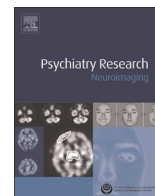




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Altered processing of visual emotional stimuli in posttraumatic stress disorder: an event-related potential study

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ABSTRACT

Patients with posttraumatic stress disorder (PTSD) display abnormal emotional processing and bias towards emotional content. Most neurophysiological studies in PTSD found higher amplitudes of event-related potentials (ERPs) in response to trauma-related visual content. Here we aimed to characterize brain electrical activity in PTSD subjects in response to non-trauma-related emotion-laden pictures (positive, neutral and negative). A combined behavioral-ERP study was conducted in 14 severe PTSD patients and 14 controls. Response time in PTSD patients was slower compared with that in controls, irrespective to emotional valence. In both PTSD and controls, response time to negative pictures was slower compared with that to neutral or positive pictures. Upon ranking, both control and PTSD subjects similarly discriminated between pictures with different emotional valences. ERP analysis revealed three distinctive components (at ~300, ~600 and ~1000 ms post-stimulus onset) for emotional valence in control subjects. In contrast, PTSD patients displayed a similar brain response across all emotional categories, resembling the response of controls to negative stimuli. We interpret these findings as a brain-circuit response tendency towards negative overgeneralization in PTSD.

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1. Introduction

Emotions are response-dispositions that are typically accompanied by physiological and behavioral changes, and can be coded on a dimensional scale of valence, i.e., positive to negative (Nesse and Ellsworth, 2009). Disrupted emotional reactivity and modulation are central features of post-traumatic stress disorder (PTSD), with symptoms such as intrusive memory, trauma flashbacks and avoidance of stimuli, persistent hyper-arousal and hyper-vigilance (American Psychiatric Association, 2013) reflecting impaired perceptual, attentional, and emotional-memory processes.

Studies in healthy controls have been conducted to identify the chronology of normal emotional processing and neurophysiological mechanisms underlying the perception of emotional stimuli. These studies have used high temporal resolution event-related

potentials (ERPs) to distinguish voluntary attention (i.e., attention that is voluntarily directed towards a stimulus) from spontaneous attention (i.e., attention that is attracted by a stimulus) to emotionally negative information during different stages of perceptual identification. Specifically, studies support a modulatory effect of negative emotion on early visual perception and attention, associated with augmentation of the visual occipital P1 component of the ERP at ~100 ms post-stimulus. Emotional processing has also been reported to be associated with increased early posterior negativity (EPN, at ~200–300 ms post-stimulus), late positive potential (LPP, occurring at latencies larger than 300 ms post-stimulus), and a sustained positive slow wave as compared with neutral contents (see reviews by Schupp et al., 2006; Olofsson et al., 2008).

ERP studies probing specifically for emotional processing abnormalities in PTSD are surprisingly limited in number and were mainly directed to test P300 abnormalities to trauma-related material. Applying a modified Stroop paradigm using personal-traumatic, personal-positive, and neutral words, Metzger et al. (1997b) tested the emotional interference effect in PTSD patients

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Table 1
Demographics and characteristics of PTSD subjects

Subject	Sex	Age (years)	Education (years)	Trauma	Medications	Bodily physical injury	Head physical injury
1	M	45	12	Work related	Venlafaxine 150 mg/d	No	No
2	M	24	12	Fall from height	None	No	No
3	M	25	12	MVA	None	No	No
4	M	37	15	Military related	None	No	no
5	M	37	12	Assault	Paroxetine 20 mg/day	Yes-mild	No
6	F	22	12	MVA	None	No	Lt. frontoparietal contusion
7	M	48	12	MVA	Paroxetine 20 mg/day	Yes	No
8	M	37	12	Military related	Paroxetine 20 mg/day	Yes	No
9	M	51	10	Fall from height	Bonserine 30 mg/day	No	No
10	F	31	15	MVA	None	No	No
11	M	23	12	MVA	Paroxetine 20 mg/day	Yes	No
12	M	26	15	Military related	Sertraline 100 mg/day	No	No
13	F	40	12	MVA	None	Yes	No
14	F	18	12	MVA	None	Yes	No

Note. Data are reported for the PTSD patients who participated in the study; MVA=Motor Vehicle Accident. Lt. = left.

