The Biology of Anxiety

By Kathleen Darling

In the United States, the most prevalent group of mental health illnesses are anxiety disorders, with 18% of adults self reporting being affected.[1] It comes in many forms that people are likely aware of, like social anxiety or other extreme phobias, as well as some people my not associate with the simple "anxiety" label, like post traumatic stress disorder. With such a saturation of these disorders in the population, it is beneficial to understand how they affect people more readily, as well as how these diseases can be combated in a healthy and productive way for the people afflicted.

It is generally accepted that anxiety stems from the innate fear response, present not just in humans, but in all animals. Often categorized as the flight half of the "fight or flight" response, it is the direct result of activation of the sympathetic nervous system. This system is based in the spinal cord and brain stem, marking it as autonomic, or, not part of conscious control. Activation of the sympathetic system releases the neurotransmitter acetylcholine into the system, and results in excitatory responses to all the body systems it has control over, including the lungs and heart. Fearful people will often feel their heart and breathing rates increase, this change is caused by the sympathetic nervous system, readying the body to fuel its muscles more effectively in the face of a threat that requires immediate action. This most basic of fear responses, however, must be separated from anxiety disorders. Where the feeling of fear is elicited in response to a clear and present concern or danger, anxiety is often categorized as being pointed toward an unknown or future danger.[2] And while these perceived dangers will be described as "real" by the people suffering from anxiety disorders, activation of the sympathetic

nervous system in these cases is obviously ineffective, as you can't exactly defend yourself or run away from an upcoming exam.

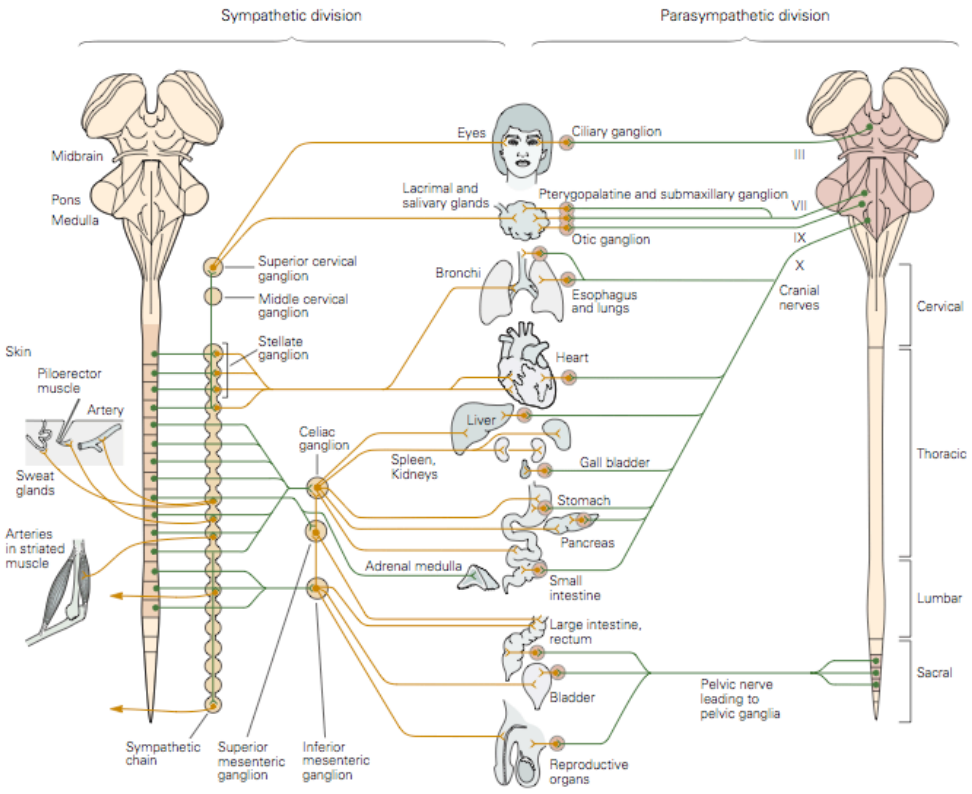

Figure 1. The signaling pathways of the symapthetic nervous system, and its sister system, the parasympathetic.[7]

