of a

conversation with Dr. Sapolsky was well-worth those minor, minor glitches. And indeed the information that he delivers us

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is tremendously valuable, interesting, and in many cases actionable as well. Before we begin, I'd like to emphasize that 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 are of the absolute highest quality. The company was founded by two All-American swimmers from Stanford, and everything about the design of the sunglasses and eyeglasses was created with performance in mind. There are several things I like about ROKA glasses so much. One of them is that the aesthetic of the glasses is great. Unlike a lot of performance glasses out there that you can wear while swimming and running but also indoors, these glasses don't make you look like a cyborg. The aesthetic of them is really terrific, and they have a lot of different styles to select from. In addition to that, the quality of the lenses on both the sunglasses and eyeglasses are superb. The optical clarity is great, you can move from brightly lit areas to shadowed areas, and you don't get any degradation in the quality of the visual image. And that's absolutely essential. If you'd like to try ROKA glasses, you can go to roka.com and enter the code Huberman to save 20% off your first order. That's [ROKA.com](https://roka.com) and enter the code Huberman at checkout. 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've long been a believer in getting regular blood work done. And now with the advent of quality DNA tests, you can get a lot of information about your genetics and how that also impacts your immediate and long-term health. The reason I'm such a fan of getting blood work done is that it is really the only way to understand what's going on in your system at a level that can really inform your decisions about your immediate and long-term health. The problem with a lot of blood and DNA tests, however, is that you get numbers back about your hormones and your metabolic factors, etc., but you don't know what to do with that information. With InsideTracker, they have a very easy to use dashboard that gives you

that information, and then gives you some suggestions and directives about things you could change about your nutrition, about your exercise and other lifestyle factors that can help you move those numbers in the direction that's best for you and for your health. If you'd like to try InsideTracker, you can go to [InsideTracker.com/Huberman](https://www.insidetracker.com/Huberman) to get 25% off any of InsideTracker plans, just use the code Huberman at checkout. Today's podcast is also brought to us by Belcampo. Belcampo is a regenerative farm in Northern California that raises organic grass-fed and finished certified humane meats. I eat meat about once a day, in general my lunch or my breakfast consists of some meat, and that meat has to be of very high-quality, and generally I'll eat some vegetable as well. And then I tend to eat pastas and rice and things of that sort later in the day or in the evening in order to facilitate the transition to sleep. So I'm eating meat about once a day, and I always insist that the meat that I eat be of the very highest quality and that the animals were raised and maintained humanely. While conventionally raised animals are confined to feedlots and eat a diet of inflammatory grains, Belcampo's animals graze on open pastures and seasonal grasses resulting in meat that's higher in nutrients and healthy fats. In addition, they raise their animals in a way that's not just better for our health, but also has a positive impact on the environment. They practice regenerative agriculture, which means the meat is climate positive and carbon negative. So you can feel good about what you're eating at the environmental level and for sake of your health. You can order Belcampo's sustainably raised meats to be delivered to you by using my code Huberman at [Belcampo.com/Huberman](https://www.belcampo.com/Huberman) and entering my code Huberman to get 20% off your first time order. I'm partial to the ribeyes or the New York steaks, so on one day I might have a ribeye, the next day I might have a New York steak, I also really like the meatballs, I'm a particular fan of the meatballs. So, again, that's [Belcampo.com/Huberman](https://www.belcampo.com/Huberman) and enter the code Huberman at checkout to get 20% off your order.

00:06:30 Stress: Short & Long-Term, Good & Bad

And now without further ado, my conversation with Dr. Robert Sapolsky. Great, well, thank you so much, Robert, for joining us today. I've been looking forward to this for a very long time and I appreciate it. - Oh yes, glad to be here. - There is an enormous range of topics that we could drill into, but just to start off, I want to return to a topic that is near and dear to your heart, which is stress. And one of the questions that I get most

commonly is, what is the difference between short and long-term stress in terms of their benefits and their drawbacks? And the reason I say benefits is that, obviously stress and the stress response can keep us alive, but stress, of course, can also sharpen our mental acuity and things of that sort. So how should we conceptualize stress and how should we conceptualize stress in the short-term and in the long-term? - Well, basically sort of two graphs that one would draw. The first one is just all sorts of beneficial effects of stress short-term, and then once we get into chronicity, it's just downhill from there. Short-term because it saves you from the predator, short-term because you're giving a presentation and you think more clearly or your focus is better, all sorts of aspects of that. And what then winds up being an argument is, how long does it take to go from short-term to long-term? And that's somewhat arbitrary, but the sorts of chronic stressors that most people deal with are just undeniably in the chronic range, like having spent the last 20 years, daily traffic jams or abusive boss or some such thing. The other curve that's sort of perpendicular to this is dealing with the fact that sometimes stress is a great thing. Like our goal is not to cure people of stress because if it's a right kind, we love it. We pay good money to be stressed that way by a scary movie or a rollercoaster ride. What you wind up seeing is when it's the right amount of stress, it's what we call stimulation. And the basic curve there is, here is an optimal level of stimulation and too little, and function goes down with what we would call boredom, and too much and function goes down

00:09:11 Valence & Amygdala

with what we would call stress. And the optimum is what all of us aim for. - In terms of the benefits of stress in the short-term, one thing that's really striking to me is, how physiologically the stress response looks so much like the excitement response to a positive event. And we can speculate that the fundamental difference between short-term stress and short-term excitement is some neuromodulator like dopamine or something like that. But is there anything else that we know about the biology that reveals to us? What really creates this thing we call valence that an experience can be terrible or feel awful, or it can feel wonderful, exhilarating depending on this somewhat subjective feature we call valence? Do we know what valence is or where it resides? - On a really mechanical level, if you're in a circumstance that is requiring that your heart races and you're breathing as fast and you're using your muscles and some such thing,

you're going to be having roughly the same brain activation profile, whether this is for something wonderful or something terrible with the one exception being that if the amygdala is part of the activation, this is something that's going to be counting as adverse. Whether that's the circumstance, an adverse circumstance recruiting the amygdala into it, and how much it's the amygdala being involved, biases you towards interpreting it as even more awful.

00:11:00 Testosterone: Common Myths vs. Actual Truths

The amygdala in some ways is kind of the checkpoint as to whether we're talking about excitement or terror. - Let's use the amygdala as a transition point to another topic that you've spent many years working on and thinking about, which is testosterone and other sex steroid hormones. I heard you say once before that among all the brain areas that bind testosterone, that where testosterone can park and create effects that the amygdala is among the most chockablock full of these parking spots, these receptors. I realize there's a lot here, but how should we think about the role of testosterone in the amygdala given that the engagement of the amygdala is fundamental in this transition point between a exhilarating, positive response and a negative stressful response? Or maybe just broadly, how should we think about testosterone and its effects on the brain? - And pertinent to the transition from whether this is a stressor that's evoking fear or revoking aggression in terms of that continuum, also because the amygdala is in the center of all four points on those axes. Basically, almost everybody out there has a completely wrong idea as to what testosterone does, which is testosterone makes you aggressive because males, virtually every species out there have more testosterone and a more aggressive and seasonal measures have testosterone surging at the time of year, they're punching it out over territory. And you take testosterone out of the picture, you castrate any mammal out there, including us, and levels of aggression will go down. And the easy thing then tends to conclude that testosterone causes aggression. And the reality is testosterone does no such thing, it doesn't cause aggression. And you can see this both behaviorally and in the amygdala. What does testosterone do? It lowers the threshold for the sort of things that would normally provoke you into being [mumbles] so that it happens more easily. It makes systems that are already turned on, turn on louder rather than turning on aggressive music or some such thing. What does that look like behaviorally? You take five male monkeys, put them together, they form a dominance

