Neural Pathways of Anxiety

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What is Anxiety?

Anxiety is a generalized term that can be used to describe feelings of worry or uneasiness that almost all people deal with intermittently in their lives. Anxiety is a stress response to a potentially dangerous stimulus that causes an accelerated heartbeat and quickened breathing. While being stressed is uncomfortable, it's not necessarily unhealthy if it does not disrupt daily life. An issue arises in those who face prolonged or recurring stress. This type of chronic stress has often been shown to predispose individuals to anxiety disorders (Sanders, 2016), including various panic disorders, phobias, and social anxiety. Another type of anxiety disorder, generalized anxiety disorder (GAD), is characterized by constant and excessive uneasiness about routine life circumstances. GAD often leads to symptoms such as difficulty sleeping or unsatisfying sleep, which can then lead to issues like irritability, muscle tension, general fatigue, and trouble concentrating (The National Institute of Mental Health, 2018). There is no single cause for GAD, but there are many associated risk factors including hormone imbalance, early-life trauma, exposure to repetitive, stressful stimuli, and a relatively slight genetic influence.

Key Brain Areas

Anatomically, GAD involves abnormalities in the functioning of the limbic system, which is a phylogenetically ancient region of the brain that functions as a control center for emotions, mood, and drives (Martin, 2009). More specifically, the hippocampus and the amygdala are the two primary structures in the limbic system that play a role in GAD. The amygdala is an almond-shaped structure that transfers nerve impulses into hormonal signals, triggering emotional responses. It plays an important role in alerting the brain about potential threats. This is noteworthy because anxiety disorders, GAD in particular, are a result of prolonged overactivity of the amygdala, which causes the brain to be in a constant state of fear or anxiety (Patriquin, 2017). Obviously, a constant state of fear would make it difficult to relax for those facing GAD, ultimately resulting in the aforementioned symptoms of anxiety disorders such as fatigue and loss of sleep that eventually contribute to a multitude of additional symptoms. The other key brain region involved in GAD, the hippocampus, is responsible for encoding threatening events into memory and relaying information to the amygdala during the process of retrieval for a rapid response to threatening stimuli ("The Effects of Stress & Anxiety on the Brain", 2018).

Phylogeny

It is important to note the phylogeny of the structures associated with GAD. Phylogeny refers to the evolutionary development of a particular feature of an organism. As mentioned before, the limbic cortex is ancient. This means that the limbic system was preserved through evolutionary history, and because of this, it is relatively autonomous, involving little voluntary action. Anxiety disorders target the structures of the limbic system rather than higher cognitive centers of the frontal lobe such as the prefrontal cortex (responsible for decision making) or the orbitofrontal cortex (controls impulses). This means that anxiety disorders are not based on irrational thoughts but on threat assessment and an uncontrollable natural response to what part of the brain perceives to be a real threat, despite higher-order brain areas providing input that there is, in fact, no immediate danger (Martin, 2009). This helps to explain the difficulty involved in controlling nervous feelings that come with anxiety disorders, as the problem is not solved by simply being cognizant of the fact that there is no real threat. Instead, victims should take actions that will directly affect the sources of the problem, such as using medication to address neurochemical and hormonal imbalances.

Neurotransmitters and Endocrine System

Anti-anxiety medication is useful in many cases as a way to counter the neurochemical imbalances associated with GAD. There are a few ways in which neurotransmitter release can result in the overactivity of the limbic system. The first way is through decreased inhibitory signaling by the major mammalian inhibitory neurotransmitter, gamma-Aminobutyric acid, also known as GABA. This would result in a greater amount of uninhibited nerve firings in the limbic cortex which would consequently lead to overactivity (Martin, 2009). The second possibility is an excess of the excitatory neurotransmitter glutamate, which would result similarly with a greater amount of nerve firings and therefore overactivity of the amygdala.

