Neurobiological and Psychological Considerations Concerning Fear and Anxiety: Analytical Essay

Neurobiological Considerations

Anxiety disorders are characterized by disruptions in neurobiological functioning, specifically in neurotransmitter and neuroendocrine pathways, and neuroanatomical structures. The limbic system, which is the emotional-processing center of the brain, contains the hypothalamus, thalamus, amygdala, hippocampus, basal ganglia, and cingulate gyrus (Martin et al., 2010). When a stressful event occurs, the cortex is activated on a cortical level, and the amygdala on a subcortical level. The amygdala then assesses the stimulus event, and if it senses danger, it transmits a distress signal to the hypothalamus, which is then transferred to both the pituitary and the sympathetic nervous system. The pituitary then transmits the distress signal it to the adrenal cortex, which releases cortisol, and the thyroid, which releases thyroxin (Preston et al., 2013). The neural pathway of the fight-or-flight response, in relation to anxiety, will be discussed in further detail.

Neuroanatomy of Anxiety

The symptoms associated with anxiety disorders appear to be partially a result of disruption in emotional regions of the brain. It was previously noted that on the subcortical level, the amygdala is activated in the presence of stimuli. The amygdala is the area of the brain responsible for the procurement and expression of fear and aggression, and emotional responses to the environment (Charney, 2003; Garakani et al., 2006; Martin et al., 2010). In addition to conditioning fear responses to explicit sensory stimuli, the amygdala is also involved in the “Development of emotional responses to environmental contexts” (Charney, 2003). Research indicates that in comparison to mentally healthy individuals, those with anxiety disorders exhibit increased activity in the amygdala (Patriquin & Matthew, 2017). This is because when in the presence of seemingly threatening stimuli, the amygdala is stimulated and can evoke feelings of fear or anxiety that correlate with emotional experiences. The plasticity within the amygdala is the mechanism that composes memory for conditioning fear-experiences over time. Plasticity in the cortex, presumably makes it “possible for explicit or declarative memories about the fear-related event to be established through interactions with the medial temporal lobe memory system”. Although fear conditioned responses “depends upon plasticity in the amygdala, learning involving higher cognitive (i.e. mnemonic and attentional) processing of fear experiences may depend upon plasticity involving cortical neurons, which is influenced by neural transmission from the amygdala to the cortex” (Charney, 2003).

On a cortical level, prefrontal structures play a vital role in modulating fear and anxiety behavior. Specifically, various areas of the orbital and medial prefrontal cortex (PFC) help decipher significant environmental stimuli on a higher level, revise behavioral responses, and determine social outcomes of behavioral responses to emotion evoking events. The PFC has a reciprocal relationship with the amygdala, because they share reciprocal projections. This connection allows the amygdala to regulate neuronal activity in the PFC, and the PFC to regulate contrived responses to emotionally significant stimuli in the amygdala (Charney, 2003). In the medial

prefrontal cortex (mPFC), the infralimbic cortex and the anterior cingulate cortex (ACC) are structures that play a critical role in mediating fear-related behavior. The relationship between the mPFC and the amygdala allow for fear-related responses to diminish, and for behavioral responses to conditioned stimuli to annihilated (Charney, 2003; Garakini et al., 2006).

The amygdala consists of 13 nuclei; three of which are associated with the pathways of fear response. These three are the basal amygdala (BA), lateral amygdala (LA), and central nuclei. The thalamus receives sensory information, which then travels from the LA, to BA, and then to the central nucleus (CA). Chemical signals are sent from the PFC, sensory cortex, and insula, to the LA (Garakani et al., 2006; Patriquin & Matthew, 2017). Afterward, a surge of excitation is projected to the hypothalamus and the locus coeruleus (LC) (Garakani et al., 2006; Preston et al., 2013). The nerve cells of the LC are moderated by the neurotransmitter norepinephrine. When it projects to the limbic system, it results in immediate hypervigilance. The hypothalamus then excites the pituitary gland and the sympathetic nervous system simultaneously. The hypothalamus emits a signal that tells the pituitary gland to either release or inhibit hormone production (Preston et al., 2013). When the hypothalamus sends an excitatory signal (i.e. in the presence of fear), the pituitary releases hormones into both the adrenal cortex and the thyroid. The adrenal cortex then secretes cortisol, and the thyroid secretes thyroxin; both are released into the bloodstream, and now the brain and body are both ready for action (Martin et al., 2010; Preston et al., 2013). The sympathetic nervous system emits a signal to the adrenal medulla, which releases hormones into the bloodstream in the form of adrenaline, and noradrenaline

Neuroendocrine and Neurotransmitter Pathways

It is necessary to consider both neuroanatomy and the neurotransmitters that transfer chemical messages between the regions of the brain. While central vasopressin (AVP) can keep the HPA axis in a state of homeostasis it can also (I). Some animal studies have found that blockage of N-methyl-D¬-aspartate (NDMA) receptors in both the hippocampus and amygdala will inhibit conditioned fear-response. While human studies on the idea are limited, preclinical finding implicate “the use of NMDA receptor antagonists and calcium channel blockers to impair memory consolidation and thereby treat anxiety symptoms” (Garakani et al., 2006). The hippocampus has the ability to inhibit the hypothalamic stress-response system, and is a key contributor to the regulation of negative feedback in the hypothalamic-pituitary-adrenal (HPA) axis (Martin et al., 2010).

