

## Erasing Fears & Traumas Based on the Modern Neuroscience of Fear | Huberman Lab Podcast #49

In this episode, I discuss fear and trauma, including the neural circuits involved in the "threat reflex" and how specific experiences and memories come to activate that system. I also discuss how our body is involved in trauma and fear. First, I describe the logic of fear mechanisms and how "top-down" processing-- meaning connections from the parts of the brain that assign meaning to our feelings, are involved in fear and erasing fears and traumas. Then I discuss what successful fear and trauma treatment must include and consider various treatments for whether they meet that standard, such as EMDR, Cognitive Behavioral Therapy, Ketamine and other drug-assisted therapies and more. I also review new data on how 5 minutes per day of deliberate, self-imposed stress can erase fear and depression. And I review the role that social connection plays in erasing or maintaining fears by activating specific molecular pathways in the brain and body. Finally, I review supplementation with over-the-counter compounds for their effects on anxiety and fear and when to take them, if at all.

#fear #trauma #stress

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- [Andrew Huberman] Welcome to the Huberman Lab Podcast, where we discuss science and science-based tools for everyday life. [bright music] - I'm Andrew Huberman, and I'm a professor of neurobiology and ophthalmology at Stanford School of Medicine. Today, we're going to talk about the Neuroscience of fear. We are also going to talk about trauma and post-traumatic stress disorders. The Neuroscience of fear has a long history in biology and in the field of psychology. However, I think it's fair to say that in the last 10 years, the field of Neuroscience has shed light on not just the neural circuits, meaning the areas of the brain that control the fear response and the ways that it does it, but some important ways to extinguish fears using behavioral therapies, drug therapies, and what we call brain machine interfaces. Today, we are going to talk about all of those, and you're going to come away with both an understanding of the biology of fear and trauma, as well as many practical tools to confront fear and trauma. In fact, we are going to discuss one very recently published study in which five minutes a day of deliberate exposure to stress was shown to alleviate longstanding depressive and fear related symptoms. We will get into the details of that study and the protocol that emerges from that study a little later in the podcast. But it stands as a really important somewhat counter-intuitive example of how stress itself can be used to combat fear. To give you a sense of where we are going, I'll just lay out the framework for today's podcast. First, I'm going to teach you about the biology of fear and trauma. Literally the cells and circuits and connections in the body and chemicals in the body that give rise to the so-called fear response. And why sometimes, but not always fear can turn into trauma. I will also describe the biology of how fear is unlearned or what we call extinguished. And there too, you're going to get some serious surprises. You're going to learn for instance, that we can't just eliminate fears. We actually have to replace fears with a new positive event.

00:02:15 Athletic Greens, InsideTracker, Helix Sleep

And again, there are tools with which to do that, and I will teach you those tools today. 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 Athletic Greens. Athletic Greens is an all-in-one vitamin mineral probiotic drink. I've been taking Athletic Greens every day since 2012. So I'm delighted that they're sponsoring the podcast. The reason I started taking Athletic Greens and the reason I still take Athletic Greens is that it covers all of my vitamin mineral and probiotic needs. Nowadays, there's a lot of data out there pointing to the fact that a healthy gut microbiome, literally little microbes that live in our gut that are good for us is important to support our immune system, our nervous system, our endocrine system, and various aspects of our immediate and long-term health. With Athletic Greens, I get all the vitamins and minerals that I need. Plus the probiotics ensure a healthy gut microbiome. It also tastes really good. I mix mine up with some water, a little bit of lemon juice. I'll have that early in the day, and sometimes a second time later in the day as well. It's compatible with intermittent fasting, it's compatible with vegan diets, with keto diets and essentially every diet that you could possibly imagine out there. It's also filled with adaptogens for recovery. It has digestive enzymes for gut health and has a number of other things that support the immune system. If you'd like to try Athletic Greens, you can go to [athleticgreens.com/huberman](https://athleticgreens.com/huberman), to claim their special offer. They'll give you five free travel packs that make it really easy to mix up Athletic Greens while you're on the road. And they'll give you a year supply of Vitamin D3 K2. There's now a lot of evidence that vitamin D3 supports a huge number of metabolic factors, immune system factors, endocrine factors. Basically we need vitamin D3. We can get it from the sun, but many people are deficient in vitamin D3 even if they are getting what they think is sufficient sunlight. And K2 is important for cardiovascular health. So again, if you go to [athleticgreens.com/huberman](https://athleticgreens.com/huberman). You can claim their special offer, the five free travel packs plus the year supply of vitamin D3 K2. 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 for the simple reason that many of the factors that impact your immediate and long-term health can only be analyzed from a quality blood test. And now with the advent of modern DNA tests, you can also get information about how your specific genes are impacting your immediate and long-term health. Now a problem with a lot of blood tests and DNA tests out there is you get the numbers back but you don't know what to do with those

numbers. With InsideTracker, they make it very simple to figure out what to do to bring those numbers into the ranges that are right for you. They have a dashboard that's very easy to use. You can see the numbers from your blood and or DNA tests. And it will point to specific lifestyle factors, nutritional factors, as well as supplementation, maybe even prescription factors that would be right for you to bring the numbers into range that are ideal for your immediate and long-term health goals. Another feature that InsideTracker has is their inner age test. This test shows you what your biological age is and compares that to your chronological age and what you can do to improve your biological age, which of course is the important number. If you'd like to try InsideTracker, you can visit [insidetracker.com/huberman](https://insidetracker.com/huberman) to get 25% off any of InsideTracker's plans. Just use the code huberman at checkout. Today's episode is also brought to us by Helix Sleep. Helix Sleep makes mattresses and pillows that are of the absolute highest quality. I've been sleeping on a Helix mattress for close to a year now, and it's the best sleep that I've ever had. Helix has a quiz that takes about two minutes to complete and matches your body type and sleep preferences to the perfect mattress for you. Some people sleep on their side, some people sleep on their backs, some people sleep on their stomach. Some people run hot, some people run cold. Some people don't know which part of their body they sleep on. You take this test, it's very brief, two minutes. And after that test Helix we'll match you to the mattress that's ideal for you. I match to the so-called Dusk, D-U-S-K mattress, because I wanted a mattress that wasn't too firm, not too soft. And I like to sleep sort of on my stomach and kind of a crawling soldier position. That seems to be always how I wake up in the morning anyway. So if you're interested in upgrading your mattress, go to [helixsleep.com/huberman](https://helixsleep.com/huberman), take their two minutes sleep quiz and they'll match it to a customized mattress and you'll get up to \$200 off all mattress orders and you'll get two free pillows.

00:06:49 What is Fear?

Again, if you're interested, please go to [helixsleep.com/huberman](https://helixsleep.com/huberman) for up to \$200 off and two free pillows. So what is fear? Well, fear falls into a category of nervous system phenomenon that we can reliably call an emotion. And it is hotly debated nowadays. And it's been hotly debated really for centuries what an emotion is and what an emotion isn't. Now that's not a debate that I want to get into today. I think it's fair to say that emotions include responses within our body. Quickening of heart rate, changes in blood flow,

things that we experience as a warming or a cooling of our skin. But that there's also a cognitive component. There are thoughts, there are memories. There's all sorts of stuff that goes on in our mind and in our body that together we call an emotion. And there's a vast amount of interest in literature devoted to try and understand how many different emotions there are, how different people experience emotions. And that's certainly a topic that we will embrace in a future podcast episode. But today I just want to talk about fear as a response. Because when we talk about fear as a physiological response and as a cognitive response, then we can get down to some very concrete mechanisms and some very concrete and practical tools that can be used to deal with fear when fear is not wanted. So let's talk first about what fear isn't. Most people are familiar with stress, both as a concept and as an experience. Stress is a physiological response. It involves quickening of the heart rate. Typically quickening a breathing, blood flow getting shuttled to certain areas of the brain and body and not to others. It can create a hypervigilance or an awareness. Typically that awareness is narrower, literally narrower in space, like a soda straw view of the world than when we are relaxed. And it is fair to say that we cannot have fear without having several, if not all of the elements of the stress response. However, we can have stress without having fear. Likewise, people are familiar with the phrase or the word rather, anxiety. Anxiety tends to be stress about some future event, although it can mean other things as well. We can't really have fear without seeing or observing or experiencing some of the elements of anxiety, but we can have anxiety without having fear. So what you're starting to realize is that fear is built up from certain basic elements that include stress and anxiety. And then there is trauma. And trauma also requires a specific, what we will call operational definition. An operational definition is just a definition that allows us to have a conversation because we both agree on or mostly agree on what the meaning of a given word is. It makes conversations much easier. In fact, I would argue if we all had operational definitions for more things in the world, that there would be fewer misunderstandings and arguments and we'd all move a lot further as a species. But that's another topic entirely. The operational definition of trauma is that some fear took place, which of course includes stress and anxiety. And that fear somehow gets embedded or activated in our nervous system, such that it shows up at times when it's maladaptive. Meaning that fear doesn't serve us well and it gets reactivated at various times. Like when you first wake up in the morning, if you're not in the presence of something that scared you, but you suddenly have what feels like a panic attack and you're in deep fear. Well, that's post-traumatic stress. That's post-

traumatic fear. So I don't want to get bogged down too much in the nomenclature but what I'm doing here is building up a sort of a series of layers where stress and anxiety form the foundation of what we're calling fear and trauma. And then there are other phrases out there that we would be remiss if we didn't mention things like phobias and panic attacks. Panic attacks are the experience of extreme fear but without any fear inducing stimulus. So it's kind of like trauma. And a phobia tends to be extreme fear of something specific. Fear of spiders, fear of heights, fear of flying, fear of dying, these kinds of things, okay? The reason for laying all that out there is not to create a word soup to confuse us rather it is to simplify the issue because now that we acknowledge that there are many different phrases to describe this thing that we call fear and unrelated phenomenon. We can start to just focus on two of these issues, fear and trauma. As it relates to specific biological processes, specific cognitive processes. And we can start to dissect how fears are formed,

00:11:45 Autonomic Arousal: "Alertness" vs. "Calmness"

how fears are unformed and how new memories can come to replace previously fearful experiences. So in this effort to establish a common language around fear and trauma, I want to point out autonomic arousal. Autonomic arousal relates to this aspect of our nervous system, that we call the autonomic nervous system. Autonomic means automatic that somewhat of a misnomer, because there are aspects of your autonomic nervous system that you can control. But your autonomic nervous system controls things like digestion, urination, sexual behavior, stress. When you want to be awake, when you want to be asleep, it basically has two branches to it. Two branches, meaning two different systems. One is the so-called sympathetic autonomic nervous system. Has nothing to do with sympathy, it has everything to do with increasing alertness. Think of the sympathetic nervous system as the alertness nervous system. It's what ramps up your levels of alertness, ramps up your levels of vigilant. Think about it as the accelerator on your alertness and attention. The other branch of the autonomic nervous system is the so-called, parasympathetic branch of the autonomic nervous system. I know that's a mouthful. The parasympathetic branch of the autonomic nervous system are the cells and neurons and chemicals and other aspects of your brain and body that are involved in the calming nervous system. So sympathetic is alerting, parasympathetic is calming. And it acts as sort of a seesaw to adjust your overall level of alertness. So for

instance, right now I'm alert, but I feel pretty calm. I'm not ready to go to sleep or anything like that. I don't feel like I need a nap. I'm alert, but I'm calm. I'm not in a state of stress or panic. So that seesaw we could imagine is more or less level. Maybe it's tilted up a little bit to the side of increased sympathetic or alertness rather than parasympathetic because I feel wide awake. If I were sleepy, the opposite would be true. The parasympathetic side would be increased relative to the sympathetic side. There are many different aspects of the autonomic nervous system, but one of the main aspects is an aspect

