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Functional neuroimaging of emotionally intense autobiographical memories in post-traumatic stress disorder

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ABSTRACT

Post-traumatic stress disorder (PTSD) affects regions that support autobiographical memory (AM) retrieval, such as the hippocampus, amygdala and ventral medial prefrontal cortex (PFC). However, it is not well understood how PTSD may impact the neural mechanisms of memory retrieval for the personal past. We used a generic cue method combined with parametric modulation analysis and functional MRI (fMRI) to investigate the neural mechanisms affected by PTSD symptoms during the retrieval of a large sample of emotionally intense AMs. There were three main results. First, the PTSD group showed greater recruitment of the amygdala/hippocampus during the construction of negative versus positive emotionally intense AMs, when compared to controls. Second, across both the construction and elaboration phases of retrieval the PTSD group showed greater recruitment of the ventral medial PFC for negatively intense memories, but less recruitment for positively intense memories. Third, the PTSD group showed greater functional coupling between the ventral medial PFC and the amygdala for negatively intense memories, but less coupling for positively intense memories. In sum, the fMRI data suggest that there was greater recruitment and coupling of emotional brain regions during the retrieval of negatively intense AMs in the PTSD group when compared to controls.

1. Introduction

Neuroimaging studies of traumatic experiences in post-traumatic stress disorder (PTSD) and other disorders (e.g., Driessen et al., 2004; Lanius et al., 2001; Lanius et al., 2004) have observed consistent differences in regions that are frequently recruited during autobiographical memory (AM) retrieval (Cabeza & St. Jacques, 2007), such as the hippocampus, amygdala, and medial prefrontal cortex (PFC). Reduced volume of the hippocampus, a region critical for memory, is frequently observed in PTSD but it is less clear whether there are also functional changes here (Shin et al., 2006). The amygdala, a region critical in the detection of emotion and the generation of physiological response, is hyperactive during negative emotional tasks in PTSD patients and the level of activity here is associated with the severity of symptoms (Etkin and Wager, 2007; Shin et al., 2006). In contrast, the medial PFC, a region associated with controlled emotional processes, is often hypoactive in PTSD patients (Etkin and Wager, 2007; Shin et al., 2006). Moreover, changes in the coupling between the amygdala and medial PFC may underlie emotional dysregulation symptoms in PTSD (Etkin and Wager, 2007; Frewen and Lanius, 2006; Milad and Rauch, 2007; Shin et al., 2006). Confirming the critical role of the amygdala and medial PFC in the pathogenesis of PTSD, a patient study by Koenigs and colleagues (Koenigs et al., 2008) found that isolated lesions to these brain regions were related to reduced occurrence of PTSD in Vietnam War veterans.

The effect of PTSD on brain regions involved in AM suggests that a broader examination of personal memory beyond traumatic experiences is warranted (Lanius et al., 2003). Moreover, in participants with PTSD or high levels of symptom severity, the effects of emotional reactions extend beyond traumatic memories to word-cued, important but non-trauma related, and positive autobiographical memories (Rubin et al., 2008b). Thus, although PTSD diagnosis relies on a single traumatic event the impact of PTSD is more widespread across AM. Little, however, is known about the neural basis of these effects.

In the present study, we investigate the neural mechanisms affected by PTSD symptoms during retrieval of a large sample of emotionally intense AMs. We employed a generic cue method that

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used emotional words to elicit AMs in order to distinguish early construction and later elaboration phases of retrieval. Further, we acquired online ratings of emotional experience for parametric analysis of functional activations associated with emotionally intense memories. We explored the hypothesis that PTSD would involve reduced recruitment of the hippocampus, increased recruitment of the amygdala and reduced recruitment of the medial PFC when recalling emotionally intense AMs.

2. Methods

2.1. Participants

Young adult participants were recruited from Duke University (18–35 years of age). Participants in the control group were recruited from a database of healthy young adults, who had participated in previous fMRI research studies. Inclusion criteria for the control group followed procedures that we have routinely used in behavioral studies in the Durham Veteran's Association Medical Clinic (VAMC), which do not include having had a previous trauma. This allowed us to examine the effect of PTSD versus a control group that was a random sample rather than one that was resilient to PTSD. Participants in the PTSD group were recruited from advertisements seeking volunteers who had experienced a traumatic memory and from a pre-screen test administered during a large group screening. The Clinician Administered PTSD Scale (CAPs) was used to determine PTSD diagnostic status in this group (Blake et al., 1995; Weathers et al., 2001). All participants in the PTSD group met the DSM-IV-TR criterion as measured by highly trained master's level clinicians who were experienced in giving the CAPS in a research setting at the Durham VAMC. There were nineteen participants in each group. All participants reported that they were not taking medication known to affect cognitive function (e.g., antidepressants, benzodiazepines, or any other psychiatric medication). The investigation was carried out in accordance with the latest version of the Declaration of Helsinki, and participants gave written informed consent for a protocol approved by the Duke University Institutional Review Board. Five controls and four participants in the PTSD group were excluded from the analyses because of technical issues (e.g., no key responses recorded) or problems with completing the task as instructed (e.g., falling asleep, not following instructions). Thus, the reported results are based on data from fourteen controls (7 females; mean Age = 24.43, *SD* = 3.73) and fifteen PTSD (11 females; mean Age = 22.21, *SD* = 4.23) participants, except where noted.

