Posttraumatic Stress Disorder (PTSD): The Prevailing Neurobiological Model and Treatment

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Abstract

Until recently, the specific neurological effects of Posttraumatic Stress Disorder (PTSD) on the brain were not well supported in the literature. It has been found that the limbic system is intimately involved in this disorder. Specifically, the hippocampus and the amygdala play a crucial role in the emotional memories in Posttraumatic Stress Disorder. Treatment for PTSD that addresses the limbic system has been shown to be highly effective in studies. Prolonged Exposure Therapy is treatment modality that activates the limbic system in order to reduce symptoms of PTSD. Counselors working with clients diagnosed with PTSD can conceptualize this disorder in a different way that demonstrates the neurobiological underpinnings that further supports the use of evidence-based treatment—prolonged exposure—to not only reduce symptoms of PTSD, but also to change the structure of the brain of these individuals. Counselors improved view of the neurobiological basis of PTSD will improve their case conceptualizations of their clients.

Post-Traumatic Stress Disorder (PTSD) is classified as an anxiety disorder that occurs after a person's exposure to a traumatic, terrifying event in which "grave physical harm" happened or was in jeopardy of happening (APA, 2004). Traumatic events that may lead to PTSD include, but are not limited to, violent personal attacks, natural disasters, vehicle accidents, physical or sexual abuse, combat, rape and terrorist attacks (APA, 2004).

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Three main clusters of symptoms prominent in PTSD are: 1) consistently re-experiencing traumatic memory 2) hyperarousal 3) avoidance of stimuli associated with trauma (Milad et al., 2009). People who suffer from PTSD often have difficulty remembering facets of the traumatic event (Werner et al., 2008). Therefore, PTSD is also seen as a disorder of memory (Bremner, 2001; Hayes et al., 2011). Milad et al. (2009) suggest that people with PTSD suffer from "deficient extinction learning" (p. 1075) where the brain fails to extinguish a conditioned fear related to PTSD (Felmingham et al., 2007; Koenigs & Grafman, 2009; Rauch, Shin & Phelps, 2006). Furthermore, PTSD could be characterized as an abnormal emotional-memory (Hayes et al., 2011). The prevailing brain structure associated with emotion and memory is the limbic system (Britton, Phan, Taylor, Fig & Liberzon, 2005), which is comprised of, in part, the amygdala, hippocampus and cingulate cortex. Moreover, Rauch et al. (2006) supports the popular neurobiological model of PTSD that emphasizes interactions of the amygdala, vmPFC and the hippocampus. To gain a clearer picture, it is pertinent to understand the neurobiological underpinnings of PTSD (Koenigs & Grafman, 2009). The amygdala plays a central role in emotional processing, perceiving threats, and fear conditioning (Britton et al, 2005; Koenigs & Grafman, 2009; Tronel & Alberini, 2007). The hippocampus is involved in learning, memory, episodic memory, and environmental contextual clues (Koenigs et al., 2008; Werner et al., 2009). In light of the three cluster symptoms of PTSD (e.g., high anxiety, memory flashback, avoidance), it is imperative to gain an understanding of neural circuitry and structure related to PTSD to provide effective treatment (Tronel & Alberini, 2007). This paper will examine the prevailing neurobiological model of PTSD, as well as, effective therapeutic interventions.

Neurobiological Model of PTSD

Neuroimaging studies have identified abnormal functioning of the limbic and paralimbic systems of the brain in pathogenesis of PTSD (Britton, Phan, Taylor, Fig & Liberzon, 2006); specifically, the amygdala, hippocampus, and medial frontal cortical regions and the dorsal anterior cingulated cortex (dACC) (Milad et al., 2009; Rauch et

al., 2006). Milad et al. stress the importance of understanding this circuitry of the brain and how it relates to PTSD's dysfunctional emotional-memory processing. Several studies support further investigation of these regions to fully appreciate their role in PTSD and individual differences among people who develop this disorder (Britton et al., 2006; Koenigs & Grafman, 2009).

