Anxiety Disorders

by Richard H. Hall, 1998

Generalized Anxiety/Panic Disorder: Behavioral Description

Anxiety disorders, as their name implies, are disorders associated with excessive feelings of anxiousness and nervousness. As with Major Depressive Disorder, Anxiety Disorders are simply a more extreme case of what all of us experience at various times. A person suffering from an anxiety disorder experiences anxiety in such a way that it significantly interferes with normal functioning. As you might suspect these cognitive feelings of anxiety and nervousness, neurologically, translate into an overly active sympathetic nervous system. In the case of **Generalized Anxiety Disorder**, these feelings of anxiousness and nervousness are constant, as is the sympathetic activation. Not only can such feelings be unpleasant, but they can also have a strong negative impact on our physical health. Thus, this type of anxiety disorder can be particularly debilitating. **Panic disorder** also includes anxious and nervous feelings, but these feelings come and go at unanticipated times. In fact, one of the defining components of Generalized Anxiety Disorder and Panic Disorder is that in neither case is the anxiety due directly to any specific external stimuli. The prototypical panic attack includes many physical components such as irregular heart rate, dizziness, faintness, shortness of breath, sweating and "clamminess". All of these are often associated with a general feeling of dissociation or unreality and even a feeling of impending death. Again, as you might suspect, a person suffering from such attacks, which com with little warning, can have significant problems in day to day functioning.

Generalized Anxiety/Panic Disorder: Neurological Basis

Although we normally think of anxiety as a largely "psychological" state that results from specific stressors in our environment, evidence is accumulating that indicates that severe anxiety disorders have an explicit basis in the nervous system. First of all, there is evidence for the heritability of Panic Disorder in that the concordance rate among monozyotic twins is greater than with dyzygotic twins. Further, analysis of family patterns of diagnosis of this disorder has lead some to the conclusion that it is controlled by a single dominant gene.

The fact that anxiety disorders are often effectively treated with pharmaceuticals is further support for the biological basis of the disorder. Most commonly, generalized anxiety and panic disorders are both treated with **Benzodiazepines**, which are drugs that act to stimulate **$GABA_A$ Benzodiazepine receptors**. As you may recall, GABA is the primary inhibitory neurotransmitter in the central nervous system, and the $GABA_A$ receptor "complex" is one of the most interesting types of receptors. The $GABA_A$ receptor consists of five binding sites each stimulated by a different type of substance. When these sites are stimulated they have an indirect effect on GABA in that they make the GABA binding site more or less sensitive to GABA, which in turn makes the GABA neuron more or less likely to release GABA. Benzodiazepines act as GABA agonists because they stimulate the Benzodiazepine receptor in such a way as to make the GABA site more sensitive (see Figure 1). This has lead some researchers to propose that generalized anxiety and panic disorders are due to underactivity of Benzodiazepine binding sites. Further evidence that Benzodiazepine binding sites may play a role in these disorders is that

drugs that block Benzodiazepine sites, thus acting as GABA antagonists, increase anxiety symptoms. Finally, research with cats indicates that cats whose mother received shots of *Valium* (a Benzodiazepine) exhibited an inordinate amount of fearfulness, and this fearfulness could be removed by injecting the cats with *Valium*. The original effect on the cats in the womb may very well have been due to subsensitivity. That is, the administration of a drug that activated Benzodiazepine receptors in the womb may have caused the receptors to be subsensitive after birth.

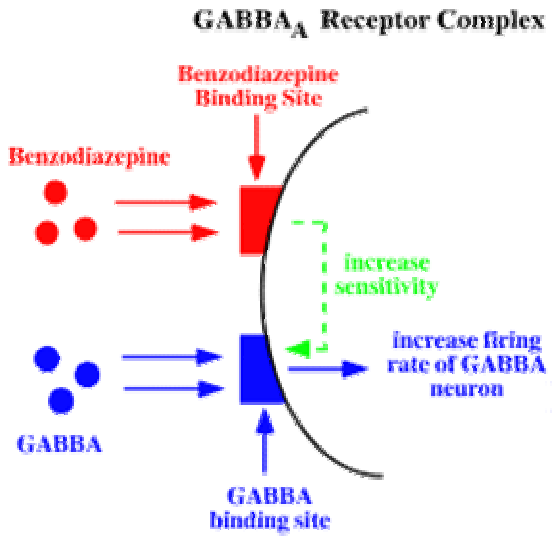

Figure 1. GABBA$_A$ Receptor Complex

It is also possible that Serotonin (5-HT) plays a role in Generalized Anxiety and Panic, in that these disorders are also often treated effectively with drugs usually used to treat depression, that are 5-HT agonists. However, although a diet low in Tryptophan (5-HT precursor) has been found to increase the symptoms of those suffering depression, the same is not true for those suffering from an anxiety or panic disorders. If the latter disorders were due strictly to underactivity of 5-HT we would expect the elimination of a precursor to increase the symptoms, but it doesn't. Thus, whether or not 5-HT plays a role in anxiety disorder, and what the role may be, remains somewhat of a mystery.