It is also possible that some combination of these two could be at play in contributing to overactivity. Other chemical messengers that play a role in anxiety disorders are cortisol and norepinephrine, in this case acting as hormones. These two hormones are normally released in response to a threat for a limited period of time. They contribute to the accelerated heartbeat and quickened breathing that normally allow for faster movement and better perception when facing danger. ("The Effects of Stress & Anxiety on the Brain", 2018). However, the brains of those with GAD constantly perceive threatening stimuli, causing the extended production of these hormones that are only intended for short periods of time. There are trade-offs for the increased awareness these hormones provide over time. High cortisol levels contribute to weight gain, muscle weakness, and suppressed immunity as the body focuses on escaping momentary danger. (The National Institute of Mental Health, 2018). Another symptom of excess levels of both cortisol and norepinephrine is difficulty sleeping, which only exacerbates the stress response to real threats, perpetuating the release of these hormones.

Physical Effects and Ramifications

The short-term effects caused by GAD are apparent, as hormone imbalances and overactivity of nerves in the limbic system lead to sleep difficulties, lack of focus, weight-gain, and other symptoms (Patriquin, 2017). However, these are merely side effects of what can be destructive functional abnormalities in and of themselves. It seems as though the constant activity of the limbic system could have some effect on the utility of the nerves themselves. In short, there are more direct and lasting effects caused by GAD on the brain itself that should be

noted in order to view the full scope of damage caused by the disorder. One such effect is on the amygdala. As discussed, GAD is linked to overactivity in the nerves of the limbic system, in particular those of the amygdala, as it is the system primarily responsible for perceiving potential danger. It has been found that the normally almond-shaped amygdala gets larger in pediatric patients with GAD. This is likely to correspond with hypertrophy seen in the amygdala of lab animals, which correlates with expectation considering the abnormal activity of the amygdala in patients with GAD (Martin, 2009). Different, yet also alarming, results have been observed in the form of hippocampal damage caused by limbic hyperactivity.

While research is still in progress on the effects of GAD on neurodegeneration within the limbic system, new research is showing that prolonged stress and anxiety can potentially cause structural degeneration of hippocampal nerves ("The Effects of Stress & Anxiety on the Brain", 2018). This is especially concerning because the volume of the hippocampus and growth of new cells is directly related to stress resiliency in anxiety and mood disorders, suggesting that if there is structural damage to the hippocampus caused by GAD, it is making the brain gradually less resilient to the stress as it persists (Martin, 2009). Another recent observation from fMRI scans of GAD patients is the ratio of grey to white matter in the brain. Grey matter is the tissue of the central nervous system that contains the cell bodies, dendrites, and axon terminals of neurons, while white matter is made up of the connecting neuron axons (Sanders, 2016). Grey matter is found mostly in regions of the brain responsible for sensory perception, memory, and emotion, which is why it is possibly related to the hyperactivity of the amygdala, where an abnormally high ratio of grey to white matter has been found in studies of patients with GAD. Conversely, possibly related to neurodegeneration associated with GAD, a greater ratio of white matter to grey matter has been found in hippocampal regions of patients with the disorder (Hilbert, 2015).

Relevance

As time goes on and the human brain becomes better understood, more information is uncovered regarding the side effects and neurological damage caused by GAD. The good news is that neurodegeneration is not totally irreversible. The plasticity of the brain will allow for regeneration to some degree, but the earlier the damage can be reversed, the better ("The Effects of Stress & Anxiety on the Brain", 2018). However, with more potential damages being uncovered, it is becoming apparent that relaxation and avoiding the risk factors of anxiety disorders should be emphasized in daily life. This is especially pertinent to those with stressful jobs and students that face difficult assignments, exams, and other stressors on a regular basis. The positive news for people that lead stressful lives is that there are ways to avoid GAD, and the genetic contribution in GAD is not as substantial as other anxiety disorders, so taking measures to stay away from avoidable stressful situations can be quite effective (Martin, 2009). However, many people, especially students, still deal with GAD. Many face GAD along with MDD (major depressive disorder), with which it has high comorbidity that ranges up to 98% in treatment studies (Patriquin, 2017). It is important to not only know how to avoid GAD, but to also be aware of the ways in which it can manifest itself in daily life, the damage it can cause, and its relationship to other mental illnesses like MDD.

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