hierarchy. Number one is great, number five is miserable, number three is right in between. Now take number three and shoot the guy up with tons of testosterone and he's going to be involved in more fights. Aha, testosterone uniformly causes aggression, but you look closely and there's a pattern to it, is number three now challenging numbers two and one for their place in the hierarchy. Absolutely not, he is brown-nosing them exactly as much as he used to. What's going on is he's just a miserable terror to poor number four and five. And in that case, what testosterone is doing is amplifying the preexisting patterns of aggression. Amplifying the social learning, that's where it'd gone into there. Now on sort of the more reductive level, so how does that translate into the amygdala? Does testosterone make amygdaloid neurons have action potentials? Does it cause those neurons to suddenly speak about fear and aggression spontaneously? Absolutely not. What they do is, if the amygdala is already being stimulated, it increases the rate of neuronal firing. What its worth? It shortens after-hyperpolarizations. So the theme there exactly is, it's not creating your aggression, it's just upping the volume of whatever aggression is already there. And once you factor that in, it's impossible to say anything about what testosterone does

00:15:15 Behaviors that Affect Testosterone

outside the context of what testosterone related behaviors, how they get treated [laughs] in your social settings. - Mm-hmm, yeah. And in terms of status and the relationship between individuals, either nonhuman primates or humans, can we say that testosterone and levels of testosterone? Or I should say, can we say that relative levels of testosterone between individuals is correlated to status within the hierarchy? - Yes, but in a way that winds up being totally uninteresting. Like you go back on whatever number of decades, the endocrinology texts, and there were two totally reliable findings in there. Let's see, I have a dog in here that's- - Oh, good, we like dogs at the Huberman Lab podcast. - Oh, okay, it is jingling with that. - They are welcome, they are absolutely welcome, yeah. - And there'd be two truisms, which is higher levels of testosterone predict higher levels of aggression in humans and other animals. Higher levels of testosterone predict higher levels of sexual activity. Whoa, testosterone causing both, and the correlation is there. And when you look closely, we've got cause and effect stuff, sexual behavior raises testosterone levels, aggression raises testosterone levels. Your levels before had were barely predictive of what's going to happen, so it's a response

rather than a cause. When you look at that though in terms of making sense of individual differences, they don't matter a whole lot. You can spend an entire career on the social circumstances that produce 3.5% more testosterone in the circulation, and expect to see all sorts of interesting implications. And that's not really the case, it's somewhat of a yes or no modulator of the much more subtle social stuff that's already there. - Very interesting.

00:17:20 Mindsets & Contexts that Affect Testosterone

I think that there are a lot of misconceptions about human biology, but testosterone seems to be one area where at least from what I can find on the internet, it's sort of at the peak of misunderstanding. Maybe we could just ask a few more questions about testosterone and sexual behavior because there's an interesting story there about castration versus non-castration and the causality, again. But before you address that, I just want to highlight something that you said that I think is so vital, which is that behaviors, such as aggressive behaviors and sexual behaviors can actually increase testosterone. Did I hear that correctly? - Yeah. - And the reverse is sort of true, but not in a causal way. Is that right? - The opposite direction of the causality, yeah. - Yeah, yeah, so if I were to increase somebody's testosterone by 30%, male or female doesn't matter, their sexual behavior may or may not change. - Essentially zero effect at all. Your brain is not that sensitive to fluctuations in testosterone levels. In terms of things like aggression, raising testosterone, this is a great footnote. If you have the right type of willing to die on the trenches devotion sort of thing, watching your favorite team play a sport will raise your testosterone levels as you sit there with the potato chips in your armchair. So it's not the physicality of aggression, it's the psychological framing of it. So, yeah, testosterone is not causing that. And a great way to appreciate that is, okay, so you had all these testosterone sexual behavior correlations, and you do the definitive endocrine intervention, which is you do a subtraction study, you've removed the testes. And as I said before, levels of sexual behavior goes down. Good, we've just shown that testosterone is somehow have caused it. Critically they go down, but not down to zero, whether you are a rat or a monkey or a human, whatever. And what predicts how much residual sexual behavior is there, how much sexual behavior there was before castration? What that's telling you is by then that's behavior that's being carried by social learning and context rather than by the hormone, exact same thing with aggression.

Drops after castration, doesn't go to zero, the more prior history of it, the more it just keeps coasting along on its own even without testosterone. - Very interesting. Can we say that there is an exception in terms of the early organizing effects of hormones? Like, for instance, if a developing animal is deprived of a testosterone or estrogen or aromatized testosterone into estrogen, there's a whole story there is, you know. But then I could imagine that the circuits of the brain that are responsible for initiating sexual behavior in the first place might not emerge, and therefore not be sensitive to the testosterone later in life. Is that right?

00:20:28 How Finger Length Ratios Reflect Prenatal Hormone Levels

Okay. - Yeah, exactly. And a great way of seeing that is this totally nutty biological factoid, which is the second to fourth digit ratio enhanced. - Oh yeah. - Totally obscure thing, the ratio of one to the other in some way reflects levels of testosterone, androgen exposure during fetal life. And I can't remember which way it goes and it's minuscule and you need a thousand people in your sample size to be able to see anything, but you see it in other primates, it's already there in fetal sonograms, all of that. So that's a readout of subtle differences in prenatal exposure, and that winds up being a predictor of a whole range of sort of stuff in adult behavior. So, yeah, at the fetal end, when you're still building everything, testosterone and the amount of that is making a huge difference. By the time you're an adult, it's just somewhat of an old and a non-signal. - Yeah, I have a confession, which is that I was a master's student at Berkeley in Marc Breedlove's arena, so I'm an author on that paper, although I'm deep within the author line, and you got the description of it exactly right that it's the D2, the index finger to the ring finger ratio is more similar in females than it is in males. In males, the index finger tends to be shorter. And for people out there who are listening to this who are now freaking out or measuring, that there is a proper way to measure this, which is, eyeballing it doesn't work all the time unless at the extremes. And there's some very interesting stories there. It actually has been replicated no fewer than five times, Marc Breedlove tells me. But yes, in terms of these early organizing effects, those seem very robust in most studies. These later effects are sort of activation of neural circuits by hormones.

