

When Instinct Turns Anxious Transcript

Earlier this week, I went to Starbucks to do homework and ordered my usual: a decaf coffee, no room for cream. I got my drink and sat down with my computer, drinking it over the course of twenty minutes. About forty-five minutes later, I started getting jitters, and then my head started to feel light and woozy. Of course, the first thing that came to my mind was that I could be dying- and as soon as I had the thought, my heart began to race, and I could barely get a full breath. Once I felt my heart speed up, my thoughts spiraled out of control; I started wondering if I should call 911, or alert someone in the store that I was having some sort of adolescent heart attack. By the time I realized that they accidentally gave me caffeinated coffee, I had effectively sent myself into one of the few panic attacks of my life, all over a case of caffeine-induced dizziness.

I'm lucky that I rarely get anxiety attacks, but when I do, they stick with me for hours. Once the panic button gets hit in my mind, it's nearly impossible to calm down. I have to spend a couple of hours distracting myself with television in order to set things straight again- doing my homework is out of the question. I certainly don't have panic attacks with enough frequency to be diagnosed with a panic disorder, which is a subset of anxiety, but this week made me incredibly sympathetic to those who do struggle with recurring panic episodes and generalized anxiety disorders. It also made me very curious about how anxiety and panic appear in the brain, and what makes them so physical. Today, I'm going to explore human anxiety, from its origins in the brain to its effects on the body. How many kinds of anxiety are there, and what do they look like? What's the evolutionary basis for anxiety? Why do some people develop anxiety but not others, and why does the incidence of anxiety increase so much in the teenage years?

Before I started researching for this episode, I didn't really understand what anxiety was. I knew it involved things like panic attacks, worrying, phobias, and stress, but my picture of the disorder was broad and shaky. Once I began to research, I realized that anxiety is difficult to define because it is, by definition, a broad range of conditions. The DSM-5, the diagnostic manual for mental illnesses, actually lists 4 different disorders under the banner of Anxiety Disorders: panic disorder, phobias, generalized anxiety disorder, and social anxiety disorder. These disorders are united by a common symptom: excessive and persistent stress and worry that is disproportional to the situation at hand. Anxiety disorders aren't just stress and fear about public speaking or the SAT; they include full-blown, uncontrollable bouts of worry and panic around events that most of us can manage fine. Anxiety is also inexplicable: sufferers can't typically explain why they feel and react the way they do, owing to the very neurological basis of anxiety that we will dig into later. Panic disorder refers to people who suffer from persistent panic attacks like the one I experienced- but unlike me, people with panic disorder have consistent attacks that can interrupt daily and social functioning. Phobias, as the name implies, are anxiety disorders related to

specific situations or objects, such as water, heights, spiders, and public spaces, which are called arachnophobia, hydrophobia, acrophobia, and agoraphobia, respectively. There's even a phobia of long words, which was cruelly named hippopotomonstrosesquipedaliophobia. Generalized anxiety disorder, which is what many of us think of as just anxiety, is a more underlying feeling of worry, restlessness, and chronic stress that leads to exhaustion and poor functioning. Finally, social anxiety disorder is specific to anxious feelings surrounding social interactions, which often prevents people from forming relationships or attending social events. Someone with panic disorder might not have general and chronic feelings of anxiety, and someone with social anxiety might never have panic attacks- each disorder has the overlapping quality of worry, but it can manifest in many different ways. If you think you might have an anxiety disorder, it's useful to think of what situations make you anxious and worried- it might turn out that you have a phobia or social anxiety disorder, not a generalized anxiety disorder, even if you feel worried much of the time. All in all, nearly one-third of people will develop an anxiety disorder at some point in their lifetime- and as we will discuss later, the majority of these people will develop it during adolescence.

