Posttraumatic Stress Disorder

Neuroimaging of Hyperaroused and Dissociative States in Posttraumatic Stress Disorder

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Abstract: Posttraumatic stress disorder (PTSD) patients can have very different responses to recalling traumatic memories during neuroimaging. Pilot studies in our laboratory have shown that approximately 70 per cent of patients relived their traumatic experience and showed an increase in heart rate while recalling the traumatic memory. The other 30 per cent of patients had a dissociative response, with no concomitant increase in heart rate. The present paper reviews the neural correlates of these distinct responses.

Résumé : Neuroimagerie des états d’hyperexcitation et de dissociation dans le syndrome de stress post-traumatique

Les patients souffrant du syndrome de stress post-traumatique (SSPT) peuvent avoir des réactions fort différentes au rappel de souvenirs traumatiques durant la neuroimagerie. Des études pilotes menées dans nos laboratoires ont indiqué que quelque 70 % des patients revivaient leur expérience traumatique et présentaient une accélération du rythme cardiaque en se remémorant le souvenir traumatique. L’autre 30 % des patients avaient une réaction dissociative sans accélération du rythme cardiaque concomitante. Le présent article examine les corrélations neurales de ces différentes réactions.

Key Words: posttraumatic stress disorder, PTSD, dissociation, psychophysiology, anterior cingulated, functional magnetic resonance imaging, fMRI

Neuroimaging has become an important means of understanding the neurochemistry, as well as the functional changes, underlying various psychiatric disorders. Neuroimaging in posttraumatic stress disorder (PTSD) has focused primarily on examining neuronal activation patterns during the recall of traumatic material. Studies using positron emission tomography (PET) have attempted to elucidate which areas of the brain are involved in the recall of traumatic events. The goal of these studies has been to examine regional cerebral blood flow (rCBF) changes, using one of two paradigms: traumatic script-driven imagery symptom provocation or exposure to photographs or sounds reminiscent of the traumatic experience. Paralimbic structures that prior neuroimaging studies have implicated in the pathophysiology of PTSD include the medial prefrontal structures of the anterior cingulate (BA 24 and 32) and the subcallosal anterior cingulate (area 25), as well as the orbitofrontal cortex. While PET studies of combat- and sexual abuse-related PTSD using trauma-specific reminders have consistently implicated paralimbic structures, they have less consistently found specific regions to be activated (1–5).

There are several explanations for the discrepancies observed in the PTSD neuroimaging literature. A history of substance use is often observed in combat-related PTSD and can alter brain structure and functioning. The existing neuroimaging literature has also included subjects with multiple comorbidities, most notably major depression. This is especially important, because some of the brain areas thought to underlie PTSD may also contribute to the pathophysiology of depression (anterior cingulate gyrus and prefrontal cortex) (6). Data analyses in previous neuroimaging studies have not considered comorbidity profiles, which may explain some of the discrepancies observed in the literature. Finally, rather large variations in posttrauma intervals may account for some of the inconsistencies.

We have recently shown that responses to recalling traumatic experience in PTSD patients can differ significantly. Approximately 70 per cent of patients relived their traumatic experience and showed an increase in heart rate while recalling the traumatic memory (7). The other 30 per cent of patients had a dissociative response, with no concomitant increase in heart rate (8).

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Dissociation is a common feature of PTSD. Dissociation involves disruptions in the usually integrated function of consciousness, memory, identity or perception of the environment. Acute dissociative responses to psychological trauma have been found to predict the later development of chronic PTSD (9–13). Moreover, individuals who experienced acute dissociative responses to psychological trauma have been shown to develop a chronic pattern of dissociation in response to minor stressors or reminders of the original trauma (13). Bremner has hypothesized that there may be two subtypes of acute trauma response, one primarily dissociative and the other predominantly intrusive or hyperaroused that represent unique pathways to chronic stress-related psychopathology (1).

In our study, the neuronal circuitry underlying hyperaroused and dissociative responses in PTSD was studied using the script-driven symptom provocation paradigm adapted to functional magnetic resonance imaging (fMRI) at a four-Tesla field strength. We studied 18 subjects with PTSD related to sexual abuse or a motor vehicle accident and 11 control subjects who had a history of sexual abuse or motor vehicle accidents but who never developed PTSD. In the script-driven symptom provocation paradigm, patients construct a narrative of their traumatic experience. These narratives are later read to patients who are instructed to recall the traumatic memory as vividly as possible. During the recall of the traumatic memory, the patient undergoes a fMRI scan that measures the oxygen use of different brain areas.

