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Soldiers With Posttraumatic Stress Disorder See a World Full of Threat: Magnetoencephalography Reveals Enhanced Tuning to Combat-Related Cues

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ABSTRACT

BACKGROUND: Posttraumatic stress disorder (PTSD) is linked to elevated arousal and alterations in cognitive processes. Yet, whether a traumatic experience is linked to neural and behavioral differences in selective attentional tuning to traumatic stimuli is not known. The present study examined selective awareness of threat stimuli and underlying temporal-spatial patterns of brain activation associated with PTSD.

METHODS: Participants were 44 soldiers from the Canadian Armed Forces, 22 with PTSD and 22 without. All completed neuropsychological tests and clinical assessments. Magnetoencephalography data were collected while participants identified two targets in a rapidly presented stream of words. The first target was a number and the second target was either a combat-related or neutral word. The difference in accuracy for combat-related versus neutral words was used as a measure of attentional bias.

RESULTS: All soldiers showed a bias for combat-related words. This bias was enhanced in the PTSD group, and behavioral differences were associated with distinct patterns of brain activity. At early latencies, non-PTSD soldiers showed activation of midline frontal regions associated with fear regulation (90–340 ms after the second target presentation), whereas those with PTSD showed greater visual cortex activation linked to enhanced visual processing of trauma stimuli (200–300 ms).

CONCLUSIONS: These findings suggest that attentional biases in PTSD are linked to deficits in very rapid regulatory activation observed in healthy control subjects. Thus, sufferers with PTSD may literally see a world more populated by traumatic cues, contributing to a positive feedback loop that perpetuates the effects of trauma.

Keywords: Affect-biased attention, Attentional bias, Attentional blink, Beamforming, Magnetoencephalography (MEG), Posttraumatic stress disorder (PTSD), Soldiers

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Posttraumatic stress disorder (PTSD) is a trauma-related mental disorder with anxious and depressive features, resulting from exposure to one or more events involving actual or threatened death or serious injury. Although the clinical presentation varies, individuals suffering from this condition experience symptoms that include re-experiencing the traumatic event, avoidance of associated situations or stimuli, negative mood and appraisals, and elevated levels of arousal and reactivity (1). It is well documented that a traumatic experience can influence a wide range of cognitive processes [e.g., (2)]. Yet, it is still not known whether a history of traumatic experience is associated with specific patterns of selective attention that may influence how an individual literally sees the world and whether neural and behavioral indices of selective attention characterize PTSD. Here, we examined these questions by investigating patterns of perceptual awareness for combat-related stimuli in Canadian soldiers with and without diagnoses of PTSD, as well as in civilians, and used magnetoencephalography (MEG) to measure the temporal-spatial patterns of associated brain activation in the soldiers.

A body of evidence indicates there is preferential allocation of attention to trauma-related stimuli following a traumatic experience. Studies of trauma-related attentional biases indicate difficulty disengaging both spatial [for review, see (3)] and temporal (4) attentional resources from trauma-related stimuli. Other studies have found enhanced perception of trauma-related stimuli as measured by an increased signal-to-noise ratio in perception for both visual (5) and auditory (6) information. However, some studies have failed to find such attentional biases (7). The specificity of attentional biases for trauma-related stimuli or threat in general has also been questioned (8,9).

The attentional blink (AB) (10) is an experimental manipulation that effectively measures biases in rapid perceptual encoding and resulting awareness. The blink itself is a phenomenon where participants are typically unable to report

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a target stimulus when it is presented within ~500 ms of a previous target in a rapid stream of stimuli. There are a number of competing interpretations of the AB phenomenon, but one interpretation that has garnered empirical support is that it reflects a failure of attentional filters to consolidate the second target into working memory when it appears too quickly after the first, resulting in impaired perceptual awareness (11). When the second target (T2) is emotionally salient (e.g., RAPE vs. ROPE), there is a reduced blink or an emotional sparing (12–14). This emotional sparing can be seen as reflecting the relative robustness of selective attention for affective stimuli (15). Fear conditioning can also elicit AB sparing for conditioned stimuli, suggesting a link between emotional learning and enhanced perceptual awareness (16), and functional magnetic resonance imaging (fMRI) research has found sparing for conditioned stimuli in healthy control subjects to be mediated by coactivation between the amygdala and visual cortices (16). Further, in healthy adults, an MEG investigation of the temporal-spatial patterns of sparing for emotionally salient words found emotional sparing to be characterized by early activation in regions of the extended amygdalae followed by later activation in key frontal regions (17).