Anyone who knows someone with anxiety or struggles with the disorder knows that it can be debilitating. The stress and worry that comes with an anxiety disorder can make it nearly impossible to function daily. Nonetheless, the biological mechanisms that trigger anxiety in the brain are actually important- even vital. In fact, the neurological system that causes anxiety is a critical system in every human and every species of animal. Fear and worry are primarily regulated by two brain systems: the amygdala and the HPA axis. The amygdala is responsible for emotion in the brain, especially the fight-or-flight response that is intrinsic in all mammal species in response to environmental threats. The amygdala also handles fear conditioning, which is when a certain situation becomes mentally associated with fear and harm. Fear conditioning was discovered in a series of experiments called the Little Albert experiments, in which infants were conditioned to fear domestic rats. At first, the infants were given rats to play with, without any aversive stimulus. However, the experimenters soon started playing a very loud noise when the rat was presented, causing the babies to cry. After a few repetitions of this pattern, rat and loud noise, the infants' amygdala began to associate the rats with the aversive loud noise. When the rats were presented to the infants without any sound, the infants still cried because the rat now triggered the feeling of fear of the loud noise.

The amygdala is our primary fear center, and in the pre-societal world, it was the system that helped us stay safe by avoiding dangers such as predatory animals and toxic foods. It conditions us to fear things, either by accidental near-death exposure, observation of others, and even innate fear responses to things like heights and loud sounds. Without the amygdala, we are helpless in the face of danger. One of the most incredible case studies of amygdala damage is the case of a woman named SM. SM had a very rare disease in which her amygdala became calcified,

meaning that her amygdala was essentially dead. If you asked SM if she liked snakes and spiders, two things that humans are conditioned to fear in the first years of life. She claimed that she hated snakes and spiders, and avoided them. However, when researchers brought SM to a pet store, she asked over and over to hold the snakes and spiders, even after being told that some species were poisonous and would bite her. When she tried to pick up a tarantula, the researchers had to restrain her to protect her from being bitten. When asked why she wanted to touch the animals, SM claimed that she was overcome with curiosity, even though she hated the animals. Without the amygdala, she could not perceive fear or exercise restraint, even when told that situations were dangerous. Evidently, we all need fully functioning amygdalas to keep ourselves safe, and have been relying on the amygdala to trigger fear for millions of years.

The other brain system involved in anxiety is the HPA axis, or hypothalamic-pituitary-adrenal axis, which is often activated by the amygdala. This system consists of the hypothalamus, pituitary gland, and adrenal glands, which actually sit right above the kidneys. The HPA axis is responsible for the feeling of stress, which is defined as a threat to homeostasis. Basically, we feel stress whenever we think that our mental or physical equilibrium is being threatened, whether by the environment, pathogens, or even thoughts. Our bodies want to be in a state of internal balance, and when this balance gets thrown off, physically or mentally, our bodies react with an immediate stress response to try to right the damage. The HPA axis performs a chain reaction to release the hormones for the stress response, most importantly cortisol. You've probably heard of cortisol, the quintessential stress hormone, but, like me, you probably haven't learned a whole lot about how cortisol affects the body.

Cortisol has been demonized for causing anxiety and worry in the human mind, but it's actually one of, if not the, most important hormone in the human body. Cortisol's job is to bring the human body back to homeostasis, or equilibrium, when the body feels threatened. In order to save us from a wide range of threats, cortisol creates a wide range of responses in the body. Cortisol raises our heart rate and blood pressure, giving us short-term access to more oxygen flow in the blood to activate our muscles. Another of cortisol's jobs is to promote gluconeogenesis, or the conversion of proteins and fats into glucose. Basically, the human body needs a supply of glucose, a carbohydrate, for energy; when our blood sugar gets low, cortisol signals our body to turn fat and protein into glucose through gluconeogenesis, picking our blood sugar level back up and giving us the energy we need to function. This is how cortisol helps to restore homeostasis during a period of fasting. Cortisol also helps us turn a food surplus into stored energy, called glycogen. When we are in a period of energy abundance, cortisol tells the liver to start converting excess calories of food into storage for later, decreasing our blood sugar and returning us to homeostasis. Cortisol also helps regulate the pH inside the body, by managing the amount of salt inside and outside the cells. This next fact stunned me: cortisol actually suppresses the human immune system by preventing inflammation and blocking a

certain groups of white blood cells, called T-cells, from fighting infection. This might seem counterintuitive, but it's actually a very intelligent system. When our bodies are really threatened, by something like a predator or intense starvation, we need all the energy we can get to run away or keep our hearts beating until we find more food. Because the immune system uses such a huge amount of energy, high cortisol levels turn the immune system off so that we have enough energy to escape from the source of stress. Finally, cortisol has a very interesting role in learning and memory. When we are in a life-or-death situation, cortisol temporarily inhibits the prefrontal cortex and old memory retrieval, instead focusing us on ingrained habits and creating new memories of the threat. When in a fight-or-flight situation, we don't have time to think our choices through, and cortisol insures that we rely on instincts to get us through stressful periods and help us remember them later.