Psychopharmalogical Considerations

The scientific treatment of anxiety disorders is primarily founded on empirical data that supports the efficacy of drug treatment. Preclinical and clinical evidence “suggest that there are neurobiological abnormalities associated with various anxiety disorders that can be reversed or normalized through pharmacological intervention” (Lydiard et al., 1996). Overall, available data currently supports the argument that most anxiety disorders are biomedical in nature, and are amenable to an array of specific behavioral and psychopharmalogical treatments. An overview of the psychopharmacological treatment of anxiety disorders will be discussed.

Antidepressants

Antidepressants are the most common medications used to treat anxiety disorders. One of the

main drawbacks of using these medications to treat anxiety is the slow onset of therapeutic effect. Individuals who are affected by panic disorder experience high levels of distress in a shorter period of time, can suffer for longer periods of time while waiting for the antidepressant to take effect. This may lead a patient to prematurely terminate pharmacotherapeutic treatment (Starcevic, 2005). The four classifications of antidepressants that are used to treat anxiety are Selective serotonin reuptake inhibitors (SSRIs), Serotonin-norepinephrine reuptake inhibitors (SNRIs), Certain tricyclic antidepressants (TCAs), and Monoamine oxidase inhibitors (MAOIs) (Lydiard et al., 1996).

SSRIs and SNRIs

SSRIs have proven effective in both the short-term and long-term treatment of various types of anxiety disorders, and they are typically well received. For these reasons, SSRIs are often the first choice for treating anxiety disorders and obsessive-compulsive disorders (Baldwin et al., 2014; Lydiard et al., 1996). However, SSRIs have the potential to cause adverse side effects such as sexual dysfunction, increased nervousness, nausea, and insomnia. In order to combat these effects doctors should start patients on a lower doses and increase the dosage over time as needed. SSRIs may react when taken simultaneously with other drugs, such as treatments for physical illness and psychotropic drugs. This is because some SSRIs, such as fluoxetine and paroxetine inhibit some cytochrome P450 enzymes in the liver. Another downfall of SSRIs is that if medication is stopped abruptly, or even decreased over time, it can cause discontinuation syndrome side effects like insomnia, flu-like symptoms, and dizziness (Baldwin et al., 2014).

In comparison to TCAs, SSRIs have been associated with fewer adverse side effects and better tolerability. However, results on the actual difference is mixed. Some side effects of SSRIs such as insomnia, may worsen anxiety symptoms (Starcevic, 2005).. Specifically, SSRIs can cause agitation when initially administered to patients with panic disorder and PTSD. Thus, because of the aversive side effects, some clinicians once chose to prescribe benzodiazepines or tricyclic antidepressants (Lyiard et al., 1996).

Some SNRIs such as duloxetine and venlafaxine have proven to be effective in the treatment of GAD. These medications have shown to be effective in both short-term and long-term treatment. Placebo-controlled trials have demonstrated the efficacy of SNRIs for the treatment and prevention of panic disorder. However, venlafaxine and duloxetine also can cause discontinuation symptoms after sudden medication termination. Studies show that SSRIs are more well received than venlafaxine and duloxetine. Although scientific evidence is limited, some patients report an increase in blood pressure while on the medication. Similarly, patients with liver disease and those at risk of hepatic dysfunction are encouraged to refrain from taking duloxetine because of the possibility of an increased risk of hepatoxicity. (Baldwin et al., 2014).

MAOIs

One of the most extensively studied pharmacological treatments for anxiety is the MAOI phenelzine. The drug has shown to be effective in the treatment on social phobia and panic disorder. Specifically, the drug moclobemide has proven to help treat social phobia (Baldwin et al., 2014). One study, compared the results of phenelzine, atenolol, and a placebo over a 16-week trial, and found that 64 percent participants responded to phenelzine, 30 percent to

atenolol, and 23 percent to the placebo. Those diagnosed while social phobia showed significant reduction in symptoms (Lydiard et al, 1996). MAOIs should be withheld from patients who are suicidal due to the risk of fatal overdose. It is also recommended that these drugs be given to those who have not responded well to other treatment options. Studies have found that those who take the MAOI agomelatine are less likely to experience sexual dysfunction than those who take SNRIs and SSRIs Baldwin et al., 2014).