#### 00:13:44 Hypothalamic-Pituitary-Adrenal Axis (HPA axis)

that's going to come up again and again and again today, it's very important that you understand what it is. It's called the HPA axis. The HPA axis stands for Hypothalamic-Pituitary-Adrenal Axis. The hypothalamus is a collection of neurons. It's an area of your brain real estate, that's deep in the brain at the base of the brain that contains many, many different areas that control things like temperature, and desire to have sex, desire to eat, thirst. It also controls the desire to not mate, to have sex, not to eat, not drink more water or any other type of fluid. So it has accelerators and brakes in there as well. The hypothalamus connects to the so-called pituitary, the pituitary lives close to the roof of your mouth. It releases hormones into your bloodstream. And so the hypothalamus has this ability to trigger the release or prevent the release of particular hormones like cortisol or the hormones that go stimulate ovaries to produce estrogen or testes to produce testosterone or adrenals to produce Adrenaline. And speaking of the adrenals that [indistinct] and the HPA are the adrenals. You have two glands that sit above your kidneys and your lower back. They receive signals by way of nerve cells neurons, and by way of hormones and other things released from the brain and elsewhere in the body. And they release different hormones and other types of chemicals into the body. And the two main ones that you need to know about today are Adrenaline also called Epinephrine and Cortisol. Both of those are so-called stress hormones, but they're not always involved in stress. They're also involved in waking up in the morning when you arrive... Excuse me, when you rise from sleep. And so this HPA axis, should be thought of in the following way. The HPA axis includes a piece of the brain, the hypothalamus, the pituitary, and the adrenals. So it's a beautiful three part system that can use your brain to alert or wake up your body and prepare it for action. And it can do that in the



short term, by triggering the release of hormones and chemicals that make you alert and ready to go right away and by triggering the release of neurotransmitters and hormones and other chemicals that give that alertness a very long tail, a very long latency before it shuts off. And that's important because one of the hallmarks of fear and one of the hallmarks of trauma is that they involve fear responses that are long lasting. Even if those fearful events, the events in the world that trigger the HPA axis can be very brief, like a car that almost hits you as you step off the curb or something... A gunshot that goes off suddenly, and it's just a very quick, like, you know, 500 millisecond or 1 second event. The fear response can reverberate through your system because the chemicals that are involved in this HPA axis have a fast component and a longer-lasting component. And the longer-lasting component can actually change not just the connections of different areas of the brain and the way that our organs work like our heart and the way that we breathe. It actually can feed back to the brain and literally control gene expression. Which can take many days and build out new circuits and new chemicals that can embed fear in our brain and body. And that might sound very depressing but there's a reason. And there's an adaptive reason why there's the slow and fast phase of the HPA axis and the fear response. And fortunately, that gene expression and the long arc of the fear response, the way it kind of lives in our system kind of like a phantom in some ways can also be leveraged to undo the fear response,

00:17:36 "The Threat Reflex": Neural Circuits for Fear

to extinguish the fear response and replace it with non fearful associations. So let's dig a little deeper into the neural circuits and biology of fear. Because in doing that, we can start to reveal the logic of how to attack fear if that's the goal. We can't have a discussion about fear without discussing the famous amygdala. Famous because I think most people by now have heard of the amygdala. Amygdala means almond. It's an almond shaped structure on both sides of the brain. So you have one on the right side of your brain, and one on the left side of your brain. The amygdala is part of what we can call the threat reflex. And this is very important to conceptualize fear as including a reflex. So much as you have reflexes that cause you to lift your foot up if you are just step on something sharp. You literally have a reflex within your spinal cord that causes you to lift up one foot and extend the other one toward the ground. Believe it or not, you always think you step on something sharp you pull your foot up. But you actually step on

something sharp, you pull your foot up and in pulling it up there's another reflex that's activated that as you extend your other legs so that you don't fall over. Similarly in the process of experiencing fear, you have a reflex for particular events in your brain and body. And that reflex involves things like, quickening of your heart rate, hypervigilance, your attentional systems pop on, increased ability to access energy stores for movement and thought and so forth. But just like that step on the tack reflex example, all of the neural circuits that are associated with being calm, with being able to go to sleep, with being able to visualize the full picture of your environment, literally to see your entire environment, or to hear other things around you. All of those get shut down when the so-called threat reflex gets activated. And the amygdala is part of the threat reflex so much so that we can really say, that it's the final common pathway through which the threat reflex flows. In other words, the amygdala is essential for the threat response. But the threat reflex and the threat response is kind of a dumb response. It's not a sophisticated thing, it's very generic. And this is also a very important point. One of the beauties of the fear system is that it's very generalizable. It's not designed for you to be afraid of any one thing. Sure, there are some debates and probably some good data out there that support the fact that human babies are innately, meaning requires no learning. Innately afraid of certain things like heights, or snakes or spiders. There's debate about this. And they depends on the quality of the experiment, et cetera. But the real capacity of the fear system is that we can become afraid of anything provided that this threat system is activated in conjunction with some external experience. So the way I'd like you to think about the amygdala is not as a fear center, but that it's a critical component of the threat reflex. I'd like you to also internalize the idea that the threat reflex involves this activation of certain systems and suppression of all the systems for calming the parasympathetic system. And now I'm going to describe the way that information flows into and through this threat reflex. And in doing that, it will reveal how specific things, like a spider, like a snake, like a physical trauma, like a car accident, like a fear of public speaking, whatever happens to scare you or scare somebody, how that gets attached to this reflex. Because this reflex is very generic. It doesn't really know what to be afraid of. It only knows how to create this sensation, this internal landscape that we think of as fear. So while the amygdala might look like an almond, it's actually part of a much bigger complex or collection of neurons called the amygdaloid complex. That complex has anywhere from 12 to 14 areas depending on who's... Which neuroanatomist is naming things and carving it up in Neuroscience and in much of biology. We like to joke that there are

lumpers and there are splitters. So some people like to draw boundaries between every little distinct difference and say, "Oh, that's a separate area and other people are lumpers." And they say, "Well, listen, you know why complicate things? Let's lump those together." I'm neither a lumper nor a splitter, I'm somewhere in between. I think the number 12 is a good number in terms of the number of different areas of the amygdala. Why is that important to us? Well, it turns out that the amygdala is not just a area for threat, it's an area for generating threat reflexes that integrates lots of different types of information. So for those of you that want to know, I'm going to give you some names, some nomenclature, for those of you that don't, you can tune out for this. But basically information from our memory systems, like the hippocampus and from our sensory systems, our eyes, our ears, our nose, our mouth, et cetera. So taste information, vision, auditory information, touch, et cetera. Flow into the so-called lateral portion of the amygdala. Flows into... Or the amygdaloid complex. It flows into the lateral portion. And then there are multiple outputs from the amygdala. And this is where things get particularly interesting because the outputs of the amygdala have a lot of different areas, but there are two main pathways. One involves the hypothalamus, which you heard about before this collection of neurons that control a lot of our primitive drives for sex, for food, for thirst and for warmth, et cetera. And it also feeds out to our adrenals. Those glands that you learned about a few minutes ago to create a sense of alertness and action. It also feeds out what I mean by feeds out, by the way, is there are neurons that send wires. We call those wires axons connections. Where they can release chemicals and trigger the activation of different brain areas. So it feeds out to other brain areas such as the PAG. PAG is very interesting for our discussion today. It's the periaqueductal gray. The periaqueductal gray contains neurons that can trigger freezing, can trigger the... Some people talk about the fawning response, which has kind of an appeasing response to traumatic events. But some people outright freeze in response to fear, right? We've heard of fight or flight. And indeed the pathway that I'm describing can create a sense of fight and cause people to want to lean in, in an aggressive way to combat things that they're afraid of or flight to run away. Essentially to avoid by mobilizing the thing that they feel they're threatened by. Now, even in the absence of some threat, somebody that has say a fear of public speaking might hesitate or move away from a podium or hesitate or move away from raising their hand. If raising their hand meant that they might be called on and would be public speaking. So there's fight and flight, but there's also the freeze response. And the freeze response is controlled by

a number of brain centers, but the periaqueductal gray, the PAG, is central for this freeze response and neurons. They're also create what are called Endogenous opioids. Many of you have heard of the opioid crisis, which is a crisis of prescription medication given out too broadly for people that don't need it, who are become addicted to opioids. Those are Exogenous opioid. But Endogenous opioids are chemicals released from neurons in the PAG and from elsewhere in the body that give us a sense of numbing. They actually numb us against pain. And you can imagine why biology would be organized this way. A threat occurs or something that we perceive as a threat, we're afraid of it. And a natural analgesic is released into our body because there's likely to be an interaction that's very uncomfortable. That's physically uncomfortable. So it's like we have our own Endogenous release of these opioids and that's occurring in the PAG. The other area and again, sorry to litter the conversation with these names of structures, but some people seem to enjoy knowing these structures. You're fine if you just understand what the structures do. If you want to know the names that's fine. But the other structure is the locus coeruleus. The locus coeruleus creates a sense of arousal, by releasing Adrenaline, Epinephrine and Norepinephrine, or related chemical into the brain. So basically the activation of the amygdaloid complex could be from any number of different things, a memory of something fearful. An actual sensory experience of something that's fearful. And but then the fear response itself is taking part because of the threat reflex gets activated. And that threat reflex then sends a whole set of other functions into action. Freezing, activation of the adrenals, activation of locus coeruleus for arousal and alertness, activation of this endogenous pain system or anti-pain system in the PAG. That's one pathway out of the amygdala. The other pathway out of the amygdala is to a very interesting area that typically is associated with reward and even addiction. So this might come as a surprise to many of you. In fact, it came as a surprise to me. I remember when these data were published, but the amygdala complex actually projects to areas of the Dopamine system. The so-called nucleus accumbens, the mesolimbic reward pathway, for those of you that want to look that up or that remember from the Dopamine episodes. We have pathways in our brain that are associated with pursuit, motivation and reward. And the neuromodulator Dopamine is largely responsible for that feeling of craving, pursuit and reward. And this threat center is actually able to communicate with and activate the Dopamine system. And later you will realize why that is very important and why you can leverage the Dopamine system in order to wire in new memories to replace fearful ones. So I've been hitting you with a lot of names of things,

but for the moment, even if you're interested in all the Neuroscience names and structures and so forth. I'd like you to just conceptualize that you have a circuit in your brain, meaning a set of cells and connections that are arranged in the following way. You have a threat reflex that can be activated at any time very easily, but what activates that threat reflex can depend on two things. One are prior memories coming from brain areas that are involved in storage of memories, or it can be immediate experiences. Things are happening in the now, okay? So were something fearful to happen right now, your threat reflex could be activated. Where you to remember something very scary that happened to you in the past? Your threat reflex could be activated. And that threat reflex circuit has two major outputs. One of the major outputs is to areas that are involved in the threat response, freezing pain management and alertness.

#### 00:28:24 Controlling Fear: Top-Down Processing

And the other major output is to areas involved in reward, motivation and reinforcement, okay? There's a fourth component. And I promise this is the last component that we need to put into this picture of the neural circuits for fear. And this is a circuit that involves an area of the brain called the prefrontal cortex and some of its subdivision. So literally in the front. And it's involved in what we call top-down processing. Top-down processing is the way that your prefrontal cortex and other areas of the brain can control or suppress a reflex, okay? A good example of this would be the step on the tack example that I gave before. So when you step on a tack, you immediately pull up your foot and you extend the other leg. That's the reflex that prevents you from injuring yourself and from falling over. However, if you wanted, not that you would want to. But if you wanted, you could for instance, place your foot onto a tack and decide not to pull your foot away. It would be difficult. And again, I don't recommend that you do that, but you could override that reflex, okay? There are other examples of reflexes, like for instance, getting into cold water, most people will start to huddle their body. Most people won't want to get into the cold water. Many people will jump out. But all of that is reflexive. And should you want to, you could override that reflex through top-down processing. You could tell yourself, "Oh, I heard on a previous Huberman Lab Podcast, or on an Instagram post that cold water exposure can be beneficial for metabolism and resilience, et cetera." And indeed it can, and you can decide to get into the water and to stretch out your body, not to huddle, and you can fight those reflexes, okay? The fighting

of reflex is carried out through top-down processing, largely through the prefrontal cortex. You provide a narrative. You tell yourself, "I want to do this or I should do this. Or even though I don't want to, I'm going to do it anyway." So top-down processing is not just for getting into cold water, and it certainly isn't for overriding reflexes that can damage us like a stepping on the tack example. It is the way in which we can override any number of internal reflexes, including the threat reflex. And the way that we do that is by giving a new story or a new narrative to this experience that we call threat. And you know the threat response, the threat response is quickening of the heart rate, quickening of the breathing. We don't generally like the feeling of Adrenaline in our system. Some people are so-called Adrenaline junkies, and they get a mixture of Dopamine and Adrenaline from certain high intensity events. I confess in previous aspects of my life, I've tended to like Adrenaline. I don't think I was at the extreme of thrill seeking, but I'm somebody that for instance, I tend to like... I like roller coasters, I've done various things where I'm familiar with and I enjoy the sensation of Adrenaline in my body. But I enjoy it because of the alertness that it brings and the hyperacuity that it brings, many people don't feel that way. In fact, most people don't like the sensation of a lot of Adrenaline in their system. That it makes them feel very uncomfortable and out of control. We will do an entire episode about Adrenaline and Adrenaline junkies and Adrenaline aversives in the future. But the threat reflex inevitably involves the release of Adrenaline into the system. And then it becomes a question of whether or not you remain still, move forward or retreat from that Adrenaline experience. And when I say the Adrenaline experience, I mean the threat reflex. So this fourth component of fear is really our ability to attach narrative, to attach a meaning and to attach purpose to what is by all accounts and purposes, a generic response. There's no negotiating what fear feels like. There's only negotiating what it means. There's only negotiating whether or not you persist, whether or not you pause or whether or not you retreat.