versus controls. Individuals with PTSD had a significantly reduced and delayed P300 across word types, as well as a slower response time (RT), especially for traumatic words. In the same study frontal P300 amplitudes were larger to both personal-positive and personal-traumatic words as compared with neutral words across groups. In a study that applied the oddball paradigm, P300 amplitudes to emotionally meaningful words were significantly related to PTSD symptoms, in particular avoidance and arousal (Blomhoff et al., 1998). Attias et al. (1996) applied a modified oddball paradigm in which subjects were requested to discriminate between animal pictures (targets), emotionally neutral pictures (trauma-irrelevant non-targets), and combat-related pictures (trauma-irrelevant non-target probes). The authors reported target stimuli (as compared with trauma-irrelevant non-targets) evoked accentuated P300 amplitudes in both controls and PTSD patients while non-target combat-related probes (as compared with trauma-irrelevant non-targets) elicited enhanced P300 and N100 amplitudes in the PTSD group only. Stanford et al. (2001) also used a modified oddball paradigm to compare Vietnam-war veterans with and without PTSD. The results revealed that PTSD patients demonstrated attenuated P300 response to neutral targets and increased responsiveness to trauma-relevant combat stimuli but not to trauma-irrelevant social-threat stimuli at frontal regions.

The preponderance of the evidence (mostly based on the oddball paradigm or a modification of it) supports the view that PTSD patients show sensitization of the P300 response specifically to trauma-related stimuli and a diminished response to neutral stimuli. Nevertheless, there are reports of non-emotional information-processing impairments in PTSD, with studies demonstrating impaired cognitive processing at early (Gillette et al., 1997; Neylan et al., 1999; Skinner et al., 1999; Ghisolfi et al., 2004; Holstein et al., 2010; Gjini et al., 2013) as well as mid-late (Paige et al., 1990; McPherson et al., 1997; Metzger et al., 2002) temporal stages. Assessment of P300 non-emotional information-processing impairments in PTSD has mainly been conducted with an auditory or visual oddball design, with studies reporting lower amplitude and longer latency P300 components in this population (McFarlane et al., 1993; Charles et al., 1995; Metzger et al. 1997a, b; Kimble et al., 2000; Felmingham et al., 2002; Araki et al., 2005; Veltmeyer et al., 2005). These findings have also been reported when using the "Go/NoGo" paradigm, with studies reporting longer latency P300 in the NoGo trials and higher P300 amplitudes in non-target trials in PTSD populations (Shucard et al., 2008). Together, these studies indicate the presence of an altered cognitive pattern of selective attention processing in early as well as late temporal stages in PTSD in addition to a vulnerability to traumatic

reminiscences. In the current study, we aimed to test the hypothesis that abnormal emotional responsiveness in early as well as late stages of stimuli processing in PTSD is evident even for non-trauma-related context using an emotional valence choice-response task. We hypothesized that abnormal emotional responsiveness would be reflected in altered brain electrical activity, as measured via ERPs. Specifically, we hypothesized that (1) the response to negative stimuli in PTSD would be altered as compared with positive/neutral stimuli, and (2) that PTSD patients would show higher amplitudes for negative stimuli as compared with control subjects.

2. Methods

2.1. Subjects

The results reported in this study are part of a larger study exploring genetic, physiological, anatomical and cognitive characteristics of PTSD patients recruited from the mental trauma clinic at Soroka University Medical Center. All patients (46 in total) were interviewed using the Clinician Administered PTSD Scale (CAPS) by a trained psychiatrist. Of those, 14 patients with extremely severe PTSD, as determined by a CAPS score ≥ 80 (Weathers et al., 2001), participated in the current study. Fourteen control subjects with no psychiatric records and/or major traumatic experience/other trauma-related disorders were recruited for the current study. All participants (PTSD patients and controls) were recruited on a voluntary basis and were not compensated for participation. Exclusion criteria for all subjects included head trauma, preexisting neuro-psychiatric disorders, alcohol abuse or use of illicit drugs. Subject characteristics were as follows: mean age (years), 33.14 ± 10.11 SD and 26.14 ± 3.33 SD, mean education (years) 12.50 ± 1.45 and 15.64 ± 2.27 , 10 and 9 males, for PTSD and controls, respectively (for full description of subject characteristics, see Table 1). All procedures were approved by the Soroka University Medical Center institutional review board. Written informed consent was obtained from all participants.

2.2. Emotional paradigm

Pictures from the International Affective Picture System (IAPS, Center for the Study of Emotion and Attention [CSEA-NIMH], 1995, University of Florida, Gainesville, FL, USA) ranked on a valence scale [from 1 (positive) to 9 (negative)] were sorted into three groups on the basis of positive, negative, or neutral emotional content. To ensure that the hypothesized effects were not a

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