Figure 1 demonstrates that, compared with control subjects, patients who had a hyperaroused response and relived their traumatic experience after being exposed to the traumatic script showed significantly less activation of the thalamus, the anterior cingulate gyrus (BA 32) and the medial frontal gyrus (BA 10,11), the occipital lobe (BA 19), and the inferior frontal gyrus (BA 47) (7). Lower levels of anterior cingulate activation and medial prefrontal activation were consistent with previous PET studies of sexual abuse-related and combat-related PTSD (5,1,2).

These patterns of brain activation are strikingly different from those observed in patients who dissociated in response to the traumatic script (8). Figure 2 shows that these patients exhibited higher levels of brain activation in the superior and middle temporal gyri (BA 38), the inferior frontal gyrus (BA 47), the occipital lobe (BA 19), the parietal lobe (BA 7), the medial frontal gyrus (BA 10), the medial prefrontal cortex (BA 9), and the anterior cingulate gyrus (BA 24 and BA 32).

In the group of patients who showed a hyperaroused response, alterations in thalamic activation may be attributable to high levels of arousal that can arise from recall of traumatic material. High levels of arousal during traumatic experiences have been hypothesized to lead to altered thalamic sensory processing (14). At extreme levels of arousal, incoherent sensory integration exists at the level of the thalamus, leading to a disruption of transmission of sensory information to the frontal cortex, cingulate gyrus, amygdala and hippocampus. This may be one mechanism underlying flashbacks in PTSD.

Activation in the superior and middle temporal gyri during dissociative states in PTSD is consistent with the temporal lobe hypothesis of dissociation. The epilepsy literature has described dissociative symptoms with seizures of various foci, including both right and left hemispheres (15,16). Penfield and Rasmussen have also reported depersonalization-like symptoms in response to stimulation of the superior and middle temporal gyrus during neurosurgery (17). Moreover, Teicher and others have explored the relation between early abuse and limbic system dysfunction as measured by the Limbic System Checklist-33 (LSCL) (18). This symptom checklist includes symptoms often experienced by people suffering from temporal lobe epilepsy. Results showed that LSCL-33 scores correlated well with the dissociative experience scale scores (18,19). Changes in brain activation of the superior and middle temporal gyri may therefore contribute to the dissociative responses experienced by the patients while recalling their traumatic experience.

Sierra and Berrios recently proposed a corticolimbic model of depersonalization (20). They postulated that depersonalization involves corticolimbic disconnection, such that left medial prefrontal activation, with reciprocal amygdala inhibition, results in hypoemotionality and decreased arousal, and right dorsolateral prefrontal cortex activation, with reciprocal anterior cingulate inhibition, leads to hypervigilance, attentional difficulties and emptiness of mental contents. In support of their model, Sierra and Berrios cited evidence for medial prefrontal involvement in both the monitoring and modulation of emotions (21,22). In this model, once a threshold of anxiety is reached, the medial prefrontal cortex inhibits emotional processing on limbic structures (the amygdala), which in turn leads to a dampening of sympathetic output and reduced emotional experiencing. Finally, several studies suggest that the prefrontal cortex has inhibitory influences on the emotional limbic system. These include PET studies showing a negative correlation between blood flow in the left prefrontal cortex and the amygdala (23,24). Our
findings partially lend support to the above model. The dissociative PTSD patients had increased activation in the dorsolateral prefrontal cortex (BA 9) and the medial frontal cortex (BA 10). They also did not exhibit increased amygdala activation. Increased activation of the medial prefrontal cortex may underlie the lack of autonomic response observed in these patients (8).

In summary, our results suggest that PTSD patients can have very different responses to traumatic script-driven imagery, which may shed light on key biological dimensions of the disorder. In our laboratory’s functional neuroimaging studies of PTSD, approximately 70 per cent of patients relived their traumatic experience and showed an increased heart rate while recalling the traumatic memory (7), while the other 30 per cent showed a dissociative response with no concomitant increase in heart rate. Interestingly, attempts to correctly classify PTSD cases using discriminant functions based on psychophysiological responses to reminders, including expected increased heart rate, have historically resulted in false-negative classifications in the range of 30 per cent or higher (25). Keane and colleagues (26) recently reported on the largest and most rigorous research of this kind, a multisite study of 1,168 Vietnam veterans, in which the best logistic model for predicting current PTSD status exhibited an approximately two-thirds rate of correct classification. The fMRI findings reported here add to the emerging evidence of experiential, psychophysiological and neurobiological differences among patients who have dissociative versus nondissociative responses to traumatic reminders. Our findings also suggest that different neuronal mechanisms may generate these two distinct reactions and, as Osuch has recently observed, that the heterogeneity of symptomatic and biological responses to traumatic reminders in PTSD should be addressed in the designs of functional imaging studies (27).
References