00:32:27 Narratives: "Protective or Dangerous"

So this is usually the point in the podcast where I think people start asking, "Okay, well, there's the biology, there's the mechanism, there's the logic. How do I eliminate fear?" Well, it's not quite that simple. Although by understanding the logic and the mechanisms by which these circuits are built, we can eventually get to that place. I do want to plant a flag around a particular type of tool or a logical framework around a particular set of tools

rather, that we are going to build out through this episode. And based on what you now know that the threat reflex gets input and it has outputs and it's subject to these top-down processing events, these narratives. You should be asking yourself, what sort of narratives should I apply to eliminate fear? Well, first let's take a step back and just acknowledged the reality, which is that fear is in some cases, an adaptive response. We don't want people eliminating fears that can get them injured or killed, right? The reason that the fear threat response and reflex exists at all is to help us from dying, to help us from making really bad decisions. It just so happens that a number of things happened to us that are not lethal, that don't harm us, but that harm us from the inside. And I think that and here I'm borrowing language from an excellent researcher who's done important work in this area at Harvard. His name is Dr. Kerry Ressler. He's both a medical doctor and a PhD, so an MD-PhD. He's the chief scientific officer at McLean Hospital. He's a professor of psychiatry at Harvard Medical School, and he's done extensive and important work on fear. I'm going to refer back to Dr. Ressler's work several times during this podcast, including important and super interesting work on transgenerational passage of trauma. He's a absolutely world-class biologist, absolutely world-class clinician. And Dr. Ressler has described fear before as containing a historical component. So it's not just about a readiness for things that might injure us or kill us in the immediate circumstance but also protecting us for the future because of our important need and ability to anticipate. And what he describes our memories as protective or memories as dangerous. You know, some memories, even if they evoke a sense of fear in us are protective. They protect us from making bad mistakes that could get us injured or killed, or put us into really horrible circumstances. Other memories are dangerous because they create a sense in us of discomfort, and they tend to limit our behavior in ways that are maladaptive. That prevent us from having healthy relationships to others, healthy job relationships, healthy relationship to ourselves, frankly. So this language of memories as protective or memories as dangerous in the context of fear is not something that I said, it's really something that I lifted from Dr. Ressler in one of his many impressive lectures. And it's an important aspect of fear because much of the fear system is a memory system. Is designed to embed a memory of certain previous experiences in us. Such that the threat reflex is activated in anticipation of what might happen, okay? So let's talk for a second about how certain memories

00:35:58 Attaching Fear to Events: Classical Conditioning & Memory

get attached to this fear system. And this brings us to a beautiful and indeed Nobel Prize winning aspect of biology and physiology, which is Pavlovian conditioning. Many of you are probably familiar with Pavlov's dogs and the famous Pavlovian conditioning experiments. They go something like this. And Pavlov did these experiments and ring a bell, a dog doesn't do much in response to a bell. It might attend to it but it doesn't salivate typically in response to the bell. However, if you pair the ringing of a bell with a presentation of food enough times, the dog will salivate in response to the food. Eventually you take away the food, you just rang the bell and the dog will salivate in response to the bell, okay? So in the context of so-called Pavlovian conditioning, these things have names like conditioned stimulus, and unconditional stimulus and responses. People often get these mixed up and it can be a little confusing, but I'm just going to make it really simple for you. The unconditioned stimulus is the thing that evokes a response unconditionally. So food is the unconditioned stimulus in the example I just gave. A foot shock or a loud bang would be the unconditioned stimulus in a... For instance say, an experiment geared toward exploring fear. That unconditioned stimulus is unconditional. It unconditionally evokes a startle or in the case of food salivating. The bell in the previous example is what we call the conditioned stimulus or the conditioning stimulus. Sometimes people mix these up. The condition stimulus is paired with the thing that naturally creates a response. And then eventually the condition stimulus creates the response itself. You might think, well, that just seems endlessly boring and simple, but this is actually the way that our fear systems work. Except unlike Pavlov's dogs, you don't need many, many pairings of a bell with some unconditioned stimulus in order to get a response. You can get what's called one trial learning. And in this circuit that involves the amygdala, the threat reflex, and all this other stuff that I was talking about earlier, the system is set up for learning. It's set up to create memories and to anticipate problems. It's a very good system because it was designed to keep us safe. And so the way to think about this is that for many people, one intense experience, one burn, one bad breakup, one bad experience, public speaking. One bad experience with somebody pet snake or whatever it happens to be can cause intense fear in the moment, a long [indistinct] experience of fear, like trouble sleeping that night and the following night. Memories of the experience that are troubling, physiological responses that are troubling. Essentially it gets wired in as a fear with one trial. Which is quite different than the other forms of neuroplasticity. Neuroplasticity, of course, just being the nervous



system's ability to change in response to experience. Other forms of neuroplasticity like learning a language, learning music, learning math, those take a while. We don't generally get one trial learning to positive or neutral experiences. We get one trial learning to negative experiences. So there's this asymmetry in how we're wired. So now you should understand how classical conditioning as it's called occurs. You go to give a piano recital as a kid, you sit down and you freeze up and it's horribly embarrassing. And even if you just freeze up for a few seconds, the heart rate increase and the perspiring, the sweating and the shame that you feel leads you to want to avoid playing instruments or public displays of performances for a long period of time unless you do something to overcome it. That's one trial learning. Some people, it tends to be more an accumulation of experiences. They have a bad relationship that lasts an entire summer, an entire year, or God forbid a decade. And then they have what they feel is of a general sense of fear about closeness to others, an attachment. These are common fears that people experience. Fears can be in the short-term, fears can be in the long-term, they can be in the medium term. Again, the fear system is very generic. It's wired to include memories that are very acute, that happened within a moment, or that include many, many events in long periods of time. That kind of funnel into a general sense of relationships are bad or this particular city or location is bad. So there's a key what we call temporal component. There's a component of the fear system being able to batch many events in time and create one specific fear or take one very specific isolated incident that happened very briefly and create one very large general sense of fears. And I'll give an example of the latter, just to kind of flesh this out a little bit. I had a friend come visit me in San Francisco some years ago, and their car got broken into. Unfortunately, a frequent occurrence in San Francisco even in the middle of the day. Never leave anything your car in San Francisco they'll break in, in the middle of the day, doesn't matter. Police can be having coffee right there in front of them they'll still do it, for reasons we could discuss, this is a problem. They got their belongings taken and they decided they were never coming back to San Francisco. This was an isolated incident that forever colored their view of the city. Which I frankly, understanding the fear system, I can understand. We can have isolated incidents that wick out to broad decisions about entire places, or we can have many experiences that funnel into very specific isolated fears about particular circumstances,

00:41:45 How Fear Learning Occurs: Long Term Potentiation, NMDA

places and things. So I like to think that by now you have a pretty good understanding of the circuits that underlie the threat reflex, the fear response, and how we have top-down control, meaning we can attach a narrative to the fear response. And that the fear response can be learned in association with particular events, okay? I haven't really talked about how the learning occurs. And so I just want to take a moment and describe that because it leads right into our discussion about how to eliminate fears, and indeed how to replace fears with more positive experiences. There's a process in our nervous system that we call neuroplasticity. Neuroplasticity broadly defined is the nervous system's ability to change in response to experience. But at a cellular level, that occurs through a couple of different mechanisms. One of the main mechanisms is something called long-term potentiation. Long-term potentiation involves the strengthening of particular connections between neurons. The connection sites between neurons we call synapses, actually technically synapses are the gaps between those connections. But nonetheless, synapses are the point of communication between neurons and those can be strengthened so that certain neurons can talk to other neurons more robustly than they happened to before. And anytime we talk about a particular event, the car, the snake, the public speaking, the trauma, the horrible experience, wiring into the fear system. What we're talking about is a change in synaptic strengths. We're talking about neurons that previously did not communicate well, communicating very well. It's like going from a old school dial up connection, or even an old school telephone connection or Morse code connection of communication to high speed ethernet, okay? To a 5G connection. It gets faster, it gets more robust, and it's very, very clear. That's what happens when you get long-term potentiation. And long-term potentiation involves a couple of cellular mechanisms that are going to be relevant to our discussion about treatments to undue fear. And I'll just throw out a couple of the names of some of those cellular elements right now. The main one is the so-called N-M-D-A receptor, N-methyl-D-aspartate receptor. And what this is, is this is a little docking site, like a little parking slot on a neuron. And when a neuron gets activated very strongly like from an intense event in the example of my friend, the intense event. Almost certainly activated and NMDA receptors related to their concept of protecting their property in their cars, the break into their car caused the NMDA receptor to be activated. Normally that NMDA receptor is not easily activated when it is activated it sets off a cascade, a series of signals within those neurons that change those neurons. It changes the genes they

express, it shuttles more parking spots to the surface of those cells so that the communication to those cells becomes easier, it becomes faster. And so the way to think about the NMDA receptor is it's used sometimes for normal things that we do every day, making cups of coffee and things like that. But it's often used for learning. It's used for creating a new associations in our nervous system. And so the activation of the NMDA receptor and LTP, and it involves some other things that you may have heard of like, brain-derived neurotrophic factor and calcium entry, things that we can leave for a discussion for a future time. But basically a whole cascade of events happen within cells that then make just even the mere thought of something or somebody or some event that happened able to activate that threat reflex, okay? So long-term potentiation is one of the main mechanisms by which we take formerly innocuous or irrelevant events, and we make them scary. We make them traumatic. Our neurons have mechanisms to do this. Now, fortunately, the NMDA receptor and long-term potentiation can also run the whole system in reverse. You can get what's called a long-term depression, and that doesn't have anything to do with the depression associated with low mood. What we're talking about is a weakening of connections. You can go from having a very high speed ethernet connection between neurons, so to speak, to a connection that's more like Morse code, or as like a poor dial up connection or really weak signal.