In the short term, cortisol is great- it keeps us safe from temporary stressors and automatically amplifies and suppresses the physiological responses that keep us out of harm's way. However, cortisol is kind of like an x-ray machine; x-ray technology is incredibly useful for helping us diagnose and treat injuries and diseases, but too much exposure to x-rays can cause cancer and a host of other problems. Likewise, cortisol is necessary in quick spurts when we are in a threatening situation, but chronic and constant elevated levels of cortisol, caused by worry and mental stress, can wreak havoc on the body. High cortisol levels can cause hypertension, heart disease, obesity, diabetes, and makes our immune systems weaker and our bodies more prone to getting sick. Cortisol disrupts prefrontal cortex functioning, that critical region for higher-level thinking, and generally puts the brain on edge in a way that's harmful day in and day out. Chronic stress, as we will soon learn, can also make us miserable.

So, now that we understand how the amygdala and HPA axis deal with fear and stress, let's talk about what goes wrong in these systems in people with anxiety. We know that both systems are critical for survival, but when they're overactivated can cause major problems. It turns out that all the anxiety disorders I mentioned- panic disorder, specific phobias, generalized anxiety disorder, and social anxiety disorder- all show brain irregularities in the amygdala or HPA axis.

According to a paper in the *Journal of Neuroscience* by Justin Kim and Paul Whalen, it appears that people with more anxious temperaments had a weaker neural pathway between the amygdala and a part of the prefrontal cortex that deals with emotion processing and regulation. This suggests that people with anxious personalities are lacking the pathway between the rational brain and fear response in the amygdala, making it difficult to regulate feelings of panic and worry. Additionally, people with fear-related anxiety disorders show greater amygdala activation than controls in an MRI scan when exposed to threatening stimuli, like loud noises and finger buzzes. People with fear disorders, such as panic disorder, social anxiety, and phobias all show increased sensitivity and activation in the amygdala, meaning that their fear response is

unusually strong compared to healthy controls. In people with generalized anxiety, it is also predicted that the amygdala is hyper vigilant and sensitive to any perceived threats. Fear is an incredibly important human response to threat, but when fear is out of proportion to the situation at hand, that is when we suffer from it in the form of anxiety disorders.

Cortisol levels also play a role in anxiety, in both fear-based disorders and stress and worry-based disorders, like generalized anxiety disorder. As we discussed before, cortisol is important for acute feelings of fear and stress, but chronic high levels of cortisol take a toll on the body and brain through constant, medium-grade stress and worry. In the normal, non-anxious brain, cortisol levels are returned to a low baseline level by a negative feedback loop. A negative feedback loop is essentially a chain reaction in which the presence of some chemical triggers the body to stop producing more of it. When the body senses that it has high levels of cortisol but that the threat has passed, it stops producing more cortisol until levels go back to baseline. However, in people with anxiety, it's often the case that cortisol levels never get back to that low baseline amount of a relaxed state. Instead, their bodies and brains are always poised to respond to stress and threat. People with panic disorder have been shown to have higher baseline cortisol levels than normal subjects, and when perceiving a threat, people with panic disorder have bigger cortisol spikes than controls. People with panic disorders are constantly on alert of fear triggers, causing their average stress levels to be higher at all times. A collaborative experiment in the Netherlands looked at the salivary cortisol levels of nearly 1500 individuals with and without different kinds of anxiety disorders. They found significantly higher cortisol levels in those with panic disorders, specific phobias, and in individuals with generalized anxiety and depression, which overlap nearly two-thirds of the time. Even people who had already recovered from anxiety disorders showed higher waking cortisol levels, indicating that people with anxiety aren't just reacting more strongly to stress, but have higher inherent levels of biological stress than others. This is likely genetic, seeing as about half of people with anxiety disorders have a close family member with an anxiety disorder as well.

So, now that we understand the biological basis for anxiety, let's put that knowledge into context. How does anxiety relate to teenagers, and what can we do about it?