TCAs

While certain TCAs have proven to be effective in the treatment of anxiety disorders, they are also correlated with more adverse side effects than SNRIs and SSRIs. As a result, it is recommended that TCAs should only be used for patients who have not responded well to, or who are not able to tolerate, SNRIs and SSRIs. Like MAOIs, TCAs also have a potential risk of fatal overdose, and therefore they are not recommended for patients who are suicidal. Like other antidepressants, TCAs are also associated with discontinuation syndrome with abrupt termination (Baldwin et al., 2014).

Benzodiazepines

Some benzodiazepines have proven to be effective in the treatment of social phobia, GAD, and panic disorder. However, these drugs should be prescribed with caution because of their dangerous side effects such as sedation and cognitive impairment (Baldwin et al., 2014). Benzodiazepines use can also lead to the development of dependence (Bandelow et al., 2014). Due to these adverse side effects, clinicians typically reserve benzodiazepines for patients who have not responded to SNRIs, SSRIs, and psychological treatment. However, many argue that the concerns about issues of long-term treatment should not prevent it being prescribed to patients with more debilitating anxiety symptoms (Baldwin et al., 2014).

Other Agents

Although antipsychotics are commonly prescribed to patients with anxiety disorders, evidence suggests that its greatest benefit it for the “acute treatment and prevention of relapse with quetiapine in generalized anxiety disorder, and the augmentation of SSRI antidepressants in anti-histamine) and buspirone (an azapirone), have also been shown to effectively treat GAD (Baldwin et al., 2014).

Psychological Considerations

CBT

Cognitive behavior therapy (CBT) has proven to be effective in the treatment of anxiety disorders, and can help improve patients’ quality of life. Exposure therapy and cognitive therapy are two of the most commonly used methods for treating anxiety disorders. CBT is typically used as a short-term treatment that focuses on the skills of the individual. Patients utilize their skills to change negative thoughts and behavior, to ultimately change maladaptive emotions. One of the benefits of CBT is that it can be revised to fit the needs of the individual, and adapted in different ways to treat different multiple anxiety disorders (Ellard &

Chronopoulos, 2016).

Exposure Therapy

Exposure therapy is commonly used to treat anxiety disorders. Emotional processing theory states that cognitive fear structures represent fear and “maintain information about the feared stimulus, fear responses (eg, escape, avoidance, psychophysiological responses), and the meaning of the stimuli and responses (eg, tiger = danger, increased heart rate = heart attack)”. In the presence of a stimulus that resembles a fear stimulus, cognitive fear structures activate the fear structure. A fear response becomes pathological when the fear does not match reality. Avoidance behaviors preserve the conditioned fear-response, which hinders new learning. (Ellard & Chronopoulos, 2016). The patient is exposed to the fearful stimuli in order to modify the fear response. The exposure activates the fear structure and then produces novel information, in order to invalidate the unrealistic associations within those cognitive structures. Research suggests that exposure to the fearful stimuli combined with cognitive restructuring, allows fear symptoms to decrease over time, in patients with anxiety. Exposure therapy is a short-term method that typically requires about ten sessions.

The exposure can either be interoceptive, in vivo, or imaginal. Interoceptive exposure is typically used to treat patients with panic disorder, because it focuses on creating physical sensations experienced at the onset of a panic attack. During imaginal exposure, the client is required to imagine a fearful situation, so they can face their anxiety symptoms head-on, as they occur. Lastly, in vivo exposure involves external stimuli in the sense that the client is exposed to familiar events, places, people, or objects that are known to activate feelings of fear or worry. Numerous studies have validated the effectiveness of exposure therapy to treat anxiety disorders, and it is typically the first treatment choice of clinicians (Ellard, K. K., & Chronopoulos).

Panic Disorder.

Interoceptive exposure therapy is typically used for treating panic disorder because it focuses on invalidating the notion that physical arousal will result in dangerous consequences such as public embarrassment, or death. One study found that introspective exposure treatment CBT with interoceptive exposure treatment yielded the largest effect sizes for panic disorder patients; however, these interventions also included cognitive restructuring in addition to exposure” (Ellard, K. K., & Chronopoulos).

GAD.

While there are a limited number of studies on the efficacy of exposure-based therapy on GAD, studies have found that it can be effectively treated with both in vivo exposure and imaginal exposure. Specifically, patients with GAD exhibited greater functioning after 12-month follow up than those who received nondirective therapy or applied relaxation. An experiment conducted by Craske and Barlow (2006), required patients to participate in self-guided exposure therapy in which the patient had to repeatedly imagine their worries. They found that the continual exposure imagined fearful stimuli helped reduce the severity of worry over time.

In vivo exposure has been shown to be less effective than the latter. Conversely, a recent study

that examined the effects of imaginal exposure, applied relaxation, and cognitive therapy found no significant differences in outcomes for treating patients with GAD. Thus, results for the efficacy and effectiveness of exposure therapy for treating GAD remain inconclusive, and require further investigation (Ellard, K. K., & Chronopoulos).