#### 00:46:10 Extinguishing (Reducing) Fears

And that's what's happening when you extinguish a fear, when you unlearn a fear. So now I'd like to talk about therapies that are carried out in humans that allow fears to be undone, that allow traumas to be reversed, such that people no longer feel bad about a particular person, place or thing. Either real interactions with that person, place or thing, or imagine interactions with that person, place or thing. That process as I just mentioned also involves things like the NMDA receptor but rather than strengthening the connections the first thing that has to happen is there needs to be a weakening of connections that associate the person, place or thing with that threat reflex. Subsequent to that, we will see there needs to be a strengthening of some new experience that's positive, okay? This is a key element of where we are headed contrary to popular belief, it is not going to work to simply extinguish a fear. One needs to extinguish a fear and or trauma and replace that fearful or traumatic memory or idea or response with a positive response. And this is something that's rarely discussed both in the scientific literature,

but certainly in the general discussion around fear and trauma. There's this idea that we can extinguish fears, we can rewire ourselves, we can eliminate our traumas and indeed we can. But that process has to involve not just becoming comfortable with a particular fearful event or trauma, but also attaching a new positive experience to that previously fearful or traumatic event. There are a lot of different approaches out there that are in clinical use to try and alleviate fear and trauma and indeed PTSD, post-traumatic stress disorder. It might be surprising to learn that many of those treatments such as SSRIs, the selective serotonin reuptake inhibitor. Things like Prozac and Zoloft and similar and other antidepressants. Or things like Benzodiazepines, which are essentially like painkillers. They create elevation in certain transmitters in the brain like GABA among others. They can have a pain relieving effect. They are generally however, considered anxiolytics, they reduce anxiety and even antipsychotic drugs or Beta blockers sometimes called adrenergic blockers. Drugs that are designed to prevent the heart from beating too fast or to reduce blood pressure, to reduce some elements of the hypothalamic-pituitary axis response that we talked about earlier. Many people experienced some degree of relief from the symptoms of anxiety and fear and PTSD in taking these various compounds. Indeed, that's why they're prescribed so broadly. But you may find it interesting to note that none of those current treatments are based on the neurobiology of fear, at least not directly, right? People that take SSRIs oftentimes will experience a reduction in anxiety. It depends on the dosage and the individual of course, right? And you have to work with a doctor, a psychiatrist, to determine whether or not they're right for you in the correct dosage, if they are right for you. But that modulation of anxiety can indirectly reduce the likelihood that one will have a panic attack or experience of fear, an intense experience of fear or reliving of a trauma. But the SSRIs themselves are not plugging into some specific mechanism related to how fear comes about in the system. It's an indirect support. That's important because if the goal of modern psychiatry and the goal of modern biology is to provide mechanistic understanding that leads to treatments. We need to think about what are the sorts of treatments that tap into the very fear circuits that we described before. The fact that there are memories attached to a generic threat reflex and response. And the threat reflex and response can be linked up with the Dopamine system and can be linked up with other systems

00:50:25 Cognitive (Narrative) Therapies for Fear

that are involved in pain, relief and anxiety and so forth. And so that brings us to which treatments are directly related to the fear circuitry and the circuitry related to trauma? And the primary one to begin with is the so-called behavioral therapies. Now, oftentimes we all wish I think from time to time that there's some specific pill that we can take or there's some machine or device that we can plug our finger into or that we can put on a headset and all of a sudden we just rewire our nervous system. Fear has gone, trauma's gone, but it doesn't work that way. And when we think of language and narrative as a tool to rewire our nervous system in comparison to those kinds of ideas about pills and machines and potions, it starts to seem a little bit weak, right? If we just think, "Oh, well, how could talking actually change the way that we respond to something?" But actually there are three forms of therapy that purely through the use of language have been shown to have very strong positive impact, meaning reduce fears and traumas. And those three are prolonged exposure therapy, cognitive processing, or CPT and cognitive behavioral therapy. And I not going to go into the entire literature around prolonged exposure, cognitive processing, and cognitive behavioral therapy. But I will just illustrate the central theme that allows them to work. Now, remember that the circuit for fear, the circuit for trauma involves this generic reflex. And then there are those top-down elements coming from the forebrain. It's very clear because it's been measured that if you look at the amount of anxiety, the pure physiological anxiety response of quickening of heart rate, flushing of the skin, sometimes quaking of the hands, that the experience of fear over time when people recount or retell their trauma that the first time they do that especially when it's recounted in a lot of detail there's a tremendous anxiety response. Sometimes even as great or greater than the actual exposure to the fearful event or trauma. And obviously this is something that is done with a clinician present, because it is very traumatic to the person. They're literally reliving the trauma in full rich detail, and they are encouraged to provide full rich detail. They're often encouraged to speak in complete sentences to flush out details about how they felt in inside, to flush out details about their memories going into this traumatic or fearful event, going through it. And after really digging into all the nuance and contours of these horrible experiences. But what's remarkable is that in the second and the third and the fourth retelling of these traumatic or fearful events that anxiety response and the amount of the physiological response, I should say that the amplitude of the physiological becomes progressively diminished with each retelling. Now, some of you might be saying, "Well, duh, you know, you tell a

story enough times, that eventually it wears off." Just like if you watch a movie enough times and you hear the same joke enough times eventually it doesn't have the same impact. But that [indistinct] be the case, right? You could imagine that this high amplitude anxiety response, this high amplitude activation of the sympathetic nervous system in retelling would actually create a even deeper routed fear response and trauma but that's not what happens. And every clinician I spoke to in anticipation of this episode which include clinical psychologists, psychiatrists and people who actually work on the fear system at a biological level said the exact same thing which is that, "A detailed recounting of the traumatic and fearful events is absolutely essential in order to get the positive effects of prolonged exposure, cognitive processing and cognitive behavioral therapy." Again, this has to be done with the appropriate support. This isn't something that should be taken lightly because as we've mentioned before the fear response can have a very long lasting contour to it. People can sometimes have trouble sleeping for days and days. And afterwards we'll talk about sleep in a little bit. But the point is that the retelling is important. And the idea here is to take what was a terrible and extremely troubling, meaning physiologically troubling, psychologically troubling story, and turn it into what is essentially a boring, bad story, okay? It never really becomes a good story at this point in the treatment process that we're describing. So a terrible event is a terrible event period. But there's a way in which the retelling of that event starts to uncouple the threat reflex from the narrative. And with each successive retelling in detail of these traumatic events, of these fearful events, the threat reflex is activated at a progressively lower and lower amplitude. Such that eventually it just becomes a really bad, really boring story. Now that's one part of the process of getting over a fear. It's what we call fear extinction. And we can bring ourselves back to our earlier example of Pavlovian conditioning, because many studies have been done both in animals and in humans showing that, for instance, if you pair a tone, a bell or a buzzer with a foot shock that an animal or a person will brace themselves for the foot shock. Eventually you can just give the bell or a tone and the person will experience that same freezing up or the same fight or flight or freeze response. So you conditioned that. But if you give the tone or the bell over and over, and there's no foot shock, there's no pain, and in human [indistinct] sometimes I'm with foot shocks, sometimes believe it or not with mild burn, even some studies, there is older studies you couldn't do those now, nor would you want to. But eventually what happens is the tone... The bell no longer evokes that response, okay? So you see this as a reversal of the classical conditioning and we call that reversal

extinction. So the retelling of this traumatic or fearful narrative, excuse me, fearful narrative is essentially an extinction process. Now, how is this done? One can do this in a therapist office face-to-face, that's sometimes done. It's sometimes done in group type settings where people actually stand up or sit in front of a group small or large and recount in detail their traumatic experience. It's sometimes done by people writing out the experience in detail. And which one of these is the most effective? Isn't really clear. The literature points to the fact that a feeling of trust obviously between the patient and the clinician or the person and the group is essential. Some people don't have access to because of finances or other limitations to therapy of that sort. In that case, journaling in detail has been shown to be effective. Although, again, I want to caution people about reactivating traumas without consideration for the kinds of social support they might need around that reactivation. And we will talk a little bit later about

#### 00:57:56 Repetition of Narrative, Overwriting Bad Experiences with Good

some of the chemicals involved in social support and why those help extinguish fears. So the thing to embed in your mind is that recognition of the early traumatic or fearful event in detail over and over is key to forming a new non-traumatic association with that event or person. So that's part one, you need to diminish the old experience. And when I say diminish, I mean, reduce the amplitude of the physiological response. Now this is just but one approach. I'm going to talk about other approaches to eliminating fear and trauma as we go forward. But I want to emphasize that diminishing the amplitude of the physiological response is the first step. So it's like a clearing away of the association between the person, place or thing and that threat reflex. But even after that's occurred, there's an essential need to relearn a new narrative. Why is their essential need to relearn a new narrative or create a new association? Well, that has to do with that fear reflect circuitry. As you recall, there outputs two areas of the brain that are associated with Dopamine release and reinforcement. And that we now know offers the capacity for these fear circuits in these circuits that underlie trauma to be mapped onto new experiences that are of positive association. So I'm going to give a kind of basic example. It's a kind of a silly example, but I'm giving it as a template for what could be any number of other different examples. Example I'll give is let's say a kid is biking to play soccer, soccer practice, and they get into a bad car accident, okay? Terrible thing to happen, but they survive. They recover. And somehow... And we really don't know why

certain fear memories get wired in more broadly or more narrowly. Somehow this kid just doesn't even want to bicycle anymore. And they actually don't even want to play sports. And they actually just don't want to go anywhere. They're kind of isolating and not interacting with friends very much at all. It's a pretty broad response. It didn't have to be that way. Some kids would just decide they don't want to cycle any more down that particular street. Well, the process of retelling the narrative to a clinician would allow an extinction of the fear response, right? So a reduction in the heart rate, a reduction in the narrowing of focus, a reduction in all the things that we consider fear. But a really good cognitive behavioral therapist or somebody that understands the Neuroscience of fear and trauma would understand that that's not sufficient. That's what it's really important is that this child, this hypothetical child relearn a new narrative that they don't just manage to bike to soccer practice or manage to spend time with friends, but that they actually start wiring in new positive associations with biking to practice, with playing soccer, with social events. And, and this is the somewhat surprising feature of this and that they link that back to that early traumatic experience. That it's not just that they're replacing that bad experience and memory with a good experience and memory, but they're actually holding in mind in these top-down narrative circuits, if you will. They're holding in mind, "Ah, I'm not just biking to soccer practice. I'm actually biking to soccer practice and I'm enjoying it despite the fact that I was in a bad car accident. Despite the fact that two months ago or two years ago, or maybe even 10 years ago, I couldn't even leave my room or I didn't want to associate with anybody." So the building up of the positive associations are key. And the linking of those positive associations with the earlier traumatic event is key for the following reason, the top-down circuitry from the prefrontal cortex to this threat reflex circuit is not like the other connections in that circuit. The other connections in that circuit are what we call glutamatergic and excitatory. They are all about activating other neurons, like a chain reaction. One neuron activates, the next activates, the next like dominoes falling. These top-down circuits that feed into the threat reflex and all its parts is what we call inhibitory. It tends to prevent activation of those given circuitries. It tends to prevent activation of the threat reflex. So it's acting as a break. And so when we think of positive experiences being associated with what was previously a negative experience, we're not talking about forgetting that the car accident was horrible or forgetting that the assault was absolutely dreadful. We're talking about attaching a new positive memory to the circuitry so that the previous fear response is far less likely to occur and that it remains extinguished. So just to make sure this is



absolutely clear, there's a first step which involves retelling and reliving in order to extinguish the fear and the trauma, to reduce the amplitude of the response. Then there's a need to replace or attach positive experiences to the earlier what would be traumatic response. The extinction has to go first, this is key. You can't simply say, "Oh, you know, the car accident was actually a good thing because I stayed home a lot that year and I got to study." You can tell yourself that and that could also be true. But that won't necessarily and probably won't eliminate the fear or the traumatic association of the car accident. And again, I'm using car accidents as a general example or a generic example here, okay? So there's a three-part process. One diminished the old experience through repetitive narrative. And almost inevitably the initial repetition of that is going to be very high amplitude and quite troubling. But over time it will reduce, right? You're turning that terrible really upsetting story into a terrible boring story. That's the extinction process. Then there's a relearning of a new narrative that includes some sort of sense of reward. And that sense of reward has to be tacked back on to the traumatic event or what was previously a traumatic event. And that is all through narrative. It's all through cognition. And I think this is a very important point. Oftentimes I think we tend to undervalue the importance of rationalization and of story and of narrative. But the prefrontal cortex is this amazing capacity of our brain real estate to create meaning, to attach meaning and purpose to things that otherwise are just reflexive. And in the example of an ice bath, it might be a little trivial. In the example of the kid with a car accident, it becomes a little more relevant. And in the example of things like people surviving, you know, genocide or attaching stories of great victory to what were previously thought of as stories of great loss of time, of people, of any number of things. That process of narrative is one of the major ways that the human brain rewires itself. Narrative should not be undervalued as a tool for relieving fear and trauma. In fact, narrative is one of the best and most potent ways that we can rewire our fear circuitry.