00:22:30 Aggression: Male-Female, Female-Male, & Female-Female

I'm absolutely fascinated by this. And I do have a couple other questions, which is, we normally associate testosterone with males, but of course, females make testosterone as well from the adrenals and presumably elsewhere too. I'm guessing if we looked hard enough, we'd probably find that there were other sources of androgens in females. Can we say that these general contours of effects on aggression also pertain to females? And I suppose I should ask in particular about female-female aggression, which does exist in many species, female-male aggression as well as maternal aggression, which is a robust aspect of our evolution, of course, that the mother will, an angry mother animal of any kind protecting her young is truly dangerous, in the best sense of the word. - And that type of post-parturition, period after birth aggression is all about estrogen, progesterone, those sorts of things. Female aggression, the rest of the time has testosterone as a major player at a much lower level on the average. On the average, one always has to say, but it's basically the same punchlines. In females, the lower levels of testosterone are essential for typical levels of aggression and sexual behavior. Nonetheless, they're not causing it, it's not sensitive to small individual differences. Same exact thing. You can get way over-impressed

00:24:05 Testosterone: The Challenge Hypothesis

with the importance of androgens in females just as readily as in males. - So in line with that, how should we conceptualize testosterone? I realize there isn't a single sentence that can capture a hormone in all its effects because hormones have so many different slow and fast effects on the brain, on other glands on their own, on the very glands that produce them. But as I've heard you talk about testosterone today and over the years, I start to get the impression that as the most misunderstood molecule [laughs] in human health in the universe, it's clearly doing something very powerful. It's shifting the way that certain neural circuits work, adjusting the gain on the amygdala, as you described, and certainly other things as well. Is there any truism about testosterone like, and its relationship to effort or its relationship to resilience, and in a way that maybe will help me and other people to sort of think about how to think about testosterone? - Yeah. Maybe three separate answers to that. The first one is, I think it's a fair summary to think that when it comes to motivated strong behaviors, what testosterone does is make you more of whatever you already are. And that to me, sexual arousal, libido, aggressiveness, spontaneous aggression, reactive aggression, things of that sort. It's upping the volume

of things that are already strongly there. Second way to think about it is, well, here's like my favorite finding about testosterone. And this was some wonderful work by a guy, John Wingfield, who's one of the best behavioral endocrinologists out there. And about 20 years ago he formulated what was called The Challenge Hypothesis of Testosterone in Action. What does testosterone do? Testosterone is what you secrete when your status is being challenged, and it makes it more likely that you'll do the behaviors needed to hold onto your status. Okay, so that's totally boringly straightforward if you are a baboon. If somebody is challenging your high rank, the appropriate response on your part is going to be aggression. All right, so we've just got in through the back door, testosterone and aggression, again. But then you get to humans, and humans have lots of different ways of achieving or maintaining status. And all you need to do is go to like some fancy private school's annual auction, and you will see all these half-drunk alpha males competing to see who can give the most money away as a show of conspicuous like property that they have. And in a setting like that, I mean, I haven't been able to take urine samples, if there's times, unfortunately, but that shows the flip side of it. If you have a species that hands out status in a very different sort of way, testosterone is going to boost that also. Okay, so that generates a totally nutty prediction. Wow, take people in a circumstance, say playing an economic game where you get status by being trustworthy and being generous in your interactions with the game. If you give people testosterone, does that make them more generous? And that's absolutely the case. Totally cool finding. I'm showing you, I don't know, basically if you took a whole bunch of Buddhist monks and shot them up with testosterone, they'd get all competitive with each other as to who could do the most random acts of kindness. And if we have a societal problem with too much aggression, the first culprit to look at is not testosterone, the first to look at is that we hand out so much damn elevated status for aggression in so many circumstances. So I find that finding to be fantastic. Third thing about subtlety of testosterone. Okay, so like some subtler behavioral effects, you give testosterone to people and they become more confident, they become more self-confident. Well, that's good, people pay to take all sorts of nonsensical self-help courses that will boost your self-esteem. And that's a good thing unless testosterone makes you more confident, that is inaccurate, and you're more likely to barrel into wrong decisions. What's shown in economic game play is that testosterone by making you more confident makes you less cooperative because who needs to cooperate because I'm on top of this all on my own. Testosterone makes people cocky and impulsive. And that might be great in one setting,

but if and the other is, you're absolutely sure your army is to get over on the other country in three days. So hell, let's start World War I, and you get a big surprise out of it. Testosterone altering risk assessment beforehand probably played a big role in that kind of miscalculation.

00:29:20 How Dopamine Impacts Testosterone & Motivation

- Super-interesting. I always think about testosterone and dopamine being close cousins in the brain, not just because of their relationship through the pituitary and hypothalamus. That, of course, but also because of dopamine's salient role in creating this bias towards exteroception. When somebody takes a drug, with it increases dopamine, or they're chockablock full of dopamine. They tend, I want to highlight 'tend' because this is, I'm really generalizing here, but they tend to focus on outward goals, things beyond the boundaries of their skin. And testosterone seems to do a bit of the same, it tends to put us into a similar mode of perceiving the outside world in ways that we're asking questions like, how do I relate to this other of my species? How do I relate to these goals? Is there anything that we can do to better conceptualize the relationship between testosterone and dopamine and motivation? Or would that just take us down the alleyways of, of neural pathways and the hypothalamus? Which is fine too. - Well, I think it's got lots to do with sort of this massive revisionism about dopamine. Everyone, since the pharaohs got brought up being taught that dopamine is about pleasure and reward. It turns out it isn't, it's about anticipation of reward, and it's about generating the motivation, the goal-directed behavior needed to go get that reward. And before you know it, you're using like elevated dopamine, your entire life to motivate you to do whatever is going to get you like entry into heaven after-life kind of, it's doing that sort of thing. So it's really about the motivation. And what testosterone does even in individuals who are not aggressive and why testosterone replacement is often a very helpful thing for aging males is it increases energy, it increases a sense of thereeness, a presence of alertness that increases motivation. So that's a whole aspect, which then takes us into is your motivation to get up and like go, hand out lots of soup in a soup kitchen for homeless people, or is it to get up and go ethnically cleanse a village. It's got much to do with what your makeup was before the testosterone got onboard. So it's activating in an energetic sense, testosterone within minutes increases glucose uptake into skeletal muscle. You're just more awake and alert and all of that, and that has a lot to do with

what dopamine does. And as one might predict then, getting just the right levels of testosterone infused into your bloodstream feels great to lab rats. They will lever press to get infused into the range that optimizes dopamine release. So there is, you are absolutely right, they're deeply intertwined. - Yeah, such beautiful biology there.

00:32:32 Estrogen: Improves Brain & Longevity BUT TIMING IS KEY

And I love the way you encapsulate their relationship. I want to ask about estrogen, we don't hear about estrogen as often, and it's always interesting to me now doing some public facing education, that testosterone is this very controversial molecule, just to say it is almost controversial. [laughs] [Robert laughs] But estrogen doesn't seem to hold the same controversial weight, and yet estrogen has a very powerful effects on both the animal brain and on the human brain of males and females. Men do not want their estrogen to go too low. Terrible things happen, they will lose cognitive function, libido can drop. So men need estrogen as well, but perhaps maybe we can put the same filter on estrogen as we did on testosterone. Are there any general themes of estrogen that people should be aware of or that you think that are generally misunderstood? Is it really all about feelings and empathy and making us more sensitive? I sense not. - No, and it's once again very context dependent. And if estrogen after giving birth is playing a central role in you wanting to shred the face of somebody getting too close to your kittens kind of thing, we know it's not just warm, fuzzy, empathic kind of stuff. Estrogen in lots of ways could be summarized by, if you've got a choice in the matter between having a lot of estrogen in your bloodstream or not, go for having a lot of estrogen. It enhances cognition, exactly as you said, it stimulates neurogenesis in the hippocampus, it increases glucose and oxygen delivery, it protects you from dementia, it decreases inflammatory oxidative damage to blood vessels, which is why it's good for protecting from cardiovascular disease in contrast to testosterone, which is making everyone of those things worse. This springs up this minefield with a question, which is, so what about post-menopausal estrogen? And all sorts of lab studies with non-human primates suggested that you keep estrogen levels high after a monkey's equivalent of menopause. And you're going to keep brain health a lot better or decreasing the risk of dementia, stroke, every such thing. Estrogen is a great antioxidant, all of that. So in the 90s I think when Healy, I'm forgetting her name, but when there was the first female head of the NIH, Bernadine Healy set up this massive prospective human study, what