It turns out that anxiety, especially social anxiety, panic disorders, and generalized anxiety, tend to be diagnosed during adolescence. Anxiety disorders typically appear right around the time of puberty- the median age of onset in the US is 11 years, according to a survey conducted by the Harvard Medical School. Half of all people who develop anxiety do so by age 14, and three-quarters develop it by age 24. About 8 percent of adolescents have diagnosed anxiety disorders, a number that has been climbing steadily since the 1950s. Surprisingly, anxiety is relatively even between the sexes in childhood, but in adolescence, twice as many girls develop anxiety disorders as boys. Evidently, something is going on just around puberty and in the years

following puberty that amps up our risk of developing anxiety disorders, especially among adolescent girls. Something is going on as our brains enter adolescence that makes us especially susceptible to anxiety disorders, and which makes girls at even higher risk. Why do we develop anxiety disorders at our age, and what makes some people- girls in particular- more susceptible than others? Why are anxiety disorders on the rise? What can we do to protect ourselves and relieve suffering?

Unsurprisingly, stress and fear do look different in the adolescent brain than the adult brain. An article from the *New York Academy of Sciences* discusses research done on juvenile and adult rats and fear response. Both groups of rats were given a random foot shock, and their corticosterone levels were measured (corticosterone is the rat equivalent to cortisol). For the juvenile rats, it took an extra 45 minutes for corticosterone levels to drop to baseline after the shock than for the adults. Unfortunately, because neuroscience is still a very young field, we have few other studies showing exactly how stress interacts with adolescent brain structures as opposed to adult ones. Researchers theorize that the adolescent amygdala, the fear center, may be more active in response to threat than the adult system. They also postulate that because our prefrontal cortex is not yet fully developed, we may have a harder time regulating stress and fear than adults do. When we get triggered to worry, our higher-level thinking part of the brain is probably not as equipped to rationalize and calm down than it would be at age 25 and beyond.

Luckily, we have a much better grasp of the factors influencing who is more likely to develop anxiety during adolescence and why. Of all the anxiety disorders, the most characteristic of adolescence is social anxiety disorder- an intense fear of social situations and avoidance of interaction. Social anxiety isn't just shyness; it's an inability to enter social situations without experiencing extreme and physical anxiety, which can prevent people from making friends and even attending school. If you've listened to the podcast episode "Like Everybody Else," you'll remember that social relationships and behavior are also very unique in adolescence. During the teenage years, our brains begin to crave social relationships with peers at record-high levels, which drops off as we age. In fact, we teenagers respond more emotionally in the limbic system even to pictures of faces flashed on a computer screen. During the teenage years, we are hyper-social animals, and this makes us hyper-aware of our social standings and sense of belonging. Unfortunately, this also comes with a dark side: if we are rejected and isolated during adolescence, we are especially likely to develop social anxiety, and go on to fear social situations for the rest of our lives. This is especially true of females. Adolescent girls are uniquely susceptible to feeling pain of social rejection, as demonstrated by computer programs that make people feel excluded during brain scans. When adolescent girls feel socially isolated, their emotional centers light up more powerfully than any other subset of the population, and report feeling more depressed and anxious after perceived social rejection.

In order to find out just how important social life is to anxiety, especially social anxiety, Annette La Greca and Hannah Harrison of the University of Miami conducted a massive study on social life and anxiety in teenagers. La Greca and Harrison collected surveys from 421 teenagers exploring four big categories: peer crowd identification, peer victimization, best friend relationships, and romantic relationships. Peer crowd identification asked kids how strongly they identified with a social group, and if this group was popular, like an athlete group, or less popular, like an alternative group. Victimization asks teens how often they've experienced things like bullying, exclusion, and having rumors spread about them by their peers. Best friendships and romantic relationships are basically what they sound like- the researchers wanted to know what role individual, intimate relationships played in social anxiety. They found that social anxiety was highest among teenagers who felt like they had no social group, who were victimized by peers, and who either reported having no close friendships or negative friendships. Additionally, having a romantic partner decreased the risk of having social anxiety. What was most interesting in their research was that both popular and unpopular kids were equally low in social anxiety, as long as they felt like they really belonged to a certain group. It wasn't the unpopular kids who had the most anxiety, but those who had no group to call home, popular or otherwise. It appears that, at our age, the most critical factor in minimizing social anxiety is having relationships with people. This might seem obvious, but I used to think that it mattered more to belong to a popular group than an unpopular one for social safety. It turns out that it doesn't. As long as we have friends that make us happy and feel included, that's all that matters for our mental health.