01:05:28 EMDR: Eye Movement Desensitization Reprocessing

And that indeed we can form completely new relationships to things over time. So basically narratives should not be undervalued as a tool to rewire our nervous system but it has to be engaged in the correct sequence. And that correct sequence is first extinction, then relearning a new narrative with positive associations and attaching those positive associations to the formerly traumatic or fearful event. Now I mentioned

prolonged exposure therapy, cognitive processing, and cognitive behavioral therapy. For those of you that are seeking relief from fear and traumatic events, you can look up licensed clinicians that can carry out those one or several of those types of therapies. I get a lot of questions about other forms of therapy. One of the ones that comes up a lot is so-called EMDR, Eye Movement Desensitization and Reprocessing developed by Francine Shapiro in the 80s. Eye Movement Desensitization and Reprocessing involves moving the eyes side to side while recounting a traumatic or fearful narrative typically with a clinician present. Why would that work? Well, basically when I first heard about EMDR from my stance as a vision scientist I thought the whole thing was kind of crazy and half-baked frankly. I heard these theories that, "Oh, it recreates the eye movements in rapid eye movement sleep or REM sleep." And that's completely false. It does not. I heard the argument EMDR activates both sides of the brain, which I guess hypothetically was thought to be important somehow. And frankly, there's no evidence whatsoever that EMDR activates both sides of the brain in a way that's beneficial. I mean, by looking from side to side, just because of the way that binocular vision circuits are organized it will do that. But it never made any sense to me why EMDR would work until several years ago when I saw. Because I reviewed no fewer than five papers. Some in animal models, others in humans looking at lateral eye movements. Meaning I moving from side to side with eyes open, not eyes up or down. And what was observed in these experiments in all of them actually, all five of those papers was a dramatic reduction in the activation and actually an inhibition a suppression of the fear or threat reflect circuitry which was a jaw dropper for me. I thought, "Wow, it actually was a jaw dropper." I widened that. For me, I thought, "Oh my goodness, maybe this EMDR stuff works according to some mechanism. And maybe this is the mechanism." And indeed many laboratories, not mine, but many laboratories are now pursuing that idea. And it's looking very likely. Why would that happen? Well, just very briefly, a lateralized eye movements of the sort that I'm describing and I'm moving my hand like this but I'll just do it with my eyes even though it's a little embarrassing to do that. Cause I know it looks strange, I don't mind cause I'm doing EMDR and EMDR reduces activation of the amygdala and related circuitries which reduces anxiety and reduces the amplitude of the threat reflex. Reduces sympathetic autonomic arousal. In other words, we feel calmer or we feel less alert, less stressed when moving our eyes from side to side. I just heard a story about this is that these are the sorts of eye movements that we do when we are ambulating, moving through space, through some sort of self-generated motion. And one can make

up a pretty reasonable story in the evolutionary context or ecological context that forward movement and fear are generally incompatible with one another. That generally a fear response involves a freezing or a retreating. Some people will advance, but that's usually a trained advance in response to fear so first responders and so forth. Most people freeze or retreat when they're afraid. Forward movement generates these eye movements. It does seem to suppress activation of this threat reflex and the amygdala in particular. So for the many EMDR practitioners out there these papers I think are a great celebration. And I think there is now increasing excitement about EMDR in the psychiatric and psychological community for its utility, for treating fear, trauma and PTSD. However, I should point out that in discussing EMDR with various colleagues of mine at Stanford and elsewhere, I was told that EMDR has been shown to be beneficial in particular for single event type traumas or fearful experiences. Not so much for relieving the trauma or feelings of fear associated. For instance, with an entire bad marriage or an entire childhood. But more for single more acute events that can be described within a very kind of brief narrative. Brief, not necessarily in time, but that the car accident, the bad interaction with another individual, the assault, God forbid, these sorts of things. And I realize we're down in the weeds of topics that are unpleasant. And so I have great sensitivity to that but I think it's also important that we be realistic about the kinds of things that traumatize people. So is EMDR useful? Well, it seems like it works for these single event or kind of constrained event type traumas that people can describe while moving their eyes from side to side generally in the presence of a clinician. However, if we think back to the model of how you extinguish and then replace a trauma or fear, remember you have to diminish the old experience the amplitude of that. You need to... That's the extinguish portion. Then you need to relearn a new narrative and attach reward to the old traumatic event. EMDR only really taps into the extinction of the physiological response to the old experience. I'm sure that there are EMDR practitioners out there that are thinking about the attaching of the new narrative and reward, but there I've heard less and I've seen fewer peer-reviewed papers on that. So let's think about this logically. Let's say, and indeed it's the case that I'm sitting down in a chair and moving eyes side to side deliberately for some period of time reduces activation of the threat reflex. I or the patient in this case, recites or repeats over and over the traumatic event or the fearful event. I'm doing that in the presence of a lower amplitude response. Remember back to where we talked about how the retelling works best if the first time it's done there's a huge amplitude response. And then with each

successive repeat that response the threat response gets lower and lower. With EMDR, you're sort of short circuiting you're kind of sneaking around the corner of that high amplitude response. And so it's taking a somewhat different approach of trying to extinguish the bad feelings in body and mind associated with an experience by reducing the physiological response. So it's somewhat different. And at least to my knowledge and EMDR practitioners please correct me, but at least to my knowledge, there isn't an active component to EMDR of relearning a new narrative and attaching reward. Now reward and attaching reward requires a somewhat high amplitude sympathetic arousal. It requires a feeling of a victory which is arousal, okay? It's positive arousal, not negative arousal, but it is arousal. So I'm not focusing on this to try and diminish the potential impact of EMDR. I know many people have achieved great relief from EMDR but it doesn't tap into all the aspects of the extinction and relearning that we talked about previously. And therefore, I think on its own at least in many cases is unlikely to be a complete therapy for fear and trauma. If there are people out there who've had terrific results with the EMDR, please let us know in the comment section, on YouTube would be the ideal place. If you've had bad experiences with EMDR or it didn't work for you also let us know. I think that EMDR practitioners like most practitioners in the psychiatric and psychological space are eager to expand their practices in order to make them more effective rather than clinging ardently to something that perhaps is incomplete or that doesn't work

#### 01:14:00 Social Connection & Isolation Are Chemically Powerful

for certain individuals. So I think they would appreciate that feedback as would I. So, as I mentioned before, most of these therapies are done in conjunction with a skilled often one would hope credentialed clinician. There are many people however, that don't have access to that or who are working through stuff. They have things in their past that are very uncomfortable to them. And I'm aware that many people are working through those things. Through journaling, through talking to a friend, through any number of different sort of non-traditional approaches. One thing that really pertains to everybody who's working through fear and trauma of any kind is the importance of social connection as it relates to the chemical systems and the neural circuits associated with fear and trauma. And this is an emerging literature in Neuroscience that is really a beautiful one because it's a very conserved biology. We see it, believe it or not in flies and fruit flies, a

commonly used model system. In mice and indeed in humans as well. And this is the work of David Anderson's group at Caltech, again, of Dr. Ressler's group at Harvard Medical and elsewhere, of course. And this is the work as it relates to Tachykinin. Tachykinin is a very interesting molecule in our brain and it turns out the Tachykinin is activated in neurons of what's called the central amygdala and some nearby structures. So really smack dab within the middle of this threat reflex. Very soon after some traumatic or fear inducing event occurs. And it actually sets in motion a number of other things including changes in gene expression and potentiation meaning long-term potentiation, activation of an NMDA receptors and so on. In the circuits that reinforce that fearful or traumatic experience. Now what's interesting about Tachykinin is also that it's been shown to lead to low to moderate levels of anxiety and even kind of aggression, irritability. Tachykinin levels are further increased by social isolation. And that social isolation is oftentimes what can exacerbate pre-existing traumas or fearful events. And in a kind of beautiful symmetry to that kind of dark and depressing story, social connection with people that we trust. And it doesn't have to be direct physical contact but just social connection conversing with, sharing a meal with, it could be physical touch if that's appropriate. Those sorts of connections actually serve to reduce the effectiveness or even the levels of Tachykinin. So the important point here is that trauma is traumatic in and of itself. Fearful events are hard in and of themselves. And if people are working through them either through clinical work or through individual work. It is important and in ideally one would still be trying to access social connection outside of that specific work-related to the trauma. Now it doesn't necessarily have to be outside of that. For instance, if you have a good relationship with a clinician or therapist to the point where there's real trust and you feel a social connection with them, wonderful. But for many people, they have a more transactional relationship to the EMDR practitioner or to their therapist, or they're working through things on their own. And it's really important to understand that regular social connection, trusting social connection of any kind is going to be very beneficial for that process. And so this is not the kind of just hand-wavy, a new agey stuff like, "Oh, you know you need social connection." There's a actual neurochemical basis for social isolation that has an amplifying effect on fear and trauma. And there is a neurochemical basis for the relief from fear and trauma and isolation. And in the ideal circumstance, one is working through these traumas and fears very intensely in a very dedicated way. But then is also engaging in the sorts of social interactions that are going to diminish the amount of Tachykinin

## 01:18:23 Trans-Generational Trauma

and going to suppress those very circuits that would otherwise be amplified. So next I'd like to talk about some really interesting and almost kind of eerie scientific findings. And that's the transgenerational passage of trauma or predisposition to fear and trauma. This is a scientific literature that's been debated many times over the last really 50 plus years. But in more recent studies have really proven that we as humans have the capacity to inherit a predisposition to trauma or fear. Now that doesn't necessarily mean that we will become traumatized or experience extreme fear just because our parents or grandparents experienced that. It's a predisposition, it's a bias. Let me explain the papers that focus on this for a little bit. And then we'll talk about what this means for each of us. One of the most important papers in this area comes to us from someone I mentioned earlier, Dr. Kerry Ressler at Harvard. And the title of the paper is, Association of FKBP5 polymorphisms and childhood abuse with risk of posttraumatic stress disorder symptoms in adults. And there are other papers as well. Another one from the Ressler's Lab, first author, Brian Dias, D-I-A-S. Parental olfactory experience influences behavior and neural structure in subsequent generations. I'm going to summarize these papers and their general contour and papers related to them. Although, feel free to look up the papers I just described. We will provide a link to them in the caption if you'd like to go further. But basically these explorations involve looking at the histories of human individuals who had trauma or abuse of some kind in their childhood. And then looking at the likelihood of fear and PTSD type symptomology in their offspring. And essentially what they identified is that indeed, if you had a parent and there does seem to be a kind of a bias toward an effect where if the father had abuse and it's severe abuse or moderate abuse. That abuse causes a change in his genetics, in his sperm that can be passed on to offspring such that the offspring have a lower threshold to develop trauma or extreme fear to certain types of events. Now what's important to point out is that predisposition or bias is not necessarily to the same sorts of events. It's not that the abuse itself gets passed from one generation to the next it's a predisposition. And the title of that paper mentioned, FKBP5, excuse me, FKBP5 polymorphisms. And the FKBP5 polymorphisms maps to a location in the genome that's associated with the so-called glucocorticoid system with cortisol release. So the predisposition that one might inherit from having a parent father or mother but stronger tendency to inherit it from the father.