was going to be the biggest one of all times, looking at the pluses and minuses of post-menopausal estrogen. And tens of thousands of women, and this was... And they had to cut the study short because what they were seeing was, estrogen was not only doing the normal bad stuff that you expect in terms of some decalcification stuff, but it was increasing the risk of cardiovascular disease, and it was increasing the risk of stroke, and it was increasing the risk of dementia. And this ground to a halt and everybody, they stopped the study and front page news and everybody panned at that point. And nobody could make sense of it who had been spending the last 20 years studying the exact same thing in primates and seeing all the protective effects. And the explanation turned out to be one of those things where like the law of unexpected consequences. Okay, menopause in women, it lasts different lengths of time, that may be a factor that's going to come. You know what, let's not start giving our study subjects more estrogen until they're totally past menopause. And when you've got that lag time in between, you shift all sorts of estrogen receptor patterns, and that's where all of the bad effects come from. - Wow! - All of the monkey studies had involved just maintaining ovulatory levels into the post-menopausal period. And you do that and you get great effects. Estrogen is one of the greatest predictors of protection from Alzheimer's disease, all of that, but it needs to be physiological. Just keep continuing what your body has been doing for a long time versus let the whole thing shutdown and suddenly like try to fire up the coal stoves at the bottom of the basement kind of thing, and get that going, there you get utterly different outcomes. And that caused a lot of human health consequences when people suddenly decided that estrogen is in fact neurologically endangering post-menopausally. - Wow, that's fascinating. And I never thought that these steroid hormone receptors could by not binding estrogen, being devoid of estrogen binding, I should say, could then set off opposite biochemical cascades. Fascinating. I guess it raises the question about testosterone replacement too, whether or not people should [laughs] talk to their doctor before too long. Men and women talk to your physicians before too long to avoid these, whatever is happening in these periods where there isn't sufficient testosterone and/or estrogen. It sounds like could cause longer-term problems even when therapies are introduced. - Two additional misery slash complications. So, okay, you're trying to understand, you look at women with a history with or without post-menopausal estrogen replacement where it's done great. And you're seeing 20 years later, estrogen is a predictor of a decreased risk of Alzheimer's. Then you got to start trying to do the unpacking prospective type studies. How much estrogen? At which times? Estrogen is a

catchall term for a bunch of hormones, estrone, estradiol, estriol. How much of each one of them? Natural or synthetic? Go try to figure all of that out. And the second complication is, it's often hard to say anything about what estrogen does outside the context of what progesterone is doing. And often it's not the absolute levels of either, it's the ratio of the two. This is such a more complicated endocrine system than testosterone. And because you have to generate dramatic cyclicity that like no male hypothalamus ever has to dream off. It's a much, much more complicated system, thus, it's a lot more complicated to understand,

00:39:40 Are Testosterone & Sperm Counts in Males Really Dropping?

let alone like figure out what the ideal benefits are of it. - Yeah. I don't know what to make of the literature on dropping rates of testosterone and endocrine disruptors. I was at Berkeley when Tyrone Hayes published his data on these frogs that were drinking water from various locations throughout the United States, not just in California, and seeing very severe endocrine disruption through blockade or, and of androgen receptors and all sorts of issues. And you hear this all the time now that sperm counts are dropping, that there are all these endocrine disruptors that there's birth control in the water, in the drinking water. It all starts to sound a little crazy, and yet I've also been fooled before by, I guess a good example would be, there's a lot of crazy stuff in the world online about all the terrible stuff in highly processed foods. And yet you've got very respectable people, endocrinologists at UCSF like Robert Lustig saying, yeah, a lot of these hidden sugars and these emulsifiers, they're causing real problems. So I've become more open-minded about the question. And so, are we suffering from drops in sperm counts and testosterone and estrogen and fertility as a consequence of endocrine disruptors in the environments and food, or because of social reasons? Is there anything that we can hang our hat on like real data that you're confident in? Or is it just a mess? - No, the phenomenon does appear to be quite real. Cross-sectional studies, human populations, or I still don't understand why this was one of the first things that Hayes spotted. Decreasing testicle size in crocodiles. [Andrew laughs] Go figure why that was one of the first contributions to this. And I think the phenomenon is absolutely real. And what you're then left with is two classic challenges, which is this is correlated with something broad environmental toxins. Which ones, how much, when, etc.? And the other one always being, well, okay, dropping is a dropping enough to make a difference.

How big of an effect is this? And those are where the juries are still out. - Yeah, it's an area that I know there's a lot of interest in, and you've got groups of people who won't touch a receipt at a store because of the BPAs that are on the inks of the... And then [laughs] you've got people who don't care about those things. It is a fascinating area.

00:42:15 Stress Mitigation & Our Sense of Control

I hope that more biology will be done there soon. I'd like to briefly return to stress. You described a study once about two rats, one running on a wheel voluntarily, one who is basically stuck in a running wheel, and it's forced to run anytime, rat number one runs. So in one case the rat is voluntarily exercising. [laughs] And in the other case, the rat is being forced to go to PE class, so to speak, but really, and seeing divergent effects on biology. And I'd like to just touch into this and use it as kind of a case study for stress mitigation in general. I'm rather obsessed in our colleague, David Spiegel, Associate Chair of Psychiatry at Stanford is obsessed with this question of, how humans can start to mitigate their own stress? What do you think about stress mitigation and what should we do as individuals and as families and as a culture to try and encourage people to mitigate their stress, but in ways that are not going to turn us into rat number two, where we're being forced to mitigate our own stress and therefore it becomes more stressful. [laughs] - And what you see is, rat number one gets all the benefits of exercise. Rat number two gets all the downsides of severe stress with the same exact muscle expenditure and movements going on. Perfectly yoked, great example that it's the interpretation on your head. And I haven't kept up with that literature, but I'll bet you, rat number two is having a whole lot more activity in its amygdala than is rat number one. Okay, so stress mitigation. Anything I should say here I should preface with, I'm reasonably good at telling people what's going to happen if they don't manage their stress, but I'm terrible at actually like managing stress or advising how to manage that. I'm much better with the bad news aspect of it. But what you see is, by now just a classic literature, half a century old, sort of showing what are the building blocks of stress. Not, ooh, you step outside and you've been gored by an elephant, and can you grow from your experience? And what doesn't kill you makes you stronger. In that you could have a stress response, but you're in the realm of the gray zone of ambiguous social interactions, that sort of thing. Some people have massive stress responses, others not at all, in between, enjoy it. Like what are the building blocks of, what makes