Amygdala and vmPFC

Koenigs and Grafman (2009) provide the following conceptualization of the role of the amygdala in PTSD. The amygdala plays a role in emotional regulation such as anxiety, fear, and stress. The amygdala may distort emotional memory of traumatic events during the encoding process that may underlie etiology of PTSD (Hayes et al., 2011). Moreover, the amygdala plays a role in fear acquisition (Milad et al., 2009) and Rogers et al., (2007) contends it plays a role in extinction learning of a conditioned fear. For example, a combat veteran exhibiting a heightened fear response to fireworks on the fourth of July because it is similar to sounds of war. Therefore, the amygdala is in a place to centrally alter symptoms of PTSD (Smith, Abou-Khalil, & Zald, 2008). The amygdala also connects to the brainstem that plays a role in the executing autonomic responses and physiological reactions (Koenigs & Grafman 2009) that supports the role of the amygdala evolutionary hypothesis of the predator model of PTSD (Clinchy, Schulkin, Zanette, Sheriff, McGowan, & Boonstra, 2011). The predator model of PTSD postulates that when an animal or human detects an anxiety/fear-provoking situation that it freezes, fights, or flees the situation. During this response, connections are made to the lower parts of the brain where there is less conscious control by the individual and perhaps this is where some dysfunctional regulation may transpire (Perry, 2009) or a conditioned fear may become abnormal (Rogers et al. 2007). So why do some people develop symptoms of PTSD while others do not?

One hypothesis set forth by Rogers et al. (2009) is that a smaller amygdala is partially responsible for the failure of fear to be extinguished in people diagnosed with PTSD. This is a notable individual difference among people who diagnosed with PTSD and non-PTSD diagnosed people. Their study was the first to control for chronic

symptoms of PTSD and reduced volume of the amygdala. Specifically, this study established that a single, intense stressful episode is associated with reduced volume of the amygdala that is related to avoidance symptoms of PTSD as shown on the assessment questionnaire, CAPS (Clinician Administered Posttraumatic Stress Disorder Scale). They also found a relationship between the anterior cingulate cortex (ACC) and the amygdala in the failure to extinguish a fear theory of PTSD. The ACC in their study showed reduced gray matter density compared to not-PTSD controls.

Another hypothesis proposed by Koenigs and Grafman (2009) contends that hyperactivity in the amygdala is responsible for symptoms of PTSD and supported by other studies (Koenigs & Grafman, 2009; Milad et al., 2009). Koenigs and Grafman (2009) performed neuroimaging on veterans with PTSD that demonstrated hyperactivity of the amygdala. Rauch et al. (2006) support the putative role of hyperactivity of the amygdala in people diagnosed with PTSD. Additionally, several studies (Britton et al., 2005; Koenigs & Grafman, 2009; Koenigs et al., 2008) found that lower activation of the amygdala seemed to inoculate against symptoms of PTSD. Perhaps this is due to the *modulation hypothesis*, which stipulates that more emotional an event, the more likely it will be remembered compared to neutral event due to the modifying effect of the amygdala (Hayes et al., 2011). What causes this hyperactivity in the amygdala? The answer lies in the medial frontal cortical area.

Medial Frontal Cortical Region

The ventral medial frontal cortex (vmPFC) is connected to the amygdala via a dense array of neuronal axons that mediates activity of the amygdala (Koenigs & Grafman, 2009). Britton et al. (2005) found a hypoactive vmPFC was related to a hyperactive amygdala. This study supports the inhibitory function of the vmPFC on the amygdala. This neural pathway communicates bidirectionally and it is not clear why the vmPFC cannot appropriately modulate the amygdala in relation to people with symptoms of PTSD (Koenigs & Grafman, 2009). Perry (2009) theorizes that that the emotional memories are being stored in a lower part of the brain where people have less conscious control of emotional memories. Therefore, if there are salient reminders

similar to the traumatic event in people with PTSD, there may be an uncontrollable emotional response due to the role of the amygdala to alert the body if danger is present (Perry, 2009). What if there is damage to the amygdala or vmPFC? Is someone just as susceptible to symptoms of PTSD with damage to this area? If not this would seemingly discount the "overactivity" theory of the amygdala.

Koenigs et al., (2008) analyzed focal lesions of the brains of combat veterans in the vmPFC, amygdala, and hippocampal regions of the limbic system to ascertain any reduction of symptoms or diagnosis of PTSD. Koenigs et al. (2008) found that lesions in either the amygdala or vmPFC reduced prevalence of PTSD in combat veterans. The reduced occurrence of PTSD in veterans was not due to the absence of symptoms, rather due to a reduction of symptom intensity. However, a damaged hippocampus did not affect whether or not PTSD developed in combat war veterans. Koenigs et al. suggest that based on these findings the overactive amygdala is a critical component in the development of PTSD in people. Moreover, Smith Abou-Khalil and Zald (2008) state that overactivity in the right amygdala is responsible for symptoms of PTSD. There could be unilateralized expression of symptoms of PTSD in the right amygdala. They support this hypothesis with a case study of a patient with a removed left amygdala that underwent a traumatic experience (hit by a car) and still suffered symptoms of PTSD. However, a limitation of this case study was that the left amygdala was removed early in life because of a seizure disorder and the right amygdala may have adapted certain functions of the left amygdala over the years.