Who experienced abuse is one in which the glucocorticoid system, the cortisol system, and that HPA axis that we talked about before the hypothalamic-pituitary-adrenal axis is sensitized or reactive in a way that sets a lower threshold to become traumatized or very afraid of certain types of events. But it's not unique to the specific type of abuse that the parent experienced. Now, this is really, really important because a lot of times out there I will hear that there's passage or transgenerational passage of actual trauma, the specific trauma. Now that could be through narrative telling, if somebody is exposed to a lot of narrative about their parents' trauma in one form or another. It may be that they start to internalize some of that trauma. And there could be because we obviously can't rule it out. There could be some other signatures of prior specific traumas they get passed on to offspring. But more likely and certainly what these data about these polymorphisms point to is that what gets passed on is a propensity for the threat reflex to get activated and attached to a wider variety or to less intense types of inputs and experiences. And the important point to take away from this is that it's not some magical, mysterious, and mystical thing that's being transplanted from parent to child. It's a gene or it's a modification in a set of genes that gives a heightened level of responsivity to fearful type events. Or even a high level of responsivity such that things that wouldn't be fear inducing or trauma inducing to certain individuals can trigger fear and trauma in these children that inherit this particular gene. Now that doesn't necessarily mean that they are fated to forever be traumatized or live in fear. It's simply not the case. It's just a genetic predisposition regardless of whether or not you had a parent or parents that were traumatized or not. There's no evidence, at least as far as I'm aware that the treatments for trauma should be any different. As far as I know there aren't gene therapies currently aimed at these particular variants, like FKBP5 and so forth that could reverse those particular genetic underpinnings of the trauma predisposition. So this transgenerational passage of trauma, I think is extremely interesting in large part because it brings us back to this idea that the threat reflex is part of a larger sensory system. You know, normally we think of seeing as a sensory system or hearing as a sensory system. But the threat detection and threat learning system, the fear learning system is in many ways a sensory system. It's just a sensory system that is very generic in its response. That generic response again is good because it allows for flexibility but it's bad because it reduces specificity, right? We can essentially become fearful or traumatized by anything if the circuit gets activated. And these particular children inherit a predisposition for more things and less intense things to traumatize them. In a few minutes, we are going to

discuss some of the behavioral treatments

01:25:00 PTSD Treatments: Ketamine, MDMA, oxytocin

including some really new exciting protocols for dealing with fear and trauma. But for a few minutes, I'd like to discuss some of the drug treatments that are starting to emerge as potential therapeutics in particular for PTSD. The two drug treatments I'd like to focus on are Ketamine-Assisted Psychotherapy, and MDMA-Assisted Psychotherapy. Currently Ketamine-Assisted Psychotherapy is legal. It is approved, provided it is prescribed by a board certified physician in the United States. I'm not certain about other areas of the world. MDMA also sometimes called Ecstasy therapy is in clinical trials in the U S, it is still an illegal drug to possess or to sell. So I want to be very clear about that. However, MDMA is being explored as a potential therapeutic for PTSD and other forms of trauma. And of course, Ketamine and MDMA are also both being explored for chronic depression, eating disorders and a number of other psychiatric disorders. But for the moment I would just like to touch on Ketamine and MDMA as they relate to the fear circuitry and trauma circuitry that we've described in the early part of the episode and throughout the episode. Because I think that in viewing them through that lens, we can gain some additional insight into how they might be providing the sorts of relief that some of the early clinical studies are starting to point to. Ketamine is a dissociative anesthetic. That's right. It's a dissociative anesthetic. It's main function is to create a state of dissociation. And I've never taken ketamine personally so I can't describe the experience of it. But a colleague of mine in psychiatry shared their experience with a patient's experience of it as making that patient feel as if, "They were getting out of the cockpit of a plane, but that they were observing themselves doing it." And this was of course, during a approved therapeutic session that they were doing this and they were in some sort of intense visualization about a traumatic experience. They were describing some of their depressive symptoms as well as the trauma. And their narrative that they basically created or took away from this. And that was relayed to me was one in which the patient felt like they were in their own body but they were also viewing their own body from the outside. So dissociative, in other words. Again, I've never had this experience. Some of you may have with Ketamine or through other means. But we might want to just take a moment and think about what Ketamine actually does and what dissociation actually does at the level of neurocircuits? And for that, we can look to this



really beautiful paper that was published by my colleagues, Karl Deisseroth in psychiatry, Robert Malenka, also in psychiatry, Liqun Luo, also at Stanford. They paired up or teamed up rather to explore how systemic Ketamine adjust circuitries in the brain. And what they discovered was that it changes the rhythm of cortical activity in certain layers of the cortex. The cortex is like a layered sandwich. The cortex of course, being the outside of the brain. And there was a particular rhythm a one to three hertz rhythm. One to three hertz just means a particular frequency of electrical activity. In this case, in these layer 5 neurons of Retrosplenial cortex. So you don't need to know much about Retrosplenial cortex or a one to three hertz rhythms. I think the important thing to just take away from this is that there is now starting to be an understanding of how drugs like Ketamine work to create this subjective experience that this patient and other patients describe as dissociation. You know, dissociation in its essence is really about not feeling what's happening. It's about viewing what's happening from a different perspective than what normally one would view that experience from. And so if we add a plug that general notion of dissociation and Ketamine induced association into the circuit that we talked about before, where we have this threat reflex involving the amygdala. These outputs for freezing or for reward and the accumbens. And we've got this prefrontal narrative coming down as top-down processing. It brings us right to that prefrontal cortical input to the threat system and that narrative. What seems to be the case in my review of the paper I just described, plus a review on how Ketamine-assisted trauma relief might work is that it somehow allows the patient, the individual to recount their trauma while feeling either none or a very different set of emotional experiences that they experienced in the actual trauma or fearful experience. So it's a remapping of new onto old. New meaning new feelings onto old feelings while staying in the exact same narrative. So it's a little bit like EMDR of suppressing the threat reflex but it seems to bring in a replacement of previous emotional experiences and sensations in the body with new ones. And so in that way we can sort of view or we can try and view Ketamine-Assisted Psychotherapy for the treatment of trauma as bringing together the three elements that we talked about before. You want to diminish the intensity, the potency of the old original trauma experience or fear experience. So that seems to be accomplished through this dissociation and maybe through the kind of anesthetic component. So it's a reduction in pain in the body, a dissociation, a kind of observing of the self that leads to the extinction of the trauma and the fear. But then there also seems to be an automatic or kind of built in a relearning of a new narrative, a new set of experiences which is the next step that

we described earlier. So it's an intriguing therapy. It's one that's really catching on and there are many, many clinics around the U S that are now doing it. Whether or not it turns out to be the ultimate treatment for trauma and for fear isn't clear. My colleagues in psychiatry tell me that that's unlikely, although it does seem to be beneficial for a number of people. Especially people that are experiencing trauma or have existing traumas and fear that are coupled with depressive symptoms. Because the data on Ketamine and depression seems to be quite strong. So now let's talk about MDMA. MDMA also sometimes called Ecstasy or Molly in its recreational form is a powerful synthetic drug that at least as far as we know, creates a state in the brain and body that is unlike any other chemical state in the brain and body that's normally experienced. What do I mean by that? Well, we have several Neuromodulator systems in our body. Neuromodulators are chemicals that change the likelihood that certain neural circuits will be active. Meaning they can make it very likely that certain circuits will be active and make it very unlikely that other neural circuits will be active. Good examples of neuromodulators are dopamine, serotonin, acetylcholine, norepinephrine. These tend to work on different systems in the brain and body but they tend to be activated more or less in parallel, right? You can have Dopamine released in your brain and also Norepinephrine. You can have Serotonin released in your brain and also Acetylcholine. So it's not an all or none kind of thing, but the degrees to which these things are activated tends to vary. And there is a little bit of a seesaw type phenomenon with Dopamine and Serotonin. Dopamine most commonly associated with activating neurocircuits related to motivation, craving, and reward. And Serotonin more typically activated in response to situations or conditions in which we are very happy and content with what we have. So Dopamine is more about pursuing and seeking. Serotonin is more about kind of pleasure and satisfaction with resources that we have in our immediate sphere. They don't tend to... Serotonin doesn't tend to place the brain and body into a mode of action quite as much as Dopamine does, more or less. MDMA is a unique compound in that it leads to very large increases in the amount of both Dopamine and Serotonin in the brain and body simultaneously. And that's a unique circumstance that is just simply not seen under normal conditions. From a subjective standpoint, people under the influence of MDMA in the therapeutic setting, tend to report immense feelings of connection or resonance with people or even things with music, with objects. Certainly if it's being done in conjunction with a family member or a partner or with a therapist, they will feel extremely connected to that person. They'll feel a very close understanding and association. Oftentimes that

goes beyond words. There is a chemical reason for that. It turns out that MDMA causes massive release of oxytocin. This neuropeptide that's associated with pair bonding and with bonding generally. The oxytocin system and the Serotonin system are closely linked to one another in the brain and body. And they tend to be co-released often at the same times and by the same sorts of events. So MDMA is one mechanism by which oxytocin is released in these massive amounts. And I should just relay some of the levels of oxytocin because they're really quite striking, gives a kind of a more vivid picture of why it is the MDMA would make people feel so associated in a positive way with the various things that are happening them while they're under the influence of the drug. So the paper related to this that I'd like to highlight is in the journal Psychoneuroendocrinology. The title of the paper is Plasma oxytocin concentrations following MDMA or intranasal oxytocin in humans. And just remarkably MDMA increased plasma oxytocin levels to 83.7, this is an average, 83.7 picograms per milliliter. About 90 to 120 minutes into the MDMA session compared to a typical level of 18.6. So this is a massive increase in oxytocin. And I think that massive increase in oxytocin is part of the reason why people have these feelings of close resonance and association. Now, the Dopamine increases are generally what lead to the feelings of euphoria inside of the MDMA session. And then the Serotonin increases it is thought are what lead to the feelings of safety and comfort. So again, a very unusual chemical cocktail that would never be seen at least not at this amplitude under any normal conditions outside of an MDMA clinical psychotherapeutic session. Why would this state of mind and body be potentially useful for the treatment of trauma? Well, indeed it is revealing itself to be useful for the treatment of trauma. Again, these are legal clinical trials where people are doing this and discovering this. What it seems to allow is a very fast relearning or new associations to be tacked on to the previously traumatic experience. So again, it brings us back to the same model of how people extinguish fears and traumas and replace them with new experiences when there is no drug treatment involved. There needs to be a diminishing of the old experience, meaning an extinction and then a relearning of a new narrative. What the chemical [indistinct] of MDMA seems to be doing is creating an opportunity for all that to happen very fast without the need for many repetitions of the original trauma and reliving of the original trauma. Probably because the reliving of it inside of one of these MDMA sessions is very acute, very intense, plus it seems to be offering the opportunity to extinguish and rewrite in or write in a new narrative associated with that trauma very quickly as well. So what this means is that treatments like MDMA that are

under investigation in these clinical trials are unlikely to be magic potions, if you will, that allow access to a particular process that would otherwise not be accessible. It's more that the typical process of trauma and fear reduction that's carried out in things like prolonged exposure, cognitive processing, cognitive behavioral therapy seems to be compacted into a much shorter session. And that session is performed at a much higher intensity. Higher intensity because the chemical [indistinct] of the brain is completely different. I mean, the experience of MDMA is one in which people have a very heightened sense of euphoria, very heightened sense of connection. So those positive experiences are essentially primed to be written in and over the traumatic experience and because of the high levels of Serotonin in the system and probably oxytocin as well, there's a safety that's written into the situation that allows people to lean into perhaps narratives or components of narratives that they would otherwise be holding back from. So these are powerful compounds, and I think the future of MDMA-assisted psychotherapy for a trauma in particular is holding great promise. As of now, meaning at the time of the recording of this podcast. Again, I want to reiterate that these are clinical trials are being done legally. These drugs are still illegal to possess or sell outside of clinical trials. Doing this sort of thing is punishable. But it does seem that the FDA and some of the related bodies that control these sorts of things are eyes open to this stuff. And I think it's very likely in the next few years, things like MDMA and certainly Ketamine has already