Obsessive-Compulsive Disorder: Behavioral Description

Another subcategory of Anxiety Disorders is **Obsessive-Compulsive Disorder (O.C.D.)**. Those suffering from this disorder are haunted by reoccurring beliefs followed by consequent compulsive behaviors (see Figure 2). These beliefs and behaviors are reoccurring and constant. Although the person experiencing the disorder recognizes that the behaviors are irrationally excessive, they feel powerless to stop. These behaviors usually fall into one of four general categories: counting, checking, cleaning, and avoidance. For example, a common OCD belief-behavior combination is a feeling of uncleanliness followed by handwashing. This behavior may occur dozens of times a day, interfering frequently with normal activities.

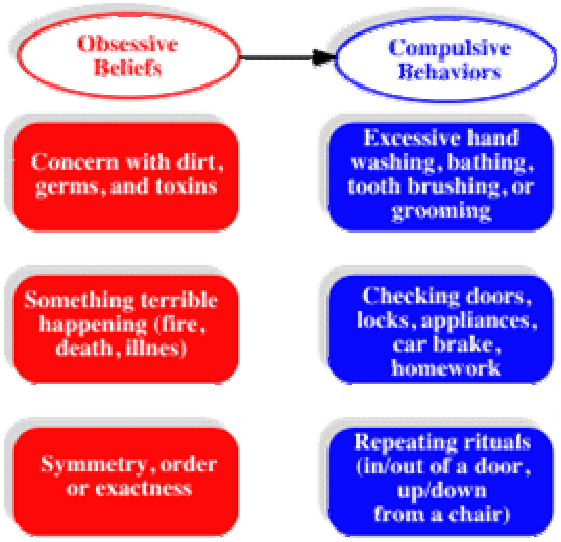

Figure 2. Illustration of Obsessive Belief and Compulsive Behavior Relationship

Some theorists propose that OCD is the result of the exaggeration of very functional, adaptable, "specifies-specific" behaviors. For example, a drive to be cleanly can serve to ward off germs associated with uncleanliness, and a feeling of fear can serve to keep us alert to dangers. A drive for order and ritual may be very helpful in helping us to be more efficient in our daily activities, and, in fact, many religious traditions rely on ritual to instill a meditative feeling of familiarity and calm. The theory is that these very important drives and behaviors simply get exaggerated in a person diagnosed with this disorder.

Obsessive-Compulsive Disorder: Neurological Basis

As with Generalized Anxiety Disorder and Panic there is evidence for heritability with OCD. One of the strongest pieces of evidence to support this is that a childhood neurological disorder Tourette's Syndrome, seems to be behaviorally associated with OCD. **Tourette's Syndrome** is characterized by stereotypical motor behavior such as facial tics. Those suffering form OCD also often exhibit such stereotypical motor behavior, and those with Tourette's Syndrome often exhibit typical OCD behavior. The similarity of these two suggests that they may both be due to the same underlying genetic factors.

There is a great deal of evidence that OCD is associated with certain types of structural brain abnormalities. First of all, the **Basal Ganglia** have been implicated. More specifically, it appears that OCD may be, at least partly, due to underactivity of this system of brain structures. OCD type behaviors often occur in diseases that are due to damage to the Basal Ganglia. Also, PET scans indicate that the Basal Ganglia are less active in those with OCD than in people not diagnosed as OCD. There is even more evidence that OCD is associated with **overactivity** of the **Prefrontal Cortex**. Brain imaging studies indicate that those diagnosed with OCD have more active Prefrontal Cortexes than non-OCD controls. Further, drug and behavioral treatments that effectively treat OCD also result in a corresponding decrease in activity in the Prefrontal Cortex. Finally, in rare cases surgery is performed to treat OCD when behavioral and drug treatments

have failed. This surgery involves the destruction of specific fiber bundles in the Prefrontal Cortex. (Obviously radically decreasing prefrontal activity in those areas).

Obsessive-Compulsive disorder is usually treated with Selective Serotonin Reuptake Inhibitors (traditionally considered anti-depression drugs). This has lead researchers to speculate that OCD is the result of too little 5-HT activity. And, in fact, 5-HT antagonists usually increase OCD symptoms. Further, consistent with the "over adaptivity" theory posed above, 5-HT has been found to **decrease** species-typical behaviors. Thus it would make sense that, if OCD were an exaggeration of such behaviors, a drug that increases the activity of a neurotransmitter that inhibits the behaviors, would effectively treat OCD. However, as with the other anxiety disorders, a low-Tryptophan diet does not effect OCD symptoms, so the exact role of 5-HT in OCD is not yet known.