Demographic and psychometric data (see Table 1) were obtained in a separate session within one week of the scanning session. As expected, the PTSD group had higher scores on the PTSD Check List (PCL; Weathers et al., 1994) when compared to the control group. The PTSD group also had higher scores on the Beck Depression Index (BDI-II; Beck et al., 1996). There were no group differences in the age, number of years of education, the Weschler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999), verbal fluency (FAS), or categorical fluency (animal names and supermarket items).

Table 1
Participant variables by group.

	M		SD		t (27)
	Controls	PTSD	Controls	PTSD	
Age (years)	24.43	22.21	3.73	4.23	1.47
Education (years)	16.50	14.70	2.28	2.56	1.95
PCL[†]	27.93	49.00	7.99	12.94	−5.19*
BDI	3.93	16.86	3.29	11.00	−4.22*
WASI-full IQ	122.36	121.50	7.66	10.14	0.25
WASI-verbal IQ	120.93	123.93	7.87	11.44	−0.81
WASI-performance IQ	118.14	114.72	7.49	10.17	1.01
Verbal fluency	47.43	51.36	10.87	10.49	−0.97
Categorical fluency	23.57	27.50	6.69	6.00	−1.63

*$p < .001$.
[†] df = 26.

2.2. Materials

Memory cues consisted of 60 emotionally arousing words selected from the affective norms for English words (ANEW) database (Bradley and Lang, 1999), such that there were 30 positive (Valence mean = 7.93, *SD* = 0.45; Arousal Mean = 5.96; *SD* = 0.83) and 30 negative (Valence Mean = 2.17, *SD* = 0.52; Arousal Mean = 6.00; *SD* = 1.03) words that were equally arousing. In order to create auditory cues the words were recorded in a female voice and constrained to an equal duration of 1 s.

2.3. Procedure

The procedure was similar to Daselaar et al. (2008); (also see Greenberg et al., 2005). During scanning participants were asked to search for AMs triggered by the auditory cue words. Participants were instructed to retrieve an AM with specific spatiotemporal coordinates. They indicated when a specific AM was found by making a response on the button-box and then continued to elaborate on the retrieved event in as much detail as possible for the rest of the trial. Thirty seconds following the onset of the auditory cue participants were given auditory instructions to rate the amount of emotion (negatively arousing to positively arousing) and reliving (low to high) associated with the memory on an 8-point scale. Rating responses were self-paced (up to 6 s) and separated by at least 0.5 s, and the order was counterbalanced between participants. There were 6 functional runs, with 10 memory cues in each run (5 positive words and 5 negative word), and an inter-trial interval at least 1.5–7.5 s. Participants were instructed to keep their eyes closed for the duration of each run so that any potential effects of visual imagery were not confounded by external attention to the stimulus.

Immediately following the scanning session participants were asked to provide a short title for the memory retrieved during scanning and to answer additional questions on a subset of the AM questionnaire (e.g., Rubin et al., 2003). Participants were asked to *date* when the event had occurred (e.g., last day to > 10 years ago), to indicate the amount of *vividness* or how clearly the event was remembered, the *perspective* or whether the memory was seen through their own eyes or through the eyes of an outside observer, the *significance* of the memory, and the *physiological* response during retrieval (e.g., heart pounding, etc.). Also, given that AM comprises different types of events (Brewer, 1986) we asked participants to indicate whether the type of memory retrieved was a unique event (referring to a particular time and place), repeated event (memory for an event with multiple occurrences), extended event (occurring longer than one day), or semantic information (long-standing facts about one's own life) (Williams, 1995).

Within two days of the scanning session, participants returned for an additional session in which they were cued by the title they had provided following the scanning session and asked to verbally recall the memories retrieved during scanning. A coder rated the narrative descriptions to determine whether they referred to the event the participant identified as a stressful experience on the PCL. A narrative was rated as referring to a PCL event if it specifically described the event (e.g., "the car flipped three times" if the given event was "car accident") or if it made reference to the event (e.g., "that happened right after the accident"). PCL-related memories