So, in anxiety disorders, somewhere in the system of recognizing and reacting to immediate dangers, there has been a disconnect in the system, where a memory or concept can falsely trigger a desperate reaction from the autonomic nervous system. The culprit in the case appears to be the amygdala. The amygdala is a small section of the cerebral cortex that is often pointed to as being integral in all emotional responses, as well as the formation of memory. It is also well known that the lesioning of the amygdala can entirely remove fear responses in mammals, suggesting that it is critical in the activation of the sympathetic pathways. It is suggested, then, that anxiety disorders stem from a hyper-excitability of the fear response in the

amygdala.[3] Hyper-excitability in the amygdala occurs when an excess number of glutamate receptors are in the receptive areas of the cells. Glutamate intake causes an excitatory response in neurons, so the ability to intake more glutamate increases the chances of a cell firing a signal. So, in an amygdala neuron that had been made hyper-excitable in this way, the mere thought of a potential stressful situation, which would normally not be powerful enough to induce a reaction, becomes potent enough to activate the fear response system as though the threat were real.[3] It is not yet entirely known how the amygdala becomes hyper-excitable, but is thought to be contributed by a number of factors, as it is difficult to point to any one genetic or environmental cue for anxiety disorders.

So then, with the underlying neural systems understood, the question then becomes, how can anxiety disorders be treated? It is unfortunately true that many people suffering from debilitating anxiety tend toward various substance abuse, such as alcohol, in attempts to self medicate. Funnily enough, because alcohol causes decreased transmission of acetylcholine, the neurotransmitter at the heart of activation of the sympathetic nervous system, it actually does decrease the effects of anxiety. However, the prolonged use of alcohol as medication obviously has negative and dangerous side effects that outweigh the benefits.[4] There are medicines made to work similarly, by inhibiting the firing of the sympathetic nervous system. Called beta blockers, they instead work on stopping the release of adrenaline, the final step in the signaling pathway of the sympathetic nervous system. These drugs are also used in patients with medical conditions which cause them to be more prone to cardiac arrest, as you'll remember that the sympathetic nervous system targets the heart.

Moving further along the system, a group of drugs called benzodiazepines are commonly prescribed in many cases of mental health disorders. These drugs work by increasing the

effectiveness of GABA (gamm amino-butyric acid) in neurons. GABA is somewhat the opposite of glutamate, inciting an inhibitory response where glutamate would cause an excitatory one. So, because neurons sum up their incoming responses before choosing whether to fire their own signal, if the neuron receives competing excitatory responses from anxiety based conditions, but more numerous inhibitory ones from the influx of GABA, the net response will be that of not firing, and so not activating the fear pathways. However, the safety of benzodiazapines has been called into question, as their initial release was rushed, and more contemporary research points to potential habit forming, dangerous withdrawal symptoms, and long term damage to the fear signaling pathway.[5]

Newer methods of treatment seek to work directly on the cells releasing glutamate themselves. Pregabalin inhibits calcium channels in the cells releasing neurotransmitters like glutamate. These calcium channels allowing calcium in is what kickstarts the release of glutamate to begin with, so blocking them entirely removes the problem of the hyper amygdala activation. However, it appears that this system also carries with it the potential for creating addictions, because in addition to affecting the fear response pathways, it likely also interacts with the reward system of dopamine, often pointed to as the cause of dependency.[6] Drugs like these, which take care of one problem but create even more debilitating issues, are obviously not ideal in helping to treat people with chronic illnesses.

Because anxiety is so wrapped up in such an integral part of the human nervous system, it appears to be very difficult to treat medically without inadvertently damaging another critical neuronal system. The nervous system is extraordinarily complex, as well as being very deeply interconnected, making pinpoint cures like the ones anxiety disorders appear to require near impossible. Currently, the most effective treatments for anxiety disorders tend to be extended

therapy, and being taught how to cope with the symptoms, rather than affecting the neuronal activation itself. However, new discoveries are made in neuroscience every day. With luck, maybe safer pharmaceutical treatment methods can be found in the years to come.

Sources

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