psychological stress stressful? And the first one is exactly what is brought up by that running study. Do you have a sense of control? A sense of control makes stressors less stressful. And the running wheel shows that or studies where you, you lab rat or you college freshman volunteer have been trained that by pressing a lever, you're less likely to get a shock. And today you're at the lever they're working away and unbeknownst to you the lever has been turned off, and it has no effect on shock frequency, but because you think you have some control, you have less of a stress response. If you were a rat and doing this day-in and day-out, you're less likely to get an ulcer. So a sense of control. And related to that is a sense of predictability. Rat get shocked, human gets shocked, whatever, and the scenario either is the shocks come now and then, or the shocks come now and then, and 10 seconds before a little warning light comes on. And when you get the warning light, the shocks are distressful. You got predictability because if you're not getting warning lights, any second you could be a half second away from the next shock. You get a warning light, and you know that if there isn't one, you've got at least 10 seconds worth of relaxation. You know what's coming, you can prepare your coping responses, and best of all afterward you know when you're finally safe, when you can recover from it. And that's enormously protective. Others outlet for frustration, you take a rat who is getting shocked, and if it could run on a running wheel, that's a protective thing, that's doing it voluntarily. If you've got a rat and he can gnaw on a bar of wood, a stressor is less stressful. Unfortunately, if you have a rat or primate or human and they're stressed, the ability to aggressively dump on somebody smaller and weaker also reduces the stress response. And the fact that displacement aggression reduces stress accounts for a huge percent triggers like unhappiness. So all of those are variables, get social support as well. That's a good one. Interpreting circumstances is being good news rather than bad. Hurray, so you've got this very simple sort of like take home recipe of go out and get as much control and as much predictability and as many outlets and as much social support as possible, and you're going to do just fine. And you go out and do that, and that's a recipe for total disaster because it's much, much more subtle than that. In one great example, okay, so you're getting shocks, you want a warning beforehand, get a little warning light 10 seconds before each shock, it's wonderfully protective. Get a warning light one second before the shock doesn't do anything. There's not enough time for you to get the psychological benefits of the anticipation. Now instead, gets the little warning coming on two minutes before each shock, and it's going to make things worse because you're not going to be sitting there

like reveling and sort of your sense of predictability, and it's soon going to be, oh. You're going to be sitting there for two minutes saying, damn, here it comes. Predictive information only works in a narrow domain. Similarly, control. Do you want to have a sense of control on the face of stress? And the answer is, only if it is a mild to moderate stressor because what's happening then, your sense of control is completely independent of the reality of whether you have control or not, but in the face of mild to moderate stressors, a sense of control gets interpreted as, wow, look how much worse things could have been. Thank God, I have control, I'm on top of this to master my fate. In contrast, if it's a major stressor, all that arbitrary sense of control does is make you think, oh my God, look how much better it could have been. I could have prevented it. And we all know that intuitively like we do that in the face of people's worst stressors. Nobody could have stopped the car the way the kids suddenly jumped out. It wouldn't have mattered and if you had gotten them to the doctor a month ago, instead of now, it wouldn't have made any... You didn't actually have any control. And what you see is, you absolutely want to have a huge sense of control over mild to moderate stressors, and especially ones that result in a good outcome. Hooray, for me, and in the face of horrible stressors, what you want to do is like self-deception, and like truth and beauty don't necessarily go hand-in-hand at that point. And that's why stress management techniques impact control and predictability wind up being far worse than neutral if you're preaching that to somebody homeless or somebody with terminal cancer, or somebody who is a refugee. Tell a neurotic middle-class person that they have the psychological tools to turn hell into heaven. And there's some truth to that. Do the same thing to somebody who is going through a real hell, and that's just privileged heartlessness to do that because that doesn't work. More and more outlets, if your outlets are damaging, that's not a good way to mitigate stress. Social support, if you're confusing mere acquaintances for real social support, you're going to have the rug pulled out from under you at some point. If you're mistaking social support for being, going and bitching and moaning and demanding supportiveness from everyone around you rather than you doing some of that reciprocally, that's not going to work very well either. It's not simple. It's not for nothing that lots of us are really lousy. It, like being good friends and things like that, and why it takes a lot of work to do it right? Because you do it wrong and it may temporarily seem like a great thing, but when it turns out to be completely misplaced faith, you're going to be feeling worse than before you started.

00:51:35 How Best to Buffer Stress

- Interesting. These days, there's a lot of interest in using physical practices to mitigate stress, trying to get out of the ruminating, and to some extent take control of neural circuits in the brain by using exercise and using breathing and hypnosis. And, of course, hypnosis has a mental component as well. What are your thoughts on stress mitigation from the standpoint of, okay, so we don't want to be rat number two, we want to select something for ourselves, so we have to take the initiative for ourselves. Being forced into exercising is not, it could actually have negative health effect perhaps. So we need to pick something that we like, we need to take control of it. In terms of supporting other people, you touched on that a bit. What is the best way to support other people? Is it to talk about the stressful thing? I mean, I'm not asking you to play psychologist here, but I find divergent data on this. We can spin ourselves up into a lather by ruminating on something. And language seems to me like it's a wonderful tool, but it's also a fairly deprived tool because it doesn't really get into the core of our physiology like something like breathing would. So what are your thoughts on more, for lack of a better way to put it, more head-centered, cognitive approaches to stress mitigation versus kind of going at the core physiology. Cold showers now are even a thing to some extent just to get people stress acclimated, voluntarily taking cold showers. - That makes some sense physiologically, preconditioning for when the real stressors come. In terms of what you bring up, oh, transcendental meditation, mindfulness, exercise, prayer, sort of reflecting on gratitude, all that sort of thing. Collectively they work on the average, they work in terms of, they can lower heart rate and cholesterol levels and have all sorts of good outcomes, but they compromise us. One is exactly the caveat that comes out of the running wheel study is, it doesn't matter how many of your friends swear by the stress management technique. If doing it makes you want to scream your head off after 10 seconds, that's not the one that's going to work for you. So read the fine print and the testimonials, but it's got to be something that works for you. Another one is the stress management type techniques that work, you can't save them for the weekend, you can't save them for when you're stuck on hold on the phone with Muzak for two minutes. It's got to be something where you stop what you're doing and do it virtually, daily or every other day, and spend 20, 30 minutes doing it. And what you see coming out of that is this like 80/20 rule from economics. 80/20, 80% of the complaints in the store come from 20% of the customers, things like that. What you see is, if your entire life consists of

every single thing on your shoulders, that you can't say no to 24/7. If you've stopped that and finally said, my wellbeing is important enough that I'm finally get to say no to some of the stuff that I can't say no to. And I'm going to do it every day for 20 minutes, whatever stress management technique you then do in those 20 minutes sort of who knows what, you're already 80% of the way there simply by having decided your wellbeing is important enough that you're going to stop every single day and have that as a priority. And that's exactly the same finding that you find people with chronic depression untreated that merely calling and getting an appointment to see a mental health professional, people start feeling better already because it's evidence that you've been activated, and you matter enough to do this, and you could conceive that this would actually have a good outcome rather than a hopeless one. Just doing something meditative or reflective every day or so, and it hardly even matters which one you're doing. And what comes out of that is thus another warning, which is do not trust anybody who says, it has been scientifically proven that their brand of stress management works better than the other ones. Just watch your wallet at that point. - Yeah, amen. I think one of the core goals of my lab and David Spiegel's lab, and I know you've worked with David and published papers with David as well is to really try and find out what are the various entry points to this thing that we call the autonomic nervous system and the stress system, and these systems that when gone unchecked really can take us down a dark path. And the idea that there are so many entry points is really the one that keeps, what the data keep telling us over and over again. So there's no magic breathing tool or exercise, it's any variety of those or one of those. And, again, we come back to this idea that it's the one that you select and the one that you make space for, and it's the one that you hopefully enjoy that's going to work best in terms of physiology. - And [mumbles] benign for those people who were stuck around you.

