Relieving anxiety by giving in to bugging thoughts: obsessive - compulsive disorde...

Health & Medicine, Mental Health

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)’s category of obsessive-compulsive and related disorders include obsessive-compulsive disorder, hoarding disorder, body dysmorphic disorder, hair-pulling disorder (trichotillomania), and skin-picking disorder (excoriation) (Sue et al., 2016). Of these illnesses, obsessive-compulsive disorder (OCD) is characterized by an inability to control troubling thoughts and brief relief after obeying these intrusive impulses, referred to as “ obsessions” and “ compulsions,” respectively. Obsessions are persistent thoughts or images that produce anxiety, and compulsions are an overwhelming need to perform mental or physical acts to counter the anxiety or prevent a feared event from occurring (Sue et al., 2016). Compulsions can include physical activities, such as hand washing, checking, and ordering objects, or mental acts, such as praying, counting, and repeating words silently. Common themes of OCD include a fear of contamination with regards to dirt, germs, body wastes, or secretions, a fear of being dirtied by coming into contact with objects, places, or people, errors of uncertainty in performance of daily behaviors, manifested by repeatedly checking if doors are locked or turning on and off appliances, thoughts of sexual acts or harming oneself or others, orderliness, and striving for perfect order or symmetry (Sue et al., 2016). In a given year, approximately 1. 2% of the United States population experiences symptoms significant enough to constitute a disorder. OCD is equally common in both males and females, and usually presents during adolescence or early adulthood. Those afflicted with OCD often describe the disorder as out of character and out of voluntary control, and many also suffer from depression and substance abuse (Sue et al. 2016). Currently,

obsessive-compulsive disorder is thought to be caused by psychological, social, and sociocultural factors, but because of its prevalence and debilitating nature, modern research is attempting to determine a neurobiological cause to create effective medications and treatments for therapeutic relief.

Obsessive-compulsive symptoms have been identified, somewhat consistently, since the seventeenth century. During this period, sufferers of OCD were viewed in a religious context and possessed by external forces, such as the devil. Exorcism was the primary treatment method, and even resulted in the successful alleviation of symptoms in some cases (Menzies and Padmal, 2003). In the nineteenth century, the disorder fell under medical jurisdiction, where it was considered a variety of “ insanity” by French psychiatrists. In 1838, OCD was described as “ neurosis” or a “ diseases of emotions” after Esquirol, a French psychiatrist, noted that his patients recognized that they were unable to resist their obsessions, indicating insight into their experience with the disorder (Menzies and Padmal, 2003). Before the 1970’s, OCD was considered a rare and strange disease, with a prevalence of 0. 005% to 0. 05% in the general population (Davis, 2008). The history of the mental illness has consisted of a variety of symptoms and behaviors that have been refined through the various editions of the Diagnostic and Statistical Manual of Mental Disorders; for example, the DSM was established in 1952, but the DSM-III codified the separation between OCD and phobias and established the obsessive-compulsive personality as distinct from the disorder (Davis, 2008). Obsessive-compulsive disorder is now one of the four mental illnesses in the top ten causes of

disability around the world, and although researchers are currently searching for the single cause of the illness, many believe that OCD requires a multi-faceted explanation, including biological, psychological, social, and cultural causes (Davis, 2008).

Although current research has not definitely determined a particular cause of obsessive-compulsive disorder, various research methods have provided considerable hypotheses. Twin and family studies have indicated that OCD has a hereditary component (Karayiorgou et al., 1999), with close relatives of individuals with the disorder four times more likely to develop the mental illnesses themselves (Sue et al., 2016), although the mode of inheritance is still unknown (Karayiorgou et al., 1999). First-degree relatives also demonstrate impairments in decision-making, planning, and mental flexibility, making these cognitive characteristics a likely endophenotype, and a possible result from impaired brain circuits and structures that mediate strong emotions and the behavioral reactions to such emotions (Sue et al., 2016). Although OCD is equally expressed in both males and females, Karayiorgou et al. (1999) genotyped the DNA for functional variants of the COMT (catechol-Omethyltransferace) and MAO (monoamine oxidase-A, which regulates monoamine metabolism) genes, and used the Transmission Disequilibrium Test (TVT) and Haplotype-based Haplotype Relative Risk (RRR) tests to investigate allele inheritance. They found a sexually dimorphic link between low COMT enzymatic activity, a MAOA gene allele, associated with high MAO-A enzymatic activity, and OCD (Karayiorgou et al., 1999). This indicates that susceptibility to OCD is may be connected to the variations of

these two genes that regulate monoamine metabolism, and that these OCD susceptibility genes propose a gender difference in genetic predisposition to the mental illness (Karayiorgou et al., 1999).