Hippocampus

The hippocampus is crucial in a person's learning and memory (Bremner, 2001). The hippocampus encodes associative stimuli; it pairs two stimuli together in a person's memory (Werner et al.,2009). Based on Koenigs et al. (2008) study that a damaged hippocampus is not involved in reducing symptoms of PTSD, does the hippocampus serve a significant role in people with PTSD? Several studies have elucidated the role of the hippocampus in the development of PTSD. Bremner (2001) contends that damage to the hippocampus due to decreased dendritic branching and neuronal loss

can lead to increased probability of developing PTSD. He suggests that high stress levels during a traumatic event can release glucocorticoids that have been found to adversely affect the formation of new memories. Bremner (2001) found that sixty-nine percent of patients could be correctly diagnosed with PTSD based solely on analyzing hippocampal volume.

Werner et al. (2009) analyzed hippocampal functioning via fMRI in patients with PTSD during an associative learning task. The hippocampus is important for encoding associative stimuli; they hypothesized that patients with PTSD would show a deficit in learning compared to non-PTSD control. Overall, they found that patients with PTSD showed less activation in the hippocampus than Non-PTSD controls, but no differences in performance on memory as previous research suggests. Perhaps this was due to the small number of subjects (n=12) that did not allow appropriate statistical analysis. Therefore, this study suggests that hippocampal activation does not play a role in PTSD like with the amygdala. How does the overall hippocampal volume affect symptoms of PTSD in individuals?

Another study conducted by Felmingham et al. (2009) looked at the role of the hippocampus in subjects with PTSD. They found that reduced right hippocampal volume is associated PTSD patients. They controlled for depression since it has been found to correlate with reduced right hippocampal volume. Moreover, a reduction in volumes in parietotemporal and frontal lobes associated with subjects diagnosed with chronic PTSD. Felmingham et al. also examined time since a trauma and right hippocampal volume and their evidence is alarming. Their study suggests that as time passes since a traumatic event and symptoms of PTSD increase, volume decreases in the right hippocampus. This study is the first to report this negative and alarming relationship between persistent symptoms of PTSD and hippocampal volume. They suggest that there is, perhaps, neuronal plasticity in the hippocampus related to environmental stressors. They reason that this may be related to glucocorticoids causing cell atrophy or inhibition of neurogenesis that impacts overall volume of the hippocampus. This study supports the view that reduced hippocampal volume

predisposes people to PTSD and increases the duration because of the lack of neurological structure to triumph over symptoms of PTSD. Reduced hippocampal volume is another important individual difference that is associated with individuals with PTSD. They also suggest that people with PTSD are not as able to engage in extinction-learning in order to break the PTSD associative learning of traumatic events with triggers as non-PTSD diagnosed people.

Hayes et al. (2010) examined hippocampal activity related to combat-related PTSD. They found that reduced activity of the hippocampus was associated with high arousal symptoms of PTSD. This suggests that under high stress and arousal, the hippocampal activity is reduced. The hippocampus functions best under moderate levels of stress (Hayes et al., 2009). They reason that during this reduced activity, details of the traumatic memory are lost and only "gists" are recalled. They also suggest that glucocorticoids may play a role to reduce hippocampal activity. Thus, the hippocampus seems vulnerable to high levels of stress that seem to have deleterious effects on its memory functioning Vermetten, Vythilingam, Southwick, Charney and Bremner, (2003). With neural plasticity, can the reduction of glucocorticoids in the hippocampus increase its volume and reduce symptoms of PTSD?

Vermetten, et al., (2003) conducted a study that demonstrated a 4.6% increase is hippocampal volume with medication, paroxetine following a nine to twelve month regimen. This was the first study to demonstrate a reversal of volume in the hippocampus due to environmentally stress induced PTSD. However, symptoms of PTSD were not reduced but declarative memory was improved with PTSD subjects. This improvement in declarative memory may be more beneficial in reducing symptoms of PTSD with psychological treatments (Vermetten et al., 2003). Tronel and Alberini (2007) support the use of pharmacological treatment and psychological treatment to treat PTSD. They found that pharmacological treatments targeting the neurotoxic effects of glucocorticoids would allow for neurogenesis among structures in the limbic system. This regeneration will possibly allow for quicker psychological therapeutic interventions to reduce symptoms of PTSD (Tronel & Alberini, 2007).