Individual differences in the degree of AB emotional sparing have been observed and may be influenced by temperament, genotype, and experience. Greater emotional sparing for threatening faces has been linked to higher levels of trait anxiety (18). Moreover, carrying a deletion variant of the *ADRA2B* gene influencing norepinephrine levels has been linked to higher levels of overall emotional enhancement of memory, including intrusive memory following trauma (19). Notably, the *ADRA2B* deletion variant is also associated with greater sparing for negatively valenced words (20). Such links between common genetic variations associated with intrusive traumatic memory, enhanced limbic activation linked to emotional sparing, and AB emotional sparing linked to threat provide convergent evidence suggesting PTSD may be associated with enhanced AB sparing for trauma-related cues.

Such enhanced AB sparing should also be related to distinct patterns of brain activity in PTSD. Although neuroimaging studies using different experimental tasks show mixed results, meta-analyses of fMRI data indicate that overall symptom provocation elicits greater activation in bilateral amygdalae, midcingulate cortex, and precuneus and reduced activation in ventromedial prefrontal cortex and frontoparietal control networks in participants with PTSD relative to control subjects (21,22). PTSD has also been linked to patterns of altered functional connectivity (23). Yet, rapidly occurring patterns of brain activity coupled with sorting salient from mundane stimuli in the AB, which may be crucially altered in PTSD, may not be captured by the slow time courses of positron emission tomography and fMRI.

The present study addressed the question of whether PTSD is linked to altered tuning of attentional filters to the visual environment under conditions of high visual competition. Here, we used MEG to examine the connection between PTSD, behavioral indices of AB emotional sparing for trauma-specific stimuli, and patterns of brain activation at a high temporal resolution. Combat veterans currently in the Canadian Armed Forces performed an AB task in the MEG scanner using combat-related and neutral words as the T2 stimuli. We predicted that AB performance would differentiate soldiers with and without PTSD, such that soldiers with PTSD would show greater AB sparing than soldiers without PTSD. For participants with no combat experience, the AB for combat-related words should not differ from that for neutral words. Based on evidence of altered structure and function of regulatory processes in PTSD, we predicted that control soldiers would show greater activation in regulatory regions of anterior cingulate cortex (ACC) in the presence of combat-related stimuli. Based on convergent evidence of the role of valuation networks in AB sparing and greater excitability of valuation networks in PTSD, we predicted that those with PTSD would show enhanced activation in nodes of valuation networks (amygdalae, orbitofrontal cortex), higher levels of visual cortex activity associated with emotional sparing, or both.

METHODS AND MATERIALS

Participants for the MEG study were active-duty service members from the Canadian Armed Forces. The initial sample included 24 soldiers diagnosed with PTSD (all male subjects; mean age = 37.7 years ± 6.8 SD; range 26–48 years) and 24 control soldiers (all male subjects; mean age = 32.9 years ± 4.6 SD; range 27–42 years). All participants were veterans of combat who had served in Afghanistan. At the time of MEG testing, 4 soldiers were excluded because of scanner incompatibility or unusable MEG data, leaving a final number of 22 soldiers with PTSD (mean age = 37.6 years; range 26–48 years) and 22 soldiers without PTSD (mean age = 32.4 years; range 27–40 years). We also collected behavioral data from an additional group of 18 age- and education-matched participants with no combat experience (all male participants; mean age = 28.05 years ± 5.84 SD; range 20–39 years) to serve as nonmilitary control subjects. These civilians were actively recruited from the hospital and university community for a separate study on traumatic brain injury and agreed to complete the behavioral version of the AB task.

Individuals with PTSD were diagnosed using a semistructured clinical interview for DSM-IV Axis I Disorders (American Psychiatric Publishing Inc., Arlington, Virginia), performed by a military psychiatrist according to Canadian Forces protocol. The diagnosis also included psychometric testing by a psychiatrist or psychologist at a Canadian Armed Forces Operational Trauma and Stress Support Centre and identified through clinicians at one of the Canadian Armed Forces Operational Trauma and Stress Support Centres (for details, see Supplement 1, and for demographic information, see Table 1). All testing was conducted in the MEG Lab at the Hospital for Sick Children and received institutional ethics approvals from both the Hospital for Sick Children and Defense Research and Development Canada. All participants gave informed written consent.

Neuropsychological and Clinical Assessments

All participants completed a short battery of neuropsychological tests as well as brief clinical assessments (Supplement 1). The tests, their means, and standard deviations for each group are contained in Table 1.