00:57:04 Power of Perception, Choice & Individual Differences

- Right, right, absolutely. And that brings me to this question of, I find it amazing that how we perceive an event, and whether or not we chose to be in that event or not can have such incredible different effects on circuitry of the brain and circuitry of the body and biology of cells. And in some ways it boggles my mind, like how can a decision made presumably with the prefrontal cortex, although other parts of the brain as well, how can that change essentially the polarity of a response in the body. And, I mean, you've talked

before about Type A personalities in there. We don't have to go into all the detail there for sake of time, but it is interesting that the effects of endothelial cells. I mean, literally of the size of, [laughs] of the portals for blood are in opposite direction, depending on whether or not somebody wants to be in a situation as a highly motivated person. Maybe you could just give us the top contour of that because I think it really illustrates this principle so beautifully. And then maybe if you would, you could just speculate on how the brain might have this switch to turn one experience from terrible to beneficial or from beneficial to terrible, it's really fascinating. - Well, all you need to do is like tonight before you're going to sleep and you're lying in bed and you're nice and drowsy and your heart's beating nice and slow, you start thinking about the fact that that heart isn't going to beat forever. [Andrew laughs] And imagine your toes getting cold afterward and imagine the flow of blood coming to a halt and all of you clotting. You're going to be doing something with your physiology at that point that 99% of mammals out there only do if they're running frantically. And you're going to be turning on your sympathetic stress response with thought, with emotions, with memory. And the measure of that is just how much the cortex and the limbic system sends projections down to all the autonomic regulators in the brain. You can think autonomic regulatory neurons into action in ways that only other animals can do with like extremes of environmental circumstances. And given that and the autonomic rule, I mean, the other big challenge in understanding it is gigantic individual differences. And that's, when you talk about the optimal amount of stress, the counts of stimulation, and in general that stress that's not too severe and doesn't go on for too long and there is overall in a benevolence setting. And under those conditions, we'd love being stressed by something unexpected and out of control predictability like a really interesting plot turn in the movie you're watching. That's great, but you get the individual differences that somehow has to accommodate the fact that for some people, the perfect stimulatory amount of stress is like getting up early for an Audubon birdwatching walk next Sunday morning. And for somebody else, it's signing up to be like a mercenary in Yemen. [Andrew laughs]

01:00:32 Context-Setting, Prefrontal Cortex & Hierarchy

And tremendous individual differences that swamp any simple prescriptions. - Yeah, the prefrontal cortex, this thinking machinery that we all harbor, it's such a double-edged sword. And what's remarkable to me is, how the areas of the brain like the hypothalamus

and the amygdala, they're sort of like switches. I mean, there is context and there is gain control. You talked about the gain control by testosterone, etc., but they're really like switches. I mean, if you stimulate ventromedial hypothalamus, you get the right neurons, an animal will try and kill even an object that's sitting next to it. You tickle some other neurons, it'll try and mate with that same object. I mean, it's really wild. I think there are probably rules to prefrontal cortex also, but it sounds like the context plural from which prefrontal cortex can draw from is probably infinite, so that we could probably learn to perceive threat in anything. Whether or not it's another group or whether or not it's science or whether or not it's somebody's version of the shape of the earth versus another. I mean, it's like, you can plug in anything to this system and give it enough data, and I think it sounds like you could drive a fear response or a love response. Is that overstepping? - Or [laughs] a mixed horribly ambivalent one that is changing by the millisecond, and then like could be mutually contradictory. No, that's absolutely the case in the prefrontal cortex, I more than once have regretted having like wasted 30 years of my life studying the hippocampus then I shoot him and studied the prefrontal cortex because it's so much more interesting what it does, and it's all this contextual stuff. It's all the ways in which it's not okay to lie in this setting, but it's a great thing in another. It's not okay to kill unless you do it to them, and then you get a medal. It's not, all of this social context and moral relativity and situational ethic stuff, that's the prefrontal cortex that's got to master that. And that winds up meaning that's the place in your brain more than anywhere where you say your perception of things can powerfully influence the reality of what's coming into you. - Yeah. - I mean, a great example, just harking back to testosterone. Okay, so exercise boosts up testosterone levels. Does exercise and success do it more than exercise and failure? A literature back in the 80s or so looking at outcomes of marathons. Did testosterone rise more in the people who win than the losers? Wrestling matches. Things of that sort with a simple prediction and the answer wound up being, you didn't see a simple answer. Okay, you win the marathon, that's not necessarily a predictor of increased testosterone. What's that about? And then you find like the winner testosterone decreases, and you find out the guy who came in 73rd is having a massive testosterone increase. Whoa, what's that about? What's that about is far more human subtlety. The guy who won the race has a decline in testosterone because he came in three minutes later than he really, really was expecting. And everybody now is going to be writing it up about how he's over the hill. And the guy who came in 73rd is having a boost of testosterone because he was assuming he'd be dead

from a heart attack by the third mile, [Andrew laughs] and instead he managed to finish. It's this interpretive stuff going on in there, and that's what prefrontal cortex is about. - Amazing, it raises this question of cognitive flexibility, Can we tell ourselves that something is good for us even if we're not enjoying it? And can we wriggle around these corners of choosing the exercise or doing the... Personally I'm not a big fan of long bouts of meditation, but I've benefited tremendously from things like dedicated breathing and shorter rounds of meditation. Can I tell myself that it's good for me and wriggle around the corner and get my physiology working the way I want? Do we have cognitive flexibility? Can I be that third place runner and tell myself, well, at least I came in, I wanted to win so badly. That was my primary goal, but another goal was to beat my previous time, and I did do that. And so, [laughs] I mean, it's... To what extent can we toggle this relationship between the prefrontal cortex and these other more primitive systems? - Well, an enormous amount. For example, being low in a hierarchy is generally bad for health in like every mammal out there, including us, but we do something special, which is we can be part of multiple hierarchies at the same time. And while you maybe low ranking in one of them, you could be extremely high ranking in another, you're like have the crappiest job in your corporation, but you are the captain of the softball team this year for the company. And you better bet that's somebody who is going to find all sorts of ways to decide that nine to five Monday to Fridays, just stupid paying the bills. And what really matters is the prestige on the weekend. You're poorer, but you're the deacon of your church here. And so we can play all sorts of psychological games with that. One of the most like consistent, reliable ones that we do and need to use the frontal cortex like crazy is, somebody does something rotten and you need to attribute it. And the answer is, they did something wrong, hmm, because they're rotten. Always have been or always will be this constitutional explanation. You do something rotten to somebody, and how do you explain it afterward? A situational one. I was tired, I was stressed in this sort of setting, I misunderstood this. We're best at excusing ourselves from bad things because we have access to our inner lives and we've got prefrontal cortexes that are great at coming up with a situational explanation rather than, hey, maybe you're just like a selfish rotten human, you need to change. And that's all prefrontal cortex, and we do that every time, we don't let somebody merge in the lane in front of us, even though you curse somebody who does the same thing to you and... Endlessly. - I love it. Your statement about the fact that we can select multiple hierarchies to participate in. To me it seems like a particularly important one nowadays