Overall, neurobiological model of PTSD suggests dysfunctions and abnormalities of specific structures in the limbic lobe. The amygdala is overactive due to the lack of inhibitory control of the vmPFC via dense neural pathways of between these two structures. Reduced volume of the hippocampus plays a role in symptoms of PTSD. Studies have suggested that this may be due to stress hormones—glucocorticoids—that cause neural atrophy and inhibit neurogenesis, thereby, reducing hippocampal volume. These individual differences (overactive amygdala, smaller hippocampus) play an important role in who may exhibit symptoms of PTSD.

Psychological Treatments of PTSD

Based on the neurobiological model of PTSD, effective treatment of PTSD needs to incorporate the extinction of fear learning (Felmingham et al., 2007) and help patients cope with distorted memories of the traumatic event (Hayes et al., 2011). Tronel and Alberini (2007) suggest that PE follows the neurobiological model by enhancing the extinction of the previously conditioned fear. Milad et al. (2009) suggest that activation of amygdala, vmPFC, and hippocampus are necessary to extinguish a conditioned fear because it must first be accessed by the same system that initiated and then use counter-conditioning (relaxation) to, in effect, inhibit the old response. In Prolonged Exposure therapy (PE), clients do activate this system by eliciting the fear and pairing it with a non-aversive stimuli (i.e. relaxation, deep breathing, etc.).

Prolonged Exposure therapy (PE) was one of the first techniques to gain acceptance in literature as being an *evidenced-based treatment* of PTSD (Cukor, Olden, Lee, & Difede, 2010). Developed by Edna Foa, PE is considered the *gold standard* for cognitive behavioral therapy for treatment of PTSD (Cukor et al., 2010). PE is grounded in learning theory (Cukor et al., 2010). It is based on the notion that people with PTSD have problems with ‘extinction’ as it relates to memories of the traumatic event (Cukor et al., 2010). There is some debate on this issue. Rauch, Foa, Furr and Filip (2004) contend that a new trauma memory is developed to inhibit activation of the old fear structure associated with the current symptoms of PTSD. Nevertheless, PE

emphasizes various learning mechanisms associated with learning theory as well as addressing memory of the traumatic event.

An individual's response to trauma with PTSD does not decrease appropriately even when there is no longer a danger present (Cukor et al., 2010). This association between the memory of the crisis event and signal of danger is still very prevalent and pathological within the individual with PTSD (Rauch et al., 2004). This association has not been adequately diminished (Rauch et al., 2004). Therefore, PE attempts to diminish or inhibit this association using a variety of exposure methods: imaginal, or *in vivo* (Foa, Keane, Friedman & Cohen, 2009). "By facilitating habituation to the [traumatic] memory, decreasing avoidance, and eliminating associations of danger" (p. 83) a client can begin to extinguish their anxious responses (Cukor et al, 2010). Rauch et al. (2004) hold that new associations developed temporally as safety cues in the therapeutic environment to establish an inhibitory response of the pathological fear associated with the PTSD symptomatology (Rauch et al., 2004).

Initially PE treatment begins with clients developing an 'anxiety hierarchy' (Foa et al., 2009). Subjective Units of Distress (SUD) is a common approach to developing a fear (anxiety) hierarchy (Foa et al., 2009). Imaginal (imagery) exposure and *in vivo* are techniques used in PE that incorporate Subjective Units of Distress.

Imaginal technique begins with a client telling and retelling of the traumatic experience (Foa et al., 2009). A client addresses her/his traumatic *memories* by closing her/his eyes to increase the vividness and experiential nature while recounting the event (Foa et al., 2009). This retelling of the memory happens repeatedly during the time frame of multiple sessions (Cukor et al, 2010). Foa et al., (2009) state the client needs to tell the story using present tense verbs and focus on the shocking feelings of the trauma. The traumatic memories need to be processed in a rich, contextualized manner that addresses the "sensations, thoughts, beliefs, and especially the feelings" (Foa et al., 2009, p. 120). By previously scaling the SUD, the therapist can monitor the client's level of distress and progress throughout therapy, (Foa et al., 2009). Milad et al. (2009) proposed that activation of a fear network is needed in order for symptoms of