#### 01:39:25 How Do You Know If You Are Traumatized?

in widespread use within the psychiatric community. And I think we're going to be seeing a lot more of that. One thing we have not touched on yet is how do you know if you're traumatized? How do you know if you have chronic fear or a debilitating fear? You know, much of the psychiatric community focuses on how many other problems people might have. Trouble sleeping, trouble eating, trouble maintaining quality work, or schoolwork and so forth. And all of those are certainly very valid criteria and necessary criteria for determining whether or not somebody meets a clinical diagnosis or not. But there's a biological component that I think we can all assess for ourselves. And that's one of interoceptive versus exteroception balance. And that sounds confusing, but it's actually really easy to understand. We can focus our perception on the external world, events going on around us, beyond the confines of our skin or within the confines of our skin. A

focus and a perception on the external world is what's called exteroception and a focus on what's happening inside us is interoception. And we have the capacity to build mental appraisal into that, right? I can for instance, stop for a moment and assess how my stomach feels, how hungry I feel, how quick my heart is beating. Some people by the way are much better at sensing whether or not their heart is beating at a particular rate and others, not so much. Some people can actually count their heartbeats without having to take their pulse by placing pressure on their wrist or their neck. Some people can't. In other words, some people have very high interoceptive awareness and other people less so. This whole business of fear and trauma relates to taking external experiences and funneling those experiences into this thing that I'm calling a threat reflex or the fear circuitry. A recent paper published in the journal Science. So absolutely spectacular journal, science, nature and cell being the apex journals of scientific publishing. Gets at this issue of where in our mind and how do we assess whether or not what we are feeling internally is reasonable given what's going on externally. And it's a really fascinating study. I'm just going to highlight a little bit of it for you and then I'll touch on some of the relevant aspects and how that can be adopted into a practice to assess and reduce fear and anxiety. The title of this paper published just a few weeks ago in Science is, Fear balance is maintained by bodily feedback to the insular cortex in mice. We've not talked too much about the insular, also called the insular cortex. This is a brain area that my lab has worked on and other labs have worked on. It's a brain area that has within it a map of our internal interoceptive landscape. It's a map of our internal bodily sensations. And it's a really interesting structure. So the way this study was carried out is that subjects were taught or conditioned to a particular danger signal through repeated presentation of a sound with a foot shock. So there's a sound and there's a foot shock. And as you know, from our earlier discussion about Pavlovian learning, conditions stimulate, an unconditioned stimulate. Eventually the sound alone comes to evoke the fear response. And that's just classic, classical conditioning. The insular is this brain area that's associated with determining whether or not one's internal sensations, gut, heart, lungs, et cetera, are reasonable or not given the external circumstances. It can even measure or is associated with our understanding of what are called arterial baroreceptors. These are blood pressure sensors. So believe or not, when you know your pulse rate increases or you feel like you're stressed out, your arterial baroreceptors are sending a signal to your insular cortex and your insular cortex is saying, wow, like I'm really stressed out, my blood pressure is up, right? You don't

actually have to measure your blood pressure with a cuff, your insular is doing it for you. It's not getting a quantitative readout, but it's getting a qualitative readout. The main effect of inhibiting or reducing the activity of the insular was that the intensity of an outside world experience led to a range of different internal effects. In other words, for most people a mild shock would induce a mild increase in heart rate, a mild increase in blood pressure. Whereas an intense shock to the skin would lead to a big increase in heart rate and a big increase in blood pressure. Turns out the insular is important for establishing that match of intensity. And when the insular is inhibited, what ends up happening is that a mild shock can create a big increase in blood pressure. And that can be maintained such that anything that's paired with that shock like a bell, or a tone would lead to a big increase in blood pressure. You've probably seen examples of this in the real world. Maybe this is even you. Some people are very jumpy in response to just even small changes in their environment. So if somebody is working and you walk in and you say, "Hello." And they'll go, they're jumpy. They have a low threshold to a big anxiety or fear response. Other people are really calm. I recall my bulldog, unfortunately passed away, but before he passed away, if you walked in the room and he said, "Hey, Costello." He might turn his eyes in your direction. He had a very high threshold to respond. He was pretty low anxiety animal. A lot of people are like that. You'd come up behind someone you say, "Hello." And they just turn around real slow, or they might just turn around at normal speeds and say, "Hello." Whereas other people jump out of their seat. The insular seems to be involved in calibrating how big or how high amplitude a given physiological response is. So it's pairing the internal landscape with the external world. And this might seem like just a mechanistic, but non-actionable point. But what you'll see from the next study that I'm going to describe is that recalibrating the relationship between outside events and internal responses, which is the job of the insular is actually something that's under our control. And through a very simple, very short protocol, we can actually recalibrate that system so much so that we can potentially reduce the amount of fear and trauma that we experience,

01:46:16 Deliberate Brief Stress Can Erase Fears & Trauma

in response to a memory or to a real event. And the entire process can occur very quickly. So I'm really excited to tell you about this next study for a number of reasons. First of all, it's extremely recent. Second of all, it's very well grounded in our current

understanding of the mechanisms of stress, trauma and PTSD and unlearning of stress, trauma and PTSD. And third, it points to a actionable protocol that while certainly is not the only approach that I think people could or should take for fear, trauma and PTSD. Is one that I think we are going to see implemented into the clinical setting very soon if it's not happening already. Now, there's a fourth reason I'm very interested in it, which is that my lab works on stress, stress-relief and tools for managing sleep and improving focus, et cetera. And one of the hallmarks of the studies we've been doing lately is very brief five minute a day interventions of the sort that was used in this particular study. Although I should emphasize, I had nothing to do with this particular study. Now this particular study was carried out in an animal model in mice. The work in my laboratory focuses on human subjects. But the similarities of the stress system at least at the level that it was explored in this study I think have great relevance maybe even direct relevance to humans. So the title of this study is, Repeated exposure with short-term behavioral stress resolves pre-existing stress-induced depressive-like behavior in mice. Again, this study was in mice. And basically what they did is they stressed out mice, got them depressed, and you actually can do that in a mouse using a restraint protocol. And that's a long lasting restraint protocol, a 15 minutes or more. Mice Don't like it, you do it often enough. They stop working so hard in their life, in their mouse life to gain food, to gain mates. They show depressive symptoms in a number of levels. They show elevated glucocorticoids. You see the same thing in humans, Okay? Chronic stress in humans lasting weeks or more does the same exact thing. So again, a very close match here in terms of mechanism overall. And then what they did was a very counterintuitive thing. Rather than give these animals stress relief at the level of reducing their anxiety with Benzodiazepines, or giving them a nice little mouse vacation, or enriched environment. Things that have been done in a lot of previous studies. What they did is they subjected them to five minutes a day of intense stress, but only five minutes a day. And what they found was miraculously, but also very convincingly. Daily short bouts of intense stress actually undid, reversed the effects of chronic stress. And it did this at the level of glucocorticoids, of hormones, of neurotransmitters and a number of other different mechanisms. Now, I find this very exciting for a number of reasons but in particular, because my laboratory in collaboration with David Spiegel laboratory, our associate chair of psychiatry at Stanford. Been exploring how five minute a day respiration protocols can alleviate stress. And while those data are not yet published, they are at the stage where I'm comfortable talking about them. And we are seeing some very

impressive and significant effects on stress reduction not just from respiration protocols that allow people to calm themselves but also respiration protocols that bring people into a heightened state

01:49:50 Erasing Fears & Traumas In 5 Minutes Per Day

of autonomic sympathetic arousal, AKA stress. As my colleague, Dr. David Spiegel, he's an MD psychiatrist and PhD. Likes to say, "When it comes to trauma, anxiety and PTSD, and the treatment of trauma, anxiety, and PTSD, it's not just the state that you are in or that you go into. It's how you got there and whether or not you had anything to do with it." And this brings us right back to those top-down mechanisms and the narrative around what we are experiencing internally. So let's zoom out and I'll explain how this works and what to do about it. We have this brain structure called the insular. We talked about the insular a few minutes ago. The insular is calibrating how we feel internally versus what's going on externally. It's involved in setting whether or not what we are feeling is appropriate given what's happening. We have a system that can generate threat responses. And in the case of trauma, PTSD, and extreme stress, chronic stress, that system gets ramped up so that it takes very little, maybe even just a memory or maybe even an association that we're not even aware of, our location trigger something, we're not even aware of it. And we start experiencing that symptomology. How do we recalibrate the system? Well, most of the approaches that are out there involving drug treatments, typical drug treatments would involve suppressing the level of internal arousal. Just trying to bring that down. Now, some of those drug treatments work. But oftentimes they don't. And if you think about it, it's probably not surprising that they don't because by taking a drug that just lowers your anxiety overall you're creating a different sort of miscalibration of the system. So what we've been doing in human subjects is having them do either breathing protocols that calm them, and I'll explain what that is in a moment, or doing breathing protocols that increase their level of autonomic arousal and seeing how that impacts their response to stress overall not just during that particular breathing protocol. So the calming protocol that we use involves these physiological size. I've talked about these previously on the podcast and elsewhere but if you just need a reminder, if you haven't heard about it. There's a pattern of breathing that we all do in sleep. When our carbon dioxide levels in our bloodstream get too high. And we do this when we get claustrophobic, meaning we do it reflexively. And that's a



double inhale through the nose followed by a long exhale. So it's, [Andrew breathing] And yes, the inhales should be through the nose and yes, the exhales should be done through the mouth, ideally. So it's a big filling of the lungs through two breaths back to back. Inhales. [Andrew breathing] Even if you could only sneak in a little air on that second one, no talking to if you're going to do it right. And then a long exhale, which allows you to offload a lot of carbon dioxide in the exhale. And we have people doing that in real time anytime they experienced stress but the particular breathing protocol that we've been giving human subjects is for them to do the repeated... What we call cyclic sign. So double inhale, exhale, double inhale, exhale, double inhale, exhale repeatedly for five minutes. Which is actually a pretty long time to repeat that. But you can do it pretty slowly and people report and the data point to the fact that it's very calming. People feel more relaxed afterwards and that relaxation wicks out into other aspects of their life. Now, we did not look at stress and trauma in that condition. We also have another condition where people do what's called cyclic hyperventilation, which is very different and creates a very different internal state and is somewhat stressful. It's five minutes a day of stress much like the study that I just described. And involves basically doing this, what I'll do in a moment for five minutes which is hyperventilating. Which is, [Andrew breathing] But not continuously for the five minutes because many people would pass out or feel extremely uncomfortable. It involves inhale, exhale, inhale, exhale, very deep inhale through the nose, exhale through the mouth. And then every 25 or 30 breaths or so doing a full exhale and holding one's breath, lungs empty for about 25, maybe 30, maybe even 60 seconds. And then continuing until five minutes is up. Subjects report and our data indicate that people feel a heightened level of autonomic arousal. In fact, I can feel it right now even from a very brief cyclic hyperventilation about I just did. You feel a heating up, you feel a... Some people will perspire, some people get wide-eyed, some people feel agitated. That's Adrenaline being released into your system. Now I'm not suggesting everyone run out and do this. And if you have a predisposition to panic attack or anxiety attacks please don't do this because it is very stimulating and can trigger those sorts of attacks. But this five minute a day protocol of cyclic hyperventilation does lead to big increases in autonomic arousal. So it's "Stressful" but to bring us back to my colleague, David Spiegel's quote. It really was him that said it, not me. It's not just about the state that you're in. It's about the state that you're in plus how you got there and whether or not you directed entry into that state. And that point one directs their own entry into a state deliberately is really key. And I think has an

important implications for whether or not their stress relief and fear relief and trauma relief from bringing oneself into a state of increased autonomic arousal. Why? Because of the way that that fear and trauma circuitry is organized. If you recall, it's got these components of how external events can trigger an internal stress response and fear response and trauma response. But there's that top-down prefrontal component that can inhibit certain aspects of that fear and threat circuitry. Now, earlier we were talking about that prefrontal circuit being engaged through narrative, through self-directed deliberate narrative. It's the person deliberately retelling the story? Here we're talking about a deliberate reactivation of the sensations in the body. So where I think this is all going, meaning where my laboratory and the Spiegel laboratory and other laboratories out there are taking this. Is you can imagine a very brief five minutes a day, two weeks was the time that they did this for five minutes a day for two weeks. Intervention in which people, with the support of a clinician we would hope, would deliberately induce a physiological state that's very stressful, right? Not shying away from the stress response but increasing their own stress response deliberately. And maybe in conjunction with recounting the traumatic or fearful circumstance. This is far and away different than the kind of state of mind and body that would come about in a Ketamine-assisted trauma induced psychotherapy session, or a MDMA-assisted trauma psychotherapy session. Or in a purely narrative based psychotherapy session aimed at alleviating fear or trauma. The reason I like these sorts of interventions is that, A, they are very low cost or even zero cost, right? One you could imagine doing this while journaling or while recounting a particular experience. Again, they're very compact five minutes a day for two weeks is what was done in this particular mouse study. We don't know if that translates directly to the human study or not. What was interesting is that if they use the longer daily bouts of stress, like 15 minutes a day, that actually exacerbated the trauma and exacerbated the fear. So one has to be very careful. Stress and deliberate entry into stress and self stressing are very potent tools. They're very sharp blades that it does appear or it's likely can help alleviate trauma and fear. But how long to do this? Exactly what the protocol should be is still something that needs to be cultivated. I know there are going to be people out there that that nonetheless are going to want to experiment with some of this. I will say that I do not think it matters how one gets into that stressed state provided it as self-directed and that therefore could be cold shower. It could be ice bath. It could be anything that induces an acute, meaning a sudden onset of Adrenaline and is self-directed that's really the key feature here. So I'm very excited about these data both the

five minute intervention data from the animal study. The work that's ongoing in my laboratory and Dr. Spiegel's laboratory, and the work that's being done on the insular. Because I think what we're starting to see now is a picture of fear and trauma and PTSD that has the sensory component, what's happening in the world around us. This internal interoceptive component, how appropriate are the signals that are occurring in my body? I mean, let's face it. If you almost get hit by a car and your heart rate is 140 beats per second. And that lasts for a little while and you're stressed out, you don't get the best night's sleep, that's pretty normal. That means you have a healthy fear system. If that persists and you're dealing with a lot of issues a week later, six weeks later, two years later. Then it's moved into the realm of trauma and PTSD. So we need to always be taking into account the different components of the circuitry. I do think that deliberate self-directed entry into these short bouts of stress is a very promising approach. And it's one that if people are going to experiment I just again, want to caution people with anxiety or panic disorders be very cautious, probably don't do it. Ideally you would do this in conjunction with support from a clinician. But I'm also aware that there are a lot of people out there that are dealing with trauma and dealing with post-traumatic stress of various kinds.

