

Neural systems for executive and emotional processing are modulated by symptoms of posttraumatic stress disorder in Iraq War veterans

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Abstract

The symptom-provocation paradigms generally used in neuroimaging studies of posttraumatic stress disorder (PTSD) have placed high demands on emotion processing but lacked cognitive processing, thereby limiting the ability to assess alterations in neural systems that subservise executive functions and their interactions with emotion processing. Thirty-nine veterans from Iraq and Afghanistan underwent functional magnetic resonance imaging while exposed to emotional combat-related and neutral civilian scenes interleaved with an executive processing task. Contrast activation maps were regressed against PTSD symptoms as measured by the Davidson Trauma Scale. Activation for emotional compared with neutral stimuli was highly *positively* correlated with level of PTSD symptoms in ventral frontolimbic regions, notably the ventromedial prefrontal cortex, inferior frontal gyrus, and ventral anterior cingulate gyrus. Conversely, activation for the executive task was *negatively* correlated with PTSD symptoms in the dorsal executive network, notably the middle frontal gyrus, dorsal anterior cingulate gyrus, and inferior parietal lobule. Thus, there is a strong link between the subjectively assessed behavioral phenomenology of PTSD and objective neurobiological markers. These findings extend the largely symptom provocation-based functional neuroanatomy to provide evidence that interrelated executive and emotional processing systems of the brain are differentially affected by PTSD symptomatology in recently deployed war veterans.

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1. Introduction

The mental health consequences of post-9/11 military deployments to Iraq and Afghanistan have garnered much attention (Miller, 2006). Large-scale studies have found significant deployment-associated neuropsychiatric

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morbidity, with posttraumatic stress disorder (PTSD) rates reported at 18–20% (Hoge et al., 2004), and cognitive impairment, notably for sustained attention (Vasterling et al., 2006). PTSD symptoms include the classic triad of (i) re-experiencing or re-living symptoms, (ii) emotional numbing or avoidance, and (iii) hypervigilance or hyperarousal (First et al., 1997). PTSD is also associated with several domains of cognitive impairment in executive processing, attention, verbal declarative memory, and autobiographical memory (Buckley et al., 2000; Danckwerts and Leatham, 2003).

Symptom-provocation paradigms involving script-driven imagery, or viewing trauma-related or other negatively valenced emotional scenes, have been used to characterize brain-activation patterns, particularly in frontolimbic regions often implicated in the emotion processing dysfunction of PTSD. For instance, when PTSD patients were compared with controls while viewing trauma-related and neutral pictures, patients had greater activation for combat pictures in the amygdala, cingulate cortex, occipitotemporal cortices, and inferior frontoparietal regions (Shin et al., 1997; Bremner et al., 1999b; Yang et al., 2004). In a comparison of fearful to neutral faces, PTSD patients had greater activation to fearful faces in the amygdala, dorsomedial prefrontal cortex (PFC), and posterior cingulate gyrus (Rauch et al., 2000; Shin et al., 2005; Williams et al., 2006). Studies using script-driven imagery have shown varied regional response patterns in frontolimbic regions, including increased activation in PTSD patients in the anterior temporal pole and inferior PFC but reduced activation in other regions such as the anterior cingulate, insula, and amygdala (Shin et al., 1999; Lanius et al., 2001, 2002, 2003a). Results in the orbitofrontal cortex show higher activity (Shin et al., 1999) whereas the ventromedial PFC show lower activity (Lanius et al., 2001; Shin et al., 2004, 2005).

In addition to emotional dysfunction, PTSD is also associated with reduced performance on executive and sustained attention tasks such as the Continuous Performance, Trails B, Digit Span, and Digit Symbol (Vasterling et al., 1998; Jenkins et al., 2000; Sachinvala et al., 2000). However, few neuroimaging studies have directly tested executive deficits in PTSD or the interplay of affective and cognitive processing. A study of the emotional counting Stroop task for combat versus neutral words found lower activation in the rostral anterior cingulate cortex (ACC) in the PTSD group (Shin et al., 2001). A subsequent study confirmed lower ACC activation in the PTSD group for the emotional Stroop condition, and lower activation in inferior parietal lobule, visual association cortex, and precuneus for the classic Stroop

condition (Bremner et al., 2004). An auditory continuous performance task study of patients with comorbid cocaine and alcohol abuse also found lower activity in rostral ACC (Semple et al., 2000). Converging support across symptom-provocation studies combined with neuropsychological assessment posits an inability of the PFC to inhibit a hyperresponsive limbic system in PTSD (Bremner et al., 1999b; Rauch et al., 2000; Shin et al., 2001).

Of particular interest is the relationship between severity of PTSD symptoms and central neural markers of executive and emotional functions. Positive correlations were reported for a trauma script condition with amygdala and anterior hippocampus activation, and negative correlations in the medial frontal gyrus and the ACC (Shin et al., 2004). Positive correlations for fearful versus happy faces were also found in the amygdala (Rauch et al., 2000; Shin et al., 2005). Finally, a negative correlation was reported between re-experiencing symptoms and ACC activity (Williams et al., 2006).

We have previously reported on the interplay of emotion processing and executive function in studies of healthy subjects using an emotional oddball paradigm (Yamasaki et al., 2002; Fichtenholtz et al., 2004; Wang et al., 2005) in which detection of a target geometric shape is interrupted by occasional task-irrelevant emotional and neutral distracters. Our earlier work demonstrated that executive and emotional functions are dissociated into parallel dorsal and ventral streams respectively, that extend into the PFC (Yamasaki et al., 2002; Fichtenholtz et al., 2004; Wang et al., 2005). Reciprocal engagement of these streams showed relative deactivation of the ventral frontolimbic regions during attentional target detection and relative deactivation of the dorsal frontoparietal regions during emotional picture processing. This reciprocal relationship between dorsal and ventral processing of executive and emotional functions may be biased towards emotional processing in patients with anxiety disorders (Drevets and Raichle, 1998), similar to that found in depression (Mayberg, 1997). Thus, our earlier work supports a model of emotion and attention processing that is well suited for investigating PTSD.

The aim of the present study was to investigate the relationship of executive and emotion-processing regions with severity of PTSD symptoms, and to assess whether the reciprocal relationship between activity in emotion and executive processing systems found in healthy adults (Drevets and Raichle, 1998; Yamasaki et al., 2002) would be a model that extended to subjects with PTSD symptoms. In the present study, the executive function block involved making a choice response to each of a short series of geometric shapes.

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