PTSD to be changed and reduced in therapy. Rauch, Foa, Furr, Filip (2004) found that high anxiety in early sessions of imaginal exposure successfully activated the fear structure related to the memory of trauma. Moreover, Rauch et al. (2004) found a significant reduction of anxiety from the first session to the sixth session, which suggests "a new trauma memory structure was formed that no longer contains the pathological associations that underlie anxious activation during imagery" (p. 464). The goal is to extinguish the conditioned reactions by providing a safe environment in therapy (Foa et al., 2009). Foa et al, (2009) contend that there is general consensus that non-reinforced exposure will lead to a reduction of anxious feelings that will enable a client to combat maladaptive cognitions (Foa et al, 2009).

What imaginal and *in vivo* techniques have in common is the exposure to "frightening yet realistically safe stimuli" (p. 143) that proceeds until the client's anxiety level is reduced (Foa et al., 2009). Most exposure-based treatments incorporate some form of relaxation training such as deep breathing or progressive muscle relaxation (Foa et al., 2009).

Clients undergoing PE for treatment of PTSD will fare better than 86% of other people treated with supportive counseling or comparable unstructured dialogue in counseling (Powers et al., 2010). These benefits are seen as "dramatic and enduring" (Powers et al., 2010). Considering the large effect size (g=1.06) for PE, it should be considered as the "treatment-of-choice" for therapists treating PTSD (Powers et al., 2010).

If there are abnormalities in the brain of someone who has PTSD, will there be changes in the brain structure of someone who has undergone Prolonged Exposure Treatment for PTSD? Essentially, can the brain rewire itself? Felmingham et al. (2007) conducted a study to answer the aforementioned question. They performed MRI's on subjects before and after an exposure-based treatment (i.e., Prolonged Exposure). Their study provides the first neuroimaging data of post-treatment PTSD subjects that suggests the brain *does* change after undergoing therapy. Specifically, their study suggests an increase in rACC (vmPFC) and reduced activity of the amygdala.

Remarkably, an increase of vmPFC and reduced activation of the amygdala is the opposite of what is found in people diagnosed with PTSD. Not only does this suggest that PE can reduce symptoms of PTSD, but it can alter neural pathways and activation sites in the brain. Essentially, the brains of post-treatment PTSD subjects look more like the brains controls of the previously mentioned subjects. Limitations of this study are the small sample size. Further investigation of the neural plasticity related to post-treatment subjects with PTSD is warranted. However, this study supports the prevailing neurobiological model of PTSD and how effective treatment that is in accord with this model can guide the practice of the clinician to provide effective treatment to ameliorate potentially debilitating symptoms of this disorder and change neural pathways of the brain.

Conclusion

PTSD is disorder affecting a person's emotional memories of a traumatic event. Three clusters of symptoms of people diagnosed with PTSD are: 1) continual re-experiencing the trauma, 2) hyperarousal, 3) avoidance of stimuli related to traumatic event. These symptoms can cause significant psychological distress and impact functioning of the brain. The neurobiological model of PTSD directs attention to the limbic system where certain abnormalities are apparent. Increased activation of the amygdala coupled with a hypoactive vmPFC seems to play a role in failure to extinguish a condition fear. Moreover, based on neuroimaging, reduced hippocampal size is evidenced in people with PTSD that may be the result of an increase of glucocorticoids—stress hormone—that may inhibit neruogenesis or cause neural atrophy that affects memory functions. Prolonged Exposure is an effective treatment of PTSD that directly helps clients cope with distorted memories and thoughts, conditioned fear, and other emotions related to the traumatic event. Moreover, there is burgeoning evidence of the neural plasticity of the brain for post-treatment patients of PTSD with Prolonged Exposure therapy that suggests neural and structural changes in the brain. Evidence suggests that counselors incorporating PE in the treatment of PTSD with their clients actually make structural changes in the brains of these clients that could perhaps

inoculate them against further development of symptoms of PTSD in the future. In light of this evidence, counselors' case conceptualization of PTSD is improved because it may no longer be seen as a client choosing to ruminate about a traumatic event, but a structural abnormality in the brain that a client cannot control. A counselor providing effective Prolonged Exposure therapy can help a client regain control of their thoughts and emotions by helping them make structural changes in their brain. Perhaps in the future, neuroimaging of the amygdala, vmPFC, and hippocampus can be used as a diagnostic tool for clinicians and doctors working with people suffering from PTSD.

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