01:59:42 Nutrition, Sleep, & Other General Support Erasing Fear & Trauma

And that they're desperate for various self directed intervention approaches. So just very briefly, I want to touch on some of the lifestyle and supplementation factors that can impact things like fear and trauma and getting over fear and trauma. To make a long story short. There are many things that we all can and should do to support our overall mental and physical health. And these are the foundational elements of quality nutrition. What that means to you? Quality sleep on a regular basis, ample sleep on a regular basis. We have an episode on how to master sleep in bed. We have four episodes that you can go to [hubermanlab.com](http://hubermanlab.com) or elsewhere and scroll down and you can find those episodes in order to get your sleep really dialed in as they say. If you're sleeping regularly and for sufficient duration, all of the systems of your fear circuitry are going to function better. Mainly because the autonomic nervous system becomes very dysregulated when we are not getting good sleep on a regular basis. Dysregulated means that out of nowhere we can have a higher propensity to have sympathetic activation or we can feel really tired and wired. That seesaw that I described earlier of

alertness and calmness of sympathetic and parasympathetic. In that analogy we can imagine that seesaw has a hinge and that hinge can neither be too tight nor too loose. If it's too tight, you can get locked into chronic activation of alertness or chronic fatigue. If it's too loose, you're bouncing all over the place and you might be [indistinct] tired and wired one moment and then really hyper alert. Sleep resets that balance and resets that hinge to the appropriate tightness, if you will. So that all these circuits and not just the circuits related to fear but also the circuits related to cognition, clear thinking to be able to spell out very clear detailed narratives, to feel like you are in control. You are deliberately bringing yourself into these protocols if that's what you intend to use. All of that functions much better when you're sleeping well and eating well. We talked about social connection. Those are all indirect supports of trauma relief and of getting over fear but they are essential, okay? I think of them sort of like the tide. When the tide is high enough a boat can leave harbor. And if the tide is not high enough, then that boat is going to be stranded on shore. And in this analogy, the boat stranded on shore is your attempt or anybody's attempt to try and work through something. Very hard to do when we're sleep deprived, very hard to do when we're not fed enough or fed the proper foods for you. And that's a highly individual thing. And social connection as we talked about earlier, creates a general sense of support for the ability to move through things. But also chemical support at the level

02:02:30 Supplements for Anxiety, Fear: Saffron, Inositol, Kava

of suppressing Tachykinin, okay? So those foundational elements are absolutely key, but they are indirect. I just want to briefly mention a few of the things that some people find great benefit from in the supplementation realm as it relates to anxiety, stress, fear and PTSD. But I want to point out that again, these are somewhat indirect in their support and most of them focus on reducing anxiety overall. The two that I want to focus on are two that I've never talked about on this podcast before because I've done podcasts before on stress and managing stress in the kind of shorter term. So we've talked about Ashwagandha in a previous podcast, check out the podcast on stress, if you're interested in how that might be relevant as well as other tools. But the two are interesting ones. The first one is Saffron of all things. But there are 12 studies, believe it or not. That orally ingested Saffron at 30 milligrams seems to be a reliable dose for reducing anxiety on the standard inventories. The Hamilton Anxiety Rating Scale, for

those of you that want to know. And these are significant effects. And these were carried out in both male and female subjects. Here I'm only referring to human studies. Several of these were double-blind studies. There's a meta analysis of the positive effects. Meaning anxiolytic affects, anxiety reducing effects that is of things like Saffron. Definitely have to check with your doctor and make sure it's right for you. But they're fairly impressive effects when you really think about it given that these are legal over the counter substances. Again, check with a doctor. The other one is a Inositol. Inositol has been shown to create a very notable decrease in anxiety symptoms. It's a fairly high dose that's used but believe it or not, the potency of this effect is on par with many of the prescription antidepressants. That's pretty impressive. These studies again are double-blind studies that all showed decreases in anxiety. These were done in males and females. The age range is very broad, which is great 18 all the way up to 64 across the studies that I at. One of the more important things is that the dosages are quite high 18 grams of Inositol taken for a full month. And it does take some time for these symptoms of anxiety to be improved. The low dose range was about 12 grams of Inositol, so as high as 18 as low as 12 grams. But then again, pretty impressive results considering that these are over the counter supplement compounds. There's even some evidence, I should just mention that the Inositol is also used for things like obsessive-compulsive disorder. We will do a full episode on OCD in the future, you can count on that. But in the meantime, Inositol does seem to have some positive effects on anxiety. And therefore it might provide a kind of supportive indirect effect for people that are trying to work through trauma and PTSD. Now, the question is when would you take it? Well, by the logic of what we spelled out today, you probably would not want to take it during a session or prior to a session where you were trying to amplify the intensity of an experience and the recounting of an experience in efforts to eventually extinguish that experience, right? Because if you put a drug or a compound of any kind prescription drug or supplement or any kind into your system you are essentially short-circuiting the extinguishing effect, right? So you could imagine doing this outside of that session as a way to kind of bring your system back to baseline, perhaps. So if you're going to use these sorts of things you want to think about them logically. And this also really points to the fact that many of the things that people are doing out there to self-medicate over use of alcohol or other substances to try and calm themselves because they have fear, anxiety and PTSD are actually driving that fear, anxiety and PTSD deeper into their system. Or at least is not allowing it to relieve itself through any attempts to recount or

replay and using these top-down narrative circuits or other approaches. And the last compound I want to mention is a particularly interesting one, because it's neither an anxiolytic, nor is it something that increases overall levels of stress and alertness. But it has some kind of MDMA ish light contour to it. It does not produce as far as we know, the same mental effects or physical effects as MDMA by any stretch but that's... The substance I'm referring to rather is Kava. Kava has been shown in eight studies to have a very potent effect on reducing anxiety. But what's interesting about kava is that kava functions by increasing GABA, this inhibitory neurotransmitter in the brain. Remember GABA is the inhibitory neurotransmitter that is used, that's employed by the very neurons in the prefrontal cortex that serve to inhibit the threat reflex. So it seems to increase GABA, but it also increases Dopamine. And that's a somewhat unusual compound. I'm not aware of many compounds that simultaneously increase GABA and increase Dopamine. And as you recall, that threat reflex has outputs that tap into the Dopamine system. Now that's a big leap to go from a compound that increases GABA and Dopamine and look at a circuit spelled out on paper in front of us and say, "Oh, there's GABA and Dopamine in this circuit and therefore this is a good compound to take." But the effects of Kava in human studies are pretty interesting as it relates to anxiety, stress, PTSD and fear. I'm not going to summarize all of these because there are eight studies that I'm aware of. But I'll just mention, again, these are double blind studies. So the trial design is solid. The age ranges are anywhere from 18 to 64 which is a nice broad age range. The number of subjects is quite high both men and women. No signs of hepatotoxic signal so meaning liver toxicity, although of course, check with your doctor. But what was interesting is that after a period of about three weeks of treatment with anywhere from 150 milligrams of what are called active kava lactones, okay? So there are dosages that relate to that kava. So a hundred milligrams of extract of Kava is a kind of a reasonable typical dose in these studies. But that spells out to a certain amount of Kava lactone. So you have to kind of boil down to what is the appropriate dosage. And it turns out it's extremely broad. You'll see evidence of 50 milligrams, you'll see evidence of 300 milligrams, is kind of all over the place. But each of these studies alone and together point to the fact that Kava does seem to produce a very potent anxiolytic and general kind of improvement in depressive symptoms and reduction in generalized anxiety across the board. So it's an interesting compound. I've never actually tried any of the compounds I just mentioned. Kava, Saffron or Inositol. So I can't report on them personally. I just know that a number of listeners of this podcast are interested in

supplements and legal over the counter approaches to their biology and psychology. And so that's why I mentioned them. Those were the three for which I found the most convincing evidence and the largest bulk of evidence. So if you're interested in exploring those

02:10:00 Synthesis

proceed with caution but they do seem quite interesting. So today we've reviewed a large amount of information about the biology of pathways in the brain and body that underlie the fear response. And they give rise to chronic fear and in some cases to trauma and PTSD. We also touched on a large variety of approaches to dealing with fear, trauma and PTSD that currently exist in the clinical landscape out there. I also touch on some of the emerging themes, for instance, this short five minute a day deliberate self-directed stress of any kind through respiration or other approaches of increasing Adrenaline. As an approach that might be viable, I should emphasize might, be viable for enhancing the speed or the potency of treatments to reduce fear or eliminate trauma. Most important I believe is to understand and really think about the logical structure of the circuits that underlie fear and PTSD. Because in doing that each of us, all of us, can think about what sorts of treatments and approaches make the most sense for them. I also hope that it will help people lean into certain practices involving re-exposure, provided that's done in a supportive environment. Re-exposure to a given traumatic event in an attempt to extinguish that. Obviously you want to do that safely, meaning psychologically safely and physically safely. There are great practitioners out there that can help you with that work. There are also a number of people out there I am certain that are carrying certain traumas or certain fears that they would like to alleviate that are not in the extreme clinical realm. And that's the reason why I touched on a number of things

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including some self-directed practices that might be useful and reasonable for them to explore. I realize we covered a lot of information today. If you're enjoying and are learning from this podcast and you're not traumatized by the amount of information covered, please subscribe to our YouTube channel. That's a terrific zero cost way to

support us. In addition, please subscribe to the podcast on apple and Spotify. And on apple, you have the opportunity to leave us up to a five star review. If you have suggestions of guests you'd like us to host on the podcast or you have topics that you'd like us to cover. Please put that in the comment section on YouTube. Also, please check out the sponsors that we mentioned at the beginning of this episode. That's a terrific way to support us. We also have a Patreon, it's [patreon.com/andrewhuberman](https://patreon.com/andrewhuberman). And there you can support this podcast at any level that you like. On this podcast episode and in many previous podcast episodes, I describe supplements. While supplements aren't necessary and perhaps aren't right for everybody many people derive great benefit from supplements. It is important however, that if you're going to use supplements that they be a very high quality and that you can trust that the amounts of supplement listed on the supplement bottle are actually what's contained in the bottle. That's a serious issue with a lot of supplements out there. For that reason, we partnered with Thorne, T-H-O-R-E. Because Thorne has the highest levels of stringency with respect to the quality of their supplements and the amounts of the supplements listed on the bottle are actually what's are contained in the bottle. They've partnered with all the major sports teams as well as the Mayo Clinic. So we have a very high degree of trust with Thorne products. If you want to see the Thorne products that I take you can go to Thorne, T-H-O-R-N-E, [.com/u/huberman](https://thorne.com/u/huberman). And there you can see the supplements that I take. You can get 20% off any of those supplements. And if you navigate deeper into the Thorne site, through that portal, [thorne.com/u/huberman](https://thorne.com/u/huberman), you can also get 20% off any of the other supplements that Thorne makes. If you're not already following Huberman Lab on Twitter and Instagram, there I do short neuroscience tutorials. I offer a lot of tools oftentimes that don't overlap with the content of the podcast. And last but not least, thank you for your interest in science. [bright music]