Finally, we cannot forget about the unique pressures that we experience as teens. The teenage years are the time when we become more autonomous, independent, and academically pressured. We are gaining independence from our parents right at the time when school, sports, and activities become high-stakes and stressful. This has never been as true as it is now, with college admissions rates plummeting as higher education becomes increasingly cut-throat. Along with the increase in competitiveness in high school, counselors across the country have noted a surge of panic disorders and generalized anxiety among some of their best and brightest students. While only about 10 percent of adolescents have diagnosed anxiety, 80 percent of students at a high-performing high school reported being somewhat or extremely stressed on a daily basis, and the majority tended towards the extreme end, according to a study by NYU. Additionally, the rates of panic attacks and anxiety-related illnesses has been noted by nurses and counselors across the country. In fact, in the last four years, the head of the National Association of School Nurses has begun to give talks about anxiety at their yearly nationwide conference, to help nurses deal with the new wave of student anxiety. It's no surprise that students are struggling to cope with today's amount of stress; there's a nearly constant stream of cortisol circulating in our veins, and for those of us with genetic and biological predispositions for anxiety, the academic world is the perfect trigger for anxious tendencies to blossom.

We live in a world full of anxiety, and unfortunately, its prevalence is on the steady rise among teenagers. Our stress systems are meant to respond to acute threats, like tigers and famine, not chronic worries like social isolation and GPAs. All of us struggle with some level of cortisol overload, and some of us have especially sensitive amygdalas that put our stress over the edge and into full-blown anxiety disorders. The picture is pretty grim, but certainly not hopeless. Remember, our brains are plastic, and especially so in adolescence. This not only means that they are susceptible to outside influence, but that we can also change our brain structure and chemistry through our own actions, behaviors, and thoughts. This holds absolutely true of anxiety disorders.

Though medication, typically antidepressants, are valuable treatment options for people with anxiety, anxiety disorders respond well to therapies like Cognitive Behavioral Therapy, or CBT. CBT is a relatively new form of psychotherapy, which focuses on our current thoughts and behaviors rather than digging into childhood traumas, Freud style. CBT has been proven to help with disorders from anorexia nervosa to PTSD, and its effects show up physically in the brain. A research study from the University of Montreal illustrates this concept well. The researchers took a group of people with a spider phobia, or arachnophobia, and scanned their brains while looking at pictures of spiders before and after CBT. Before CBT, the patients showed activation in many brain regions related to their fear. However, after CBT, the patients showed brain activity that was similar to controls. By targeting and managing fearful thoughts, CBT teaches us how to rewire our brain responses to perceived threats. If you're interested in CBT, visit the show notes for this episode for more information about CBT and finding a therapist in your area.

We have the power to overcome anxiety through deliberate practice and by challenging the thoughts and feelings that arise when we feel worry and stress. Though the brain is a physical organ, that doesn't mean we can't control how it responds and behaves. Just like we can learn motor skills like hitting a golf ball or doing a pirouette, our brains can be trained to respond in new and healthier ways to the world. With help from a therapist, family, and possible medications, we can change our brains for the better. For those of us who struggle with anxiety, the most important thing is not to give up, and to continue confronting situations that make us anxious and worried. The brain cannot change without exposure to the things that make it uncomfortable. With the help of a support network, you can learn to retrain your brain when it is exposed to your anxiety triggers. Anxiety is a physical, neurobiological problem, not a character fault. With treatment and perseverance, you can and will put the worst of your anxiety behind you.

After having my little caffeine-induced panic attack, I found myself revisiting meditation and spiritual practices that I hadn't thought about in years, and for that I'm grateful. Anxiety is not

fun, and it's not ideal, but it does have the power to give us a lot of perspective about life, happiness, peace, and meaning. If you have anxiety, try not to regret the stress and worry, but to welcome in a period of healing and transformation that can only happen when we hit bumps in the road.