with social media being so prevalent. I know you're not particularly active on social media although you might be pleasantly, or I don't know unpleasantly surprised to find out that there's a lot of positive discussion about you and your work, so you don't even need to be on there. We'll just continue to discuss [laughs] your work. But what's interesting about social media I've found is that the context is very, very broad. I mean, one could argue that who one selects to follow and which news articles you're reading, etc. can create a kind of a funneling of information that itself can be dangerous. More verification of crazy ideas or even just less exposure to new ideas. But there's also this idea that social media is an incredibly broad context. So as you scroll through a feed, it's no longer like being in your eighth grade classroom or your office or your faculty meeting. You are being exposed to thousands, if not millions of contexts, this meal, that soccer game, this person's body, this person's intellect. YouTube is another example. It's a vast, vast landscape. So the context is completely mishmash whereas I'm assuming we evolved. I think we did evolve under contexts that were much more constrained. We interacted with a limited number of individuals and a limited number of different domains, seasons tended to be constrain us all. Of course, then we got phones and televisions, and this started to expand, but now more than ever, our brain, our prefrontal cortex and our sense of where we exist in these multiple hierarchies has essentially wicked out into infinity. How do you think this might be interacting with some of these more primitive systems and other aspects of our biology? - Well, I think what you get is, in some ways the punchline of, what's most human about humans, which is over and over we use the exact same blueprint, the same hormones, the same kinases, the same receptors, the same, everything were built out of the exact same stuff as all these other species out there, and then we go and use it in a completely novel way. And usually in terms of being able to abstract stuff over space and time in dramatic ways. So, okay, you're a low ranking baboon and you can feel badly because you just like killed a rabbit and you're about to eat and some higher ranking guy boots you off and takes it away from you, and you feel crummy and it's stressful and you're unhappy. We are doing the exact same things with like our brain and bodies when we're losing a sense of self-esteem, but we can do it by watching a movie character on the screen and feeling inadequate compared to like how wonderful or attractive they are. We can do it by somebody driving past us in an expensive car, and we don't even see their face, and you can feel belittled by your own socioeconomic status. You can watch like the Lifestyles of the Rich and Famous or read about what Bezos is up to. And for some reason, decide your life is less fulfilling

because you didn't fly into space for 11 minutes. And so you can feel miserable about yourself in ways that no other organism can, simply because we can have our meaningful social networks include like the party you're reading about on Facebook that you weren't invited to because it's taking place in Singapore, and you don't know any of those people, but nonetheless, somehow that could be a means for you

01:11:20 How Dr. Sapolsky Accomplishes Deep Thinking

to feel less content with who you've turned out to be. Do you take steps in your own life to actively restrict the contexts in which you think and live and contemplate in order to enhance your creative life, your intellectual life? Are those steps that you actively take? - Well, I very actively don't know how to make use of anything [laughs] with social media. So I guess that counts as my having thus actively chosen not to learn how. So that's the case certainly for the last year and a half, like lots of people, I've gone through stretches where I've managed to sort of enforce a moratorium on looking at the news, and that was wonderfully freeing. I think in the larger sense though, in addition to me being a neurobiologist, I'd sort of spent decades spending part of each year studying wild baboons out in a national park in East Africa. And I'd spend three months a year without electricity, without phone calls, with going 12 hours a day without saying a word to somebody. And when I finally would, it would be somebody nomadic pastoralist guy in a different language. Yeah, I did 90% of my like insightful thinking about anything in the laboratory during those three months each year, and not one in the lab, and not when inundated with stuff. - Well, I think there is a shifting trend towards trying to create a narrowing of context that... And I like what I see, I have a niece, she's 14-years-old and she and her friends are very good at putting their phones away. They say, we're not going to have our phones for this interaction, especially after... And I realized we're still somewhat in this. It's unclear where it's headed,

01:13:17 Do We Have Free Will?

but 2020 was so restrictive and she was so separated from her friends. Now it's, let's really focus on being together and not bring in all these other elements from our phones. And that brings me great hope for that generation, [laughs] maybe they will... Or who knows, maybe they'll run off and study baboons, we need more field researchers. So

along the lines of choice, I'd like to shift gears slightly and talk about freewill, about our ability to make choices at all. - Well, my personal way out in left field inflammatory stance is, I don't think we have a shred of freewill despite 95% of philosophers. And I think probably the majority of neuroscientists are saying that we have freewill in at least some circumstances. I don't think there's any at all. And the reason for this is, you do something, you behave, you make a choice, whatever. And to understand why you did that, where did that intention come from? Part of it was due to like the sensory environment you were in the previous minute. Some of it is from the hormone levels in your bloodstream that morning. Some of it is from whether you had a wonderful or stressful last three months and what sort of neuroplasticity happened. Part of it is what hormone levels you were exposed to as a fetus. Part of it is what culture your ancestors came up with, and thus how you were parented when you were a kid. All of those are in there, and you can understand where behavior is coming from without incorporating all of those. And at that point, not only are there all of these relevant factors, but they're ultimately all one factor. If you're talking about what evolution has to do with your behavior, by definition you're also talking about genetics. If you're talking about what your genes have to do with behavior, by definition you're talking about how your brain was constructed or what proteins are coded for. If you're talking about like your mood disorder now, you're talking about the sense of efficacy you were getting as a five-year-old. They're all intertwined. And when you look at all those influences, basically like the challenge is, show me a neuron that just caused that behavior, or show me a network of neurons that just caused that behavior. And show me that nothing about what they just did was influenced by anything from the sensory environment one second ago to the evolution of your species. And there's no space in there to fit in a freewill concept that winds up being in your brain, but not of your brain. There's simply no wiggle room for it there. - So I can appreciate that our behaviors and our choices are the consequences of a long line of dominoes that fell prior to that behavior. But is it possible that I can intervene in the domino effect, so to speak. In other words, can my recognition of the fact that genes have heritability, there is an epigenome that, there is a hormonal context, there is a historical context. Can the knowledge of that give me some small shard of freewill? Meaning, does it allow me to say, ah, okay, I accept that my choices are somewhat predetermined, and yet knowing that gives me some additional layer of control? Is there any philosophical or biological universe in which that works? - Nah. All of that can produce the wonderfully positive belief that change can happen. Even a