Like the genetic basis of the mental illness, the pathophysiology and neuroanatomy of OCD has not been yet undoubtedly determined as well. Although X-ray CT studies have not shown any diagnosable abnormalities, EEGS of individuals suffering from OCD have shown increased metabolic activity in the frontal lobe of the left hemisphere of the brain (Garber et al., 1989), suggesting a connection between a dysregulation of the orbitofrontal-caudate circuit and obsessive-compulsive symptoms. The orbitofrontal cortex notifies the rest of the brain when something “ feels wrong”; when this cortex becomes hyperactive, it may not only trigger the feeling that something is not right, but also persistently create this feeling, a symptom of OCD (Sue et al., 2016). The decreased activity in the caudate nuclei, a brain region that regulates the transmission of impulses, may allow distressing thoughts to occur unchecked. In fact, MRI scans of individuals who have successfully undergone cognitive-behavioral therapy have reported increased activity in the caudate nuclei (Sue et al., 2016). PET (positron emission tomography) studies have also discovered increased glucose metabolism in the caudate nuclei of the left orbital gyrus and right orbital cortex, indicating these areas may also be important anatomical substrates of the disorder (Garber et al., 1989). Because magnetic resonance imaging (MRI) of hydrogen protons is more sensitive than CT for detecting neuropsychiatric disorder abnormalities in the brain, Garber et al. (1989)

used a spin-lattice relaxation time to demonstrate reactions between excited protons and molecular motion. These resonance signals, measured by spin-lattice relaxation time, indicated abnormalities that suggest involvement of the frontal regions of the brain (Garber et al., 1989). Neuroimaging techniques have also recorded excessive neural connectivity between the orbitofrontal cortex and the prefrontal cortex, an area associated with the executive function of impulse control (Sue et al., 2016).

The discovery that selective serotonin reuptake inhibitors (SSRIs), which increase the availability of serotonin in the brain, reduce obsessive-compulsive symptoms has led to the serotonin hypothesis, which links serotonin to OCD. This connection is evidenced by the SSRIs' effective treatment of OCD by targeting overactive neural connections and abnormalities in serotonin availability, and because medications that are effective with other anxiety disorders, but do not increase the availability of serotonin, are not useful in treating the mental illness (Sue et al., 2016). The serotonergic basis of OCD has been supported by functional imaging studies that have identified a cortico-striatal-pallido-thalamic-cortical tract dysfunction. Because this tract receives much serotonergic innervation from the raphe nuclei, its dysfunction supports the hypothesis that serotonin plays a role in OCD (Chakrabarty et al., 2005). However, because only 60% of people with OCD respond to SSRIs, and oftentimes reduction in symptoms is only partial (Sue et al., 2016), there may also be additional and different mechanisms implicated in OCD (Chakrabarty et al., 2005).

Research has also proposed that OCD may be a product of disrupted transmissions of glutamate, an excitatory neuron that activates neuron firing (Sue et al., 2016). To investigate this glutamate hypothesis, Chakrabarty et al. (2005) analyzed the CSF glutamate levels in adults with OCD and found that they were significantly higher than the levels of the control individuals who did not have the diagnosable condition. This study provided initial evidence of the connection between glutamatergic excess and the pathophysiology of OCD (Chakrabarty et al., 2005). However, the glutamate hypothesis has also stemmed from the discovery that individuals who are given a single infusion of ketamine, a drug that causes the release of glutamate, experience a rapid reduction of obsessive-compulsive symptoms (Sue et al., 2016). Because Chakrabarty et al.'s study only provided initial evidence of a glutamatergic implication with OCD and other studies have discovered conflicting reports on levels of glutamate, research must continue to explore the role of glutamate in OCD to determine if targeting this neurotransmitter can successfully alleviate OCD symptoms in more individuals and individuals who do not respond to SSRIs.

Behavioral treatments may also induce neuroplasticity that results in functional connectivity by retraining the brain so that obsessive or compulsive cues no longer activate the fear circuit (Sue et al., 2016). Schwartz et al. (1996) used PET scans to discover that successful behavioral therapy of OCD coincided with a bilateral decrease of glucose metabolic rates in the caudate nucleus, implicating a prefrontal cortico-striato-thalamic brain system as a mediating system of OCD. The most improvement in

symptoms is achieved when behavioral treatments and SSRIs are combined; however, if individuals do not respond to SSRIs, antipsychotics can also be used, although some have adverse reactions (Sue et al., 2016).

Because of the discovery of the effectiveness of ketamine, current research is increasingly interested in investigating the use of medications that moderate glutamate in the treatment of obsessive-compulsive disorder (Sue et al., 2016). Although Chakrabarty et al. (2005)’s study provided initial evidence for the glutamate hypothesis, in comparison to other areas of research, glutamate and its mechanism of action with respect to OCD is still significantly understudied. Despite the etiology of OCD indicating a genetic component and clinical and pharmacological studies suggesting the involvement of serotonergic and dopaminergic systems, various studies have not found any statistically significant genotypic or allelic associations in polymorphic variants in serotonin receptor 2A and 1D, dopamine transporter (DAT), dopamine receptor type 4 (DRD4), monoamine-oxidase A (MAO-A) (Hemmings et al., 2003), tryptophan hydroxylase (TPH), serotonin 2C receptor (HTR2C), serotonin transporter (5-HTT), and dopamine transporter (DAT1) (Frisch et al., 2000). Because cognitive-behavioral therapies have been most effective in the treatment of OCD, specialized therapy programs for OCD, treatment protocols that can be used for a variety of anxiety disorders, and technology that can improve cognitive behavioral therapy are being investigated (Sue et al., 2016). Although obsessive-compulsive disorder is a mental disorder likely caused by a variety of factors, sufferers of this mental illness need a definite neurobiological

cause that can be targeted by treatments for therapeutic relief; glutamate is currently the most promising avenue.