traumatic change, even in the worst of circumstances, most unlikely people, and change can happen, things can change. Don't be fatalistic, don't decide because we're a mechanistic, biological machines that nothing can ever... Change can happen, but where people go off the rails is translating that into, we can change ourselves. We don't, we can't because there's no freewill. However, we can be changed by circumstance. And the point of it is, like you look at an Aplysia, a sea slug that has learned to retract its gill in response to a shock on its tail, you can do like conditioning, Pavlovian conditioning on it, and it has learned, its behavior has been changed by its environment. And you hear news about something like horrifically depressing going on, and refugees in wherever. And as a result, you feel a little bit more helpless and a less of a sense of efficacy in the world, and both of your behaviors have been changed. Okay, okay, yeah, I guess that, but the remarkable thing is, it's the exact same neurobiology. The signal transduction pathways that were happening in that sea snail incorporate the exact same kinases and proteases and phosphatases that we do when you're having mammalian fear conditioning, or when you're alert, it's conserved. It's the exact same thing, it's simply playing out in obviously a much, much fancier domain. And because you have learned that change is possible despite understanding mechanistically that we can't change ourselves volitionally, but because you understand change is possible, you have just changed the ability of your brain to respond to optimistic stimuli. And you have changed the ability of your brain to now send you in the direction of being exposed to more information that will seem cheerful rather than depressing. Oh my God, that's amazing, what Nelson Mandela and Martin Luther king and all these folks did. Wow, under the most adverse of circumstances, they were able to do. Maybe I can also, maybe I can go read more about people like them to get even more data points of change the neurochemistry, so that your responses are different now. And you're tilted a little bit more in that direction of feeling like you can make a difference instead of it's all damn hopeless. So enormous change can happen, but the last thing that could come out of a view of, we are nothing more or less than the sum of our biology and its interactions with environment,

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is to throw up your hands and say, and thus it's no use trying to change anything. - So we can acknowledge that change is extremely hard to impossible, that circumstances

can change, and yet that striving to be better human beings is still a worthwhile endeavor. Do I have that correct? - Absolutely. Because simply the knowledge, either from experience or making it to the end of the right neurobiology class has taught you that change can happen within a framework of a mechanistic neurobiology. You were now more open to being made optimistic by the good news in the world around you. You are more likely to be inspired by this or that, you were more resistant to getting discouraged by bad news, simply because you now understand it's possible. - Mm-hmm, yeah, somebody who spent much of his career working on the hippocampus, I have to assume that you are a believer in neuroplasticity, that neural circuits can change in response to experience, and that some of the same so-called top-down mechanisms of prefrontal cortex that we were talking about before can play a role there, that the decision to try and change and the pursuit of knowledge and the pursuit of experience can shape our circuitry, and therefore make us different machines, so to speak. - Yeah. And not only can say prenatal hormone exposure changed the way your brain is being constructed, but learning that prenatal hormone exposure can change the construction of your brain will change your brain right now, and how you think about where your intentions came from. Wow, maybe that had something to do with it. The knowledge of the knowledge is an effector in and of itself. - That's such an important and powerful statement to hear. I think that many people think that if a tool, if it doesn't involve a pill or a protocol, that it's useless. And certainly there are pills and protocols that are very useful in a variety of context for a variety of things, but the idea that knowledge itself, whereas you put it, knowledge of knowledge is itself a tool, I think is a very important concept for people to embed in their minds. And, listen, I'm so grateful for this discussion and for you raising these topics. I think that people, many people know your work on testosterone, on stress, and we've covered some of that today, the work on freewill and this idea that we are hopeless or that we are in total control. I think I'm realizing in listening to you that it's neither is true, and that the solution resides

01:23:44 Robert's New Book: "Determined: The Science of Life Without Free Will"

in understanding more about freewill and lack of it, [laughs] and also neuroplasticity. You're working on a book about freewill, are you willing to tell us a little bit about that book and where you are in that process and what we can look forward to? - Yeah, it's going really slow. Title is, "Determined: A Science of Life Without Freewill." And

essentially the first half of the book is trying to convince a reader, okay, if not that there's no freewill whatsoever, but at least there's a lot less than is normally assumed. And I'm going through all the standard arguments for freewill, and why that doesn't make sense with 21st century science? And that has led to reading a lot of very frustrating philosophers who basically are willing to admit that stuff is made out of like atoms and molecules. And like there's a physical reality sort of world, they're not just relying on magic, but that they believe in freewill for magical reasons, and where it doesn't make sense. Okay, so the first half of the book is to hopefully convince people that there's much less freewill than we used to think. And then the second half is this gigantic juncture built around the fact that I haven't thought there's any freewill since I was like an adolescent. And despite thinking that way, I still have absolutely no idea how you're supposed to function with that belief. How are you supposed to go about everyday life if anything you feel entitled to isn't true? If any angers and hatreds you feel aren't justified, if there's no such thing as appropriate, blame or punishment or praise or reward, and none of it makes any sense, and somebody like even compliments you on your haircut, and you've been conditioned to say, oh, thanks, as if you had something to do. How are we supposed to function with that? And so the second half is wrestling with that, and what the punchline there is, is it's going to be incredibly hard. And if you think it's going to be hard to subtract a notion of freewill out of making sense of like serial murderers, it's going to be a thousand times harder making sense of when somebody says "good job" to you. [Andrew laughs] And because it's the exact same on reality of sort of our interpretations. It's going to be incredibly hard, but nonetheless when you look at the history of how we have subtracted the notion of agency out of all sorts of realms of blame, starting with thinking that witches caused hailstorms 500 years ago to the notion that psychodynamically screwed up mothers cause schizophrenia, we've done it. We've done it endless number of times, we've been able to subtract out a sense of volition in understanding how the world works around us. And we don't have murderers running amuck on the street, and society hasn't collapsed into a puddle, and in fact, it's a more humane society. So the good news is it's possible because we've done it repeatedly in the past, but it's going to be hard as hell. And it's hard as hell to try to write about that coherently, [laughs] I'm discovering, so it's going slowly. - Well, I speak for many, many people when I say that we're really excited for the book when it's done and we will patiently wait, but with great excitement for the book, "Determined". You said it's the title, correct? - Yeah, "Determined: The Science of Life Without Freewill". It seems like you

can't publish your book these days without a sub-title, so that's it? - Fantastic. Well, very excited to read the book. I'm very grateful to you for this conversation today, I learned a ton. Every time you speak I learn, and for me it's really been a pleasure and a delight to interact with you today and over the previous years, I should say, as colleagues. And thank you again, Robert, for everything that you do and all the hard, hard work and thinking that you put into your work because it's clear that you put a lot of hard work

01:28:27 Reflections, Support of Podcast, & Supporting Stress Research

and thinking, and we all benefit as a consequence. - Thanks, and thanks for having me, this was a blast. - Thank you for joining me for my conversation with Dr. Robert Sapolsky. If you're enjoying this podcast and learning from it, please subscribe to our YouTube channel. In addition, you can leave us comments and suggestions for future episodes and guests in the Comments section on YouTube. Please also subscribe on Apple and on Spotify, and on Apple you have the opportunity to leave us up to a five-star review and a comment. In addition, please check out the sponsors that we mentioned at the beginning of this podcast. That's a terrific way to support us. And for those of you that are interested in supporting research on stress, on sleep, and how to better access sleep and combat stress, you can do that by supporting the research being done on those topics in my laboratory. You can go to HubermanLab.stanford.edu, and there you'll see a tab entitled, Support Research in the Huberman Lab. So that's for work at the Huberman Lab at Stanford, not the Huberman Lab podcast. And there's a Make a Donation tab where you can make a tax deductible donation. And if you're not already following the Huberman Lab on Instagram, please check out Huberman Lab on Instagram and on Twitter. On both those channels, I post information about science and science related tools anywhere from one to five minutes. Some of that information overlaps with the podcast, but a lot of it is unique and different from the information on this podcast. And last but not least, thank you for your interest in science.