



Atypical visual processing in posttraumatic stress disorder



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ABSTRACT

Background: Many patients with Posttraumatic Stress Disorder (PTSD) feel overwhelmed in situations with high levels of sensory input, as in crowded situations with complex sensory characteristics. These difficulties might be related to subtle sensory processing deficits similar to those that have been found for sounds in electrophysiological studies.

Method: Visual processing was investigated with functional magnetic resonance imaging in trauma-exposed participants with (N = 18) and without PTSD (N = 21) employing a picture-viewing task.

Results: Activity observed in response to visual scenes was lower in PTSD participants 1) in the ventral stream of the visual system, including striate and extrastriate, inferior temporal, and entorhinal cortices, and 2) in dorsal and ventral attention systems ($P < 0.05$, FWE-corrected). These effects could not be explained by the emotional salience of the pictures.

Conclusions: Visual processing was substantially altered in PTSD in the ventral visual stream, a component of the visual system thought to be responsible for object property processing. Together with previous reports of subtle auditory deficits in PTSD, these findings provide strong support for potentially important sensory processing deficits, whose origins may be related to dysfunctional attention processes.

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1. Introduction

Posttraumatic Stress Disorder (PTSD) is a serious condition that can develop in the aftermath of a traumatic event. The disorder has a substantial impact on quality of life and functioning (Zatzick et al., 1997). Despite therapeutic advances over the past two decades, PTSD remains a rather treatment refractory condition (Bradley et al., 2005). Current classification schemas, including DSM-5 (American Psychiatric Association, 2013) and ICD-10 (World Health Organization, 2010), define PTSD based on symptoms of persistent re-experiencing of traumatic memories, avoidance of stimuli reminiscent of the traumatic event, negative cognition and mood, and increased arousal. In addition to these core

features, PTSD patients often present with a range of other symptoms such as dissociation, included now in DSM-5 as a PTSD subtype, and medically unexplained symptoms including pain, gastrointestinal complaints, chronic fatigue, and visual problems (Engel et al., 2000; Foa et al., 2006; McFarlane, 2010; Pacella et al., 2013; Trachtman, 2010; Wolf et al., 2012).

Many PTSD patients feel overwhelmed or insecure in situations with high levels of complex sensory input, including large crowds, heavy traffic, large cities, public transportation, or crowded shopping malls. Electrophysiological methods have identified sensory processing disturbances at early, relatively automatic processing stages (Ge et al., 2011; Holstein et al., 2010; Hunter et al., 2011) that are thought to underlie hyperarousal symptoms in PTSD (Clark et al., 2009; Newport and Nemeroff, 2000). Further evidence for visual system dysfunction in PTSD patients are reports of feeling flooded and overwhelmed by multiple, simultaneous sensory stimuli, and experiencing lights or noises as unusually intense (Stewart and White, 2008). These puzzling symptoms are not fully subsumed under the hyperarousal cluster in DSM-V (American Psychiatric Association, 2013), and PTSD patients frequently struggle to articulate and understand these phenomena.

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Both electrophysiological and magnetoencephalographic studies have provided preliminary evidence for atypical visual processing following traumatic experiences, evidenced by reduced occipital responses to neutral or angry faces (Felmingham et al., 2003), and positive or negative scenes (Adenauer et al., 2010, 2011; Catani et al., 2009) in PTSD compared to trauma-exposed and non-trauma-exposed healthy individuals. Structural imaging studies have demonstrated reduced regional gray matter volume in visual cortex in both individuals with PTSD (Chao et al., 2012; Zhang et al., 2011) and adult survivors of child sexual abuse (Tomoda et al., 2009, 2012), suggesting the possibility of lasting macrostructural alterations in regions specialized for visual processing. However, functional imaging studies in PTSD employing visual stimuli have primarily focused on the contrast between processing of pictures with either emotional or neutral valence (Bremner et al., 1999; Brunetti et al., 2010; Chao et al., 2012; Fani et al., 2012; Hendler et al., 2003; Hou et al., 2007; Phan et al., 2006; Shin et al., 1997, 2005; Williams et al., 2006). Concerning visual cortex, these studies have yielded inconsistent results, showing lower (Fani et al., 2012), higher (Bremner et al., 1999; Williams et al., 2006) or comparable (Brunetti et al., 2010; Chao et al., 2012; Hendler et al., 2003; Hou et al., 2007; Phan et al., 2006; Shin et al., 1997, 2005) activity in PTSD in response to threat-related and trauma-related visual stimuli. Because these studies (with one exception discussed below) did not test general visual processing by contrasting picture with non-picture conditions, they may have failed to detect atypical, more general visual processing abnormalities in PTSD. In this fMRI study we asked PTSD patients and trauma-exposed healthy controls to view pictures with varying emotional contents and found substantial reductions in task related activity in the ventral visual processing stream, perhaps related to atypical modulation by both dorsal and ventral attention systems. Surprisingly, these reductions were unrelated to the pictures' emotional content.

2. Method

2.1. Participants

Participants were right-handed (Oldfield, 1971), trauma-exposed (meeting DSM-IV criteria A1) individuals with ($N = 18$) and without ($N = 21$) a current DSM-IV PTSD diagnosis as assessed using the Clinician-Administered PTSD Scale (CAPS) (Blake et al., 1995). A CAPS score of greater than 50 was required for PTSD participants and less than 34 for trauma-exposed controls. Trauma history was assessed using the CAPS, the trauma checklist from the Posttraumatic Diagnostic Scale (PDS) (Foa et al., 1997), and the Childhood Trauma Questionnaire (CTQ) (Bernstein et al., 2003). No PTSD participant had a current comorbid dissociative disorder assessed using the Structured Clinical Interview for DSM-IV Dissociative Disorders-Revised (SCID-D-R) (Steinberg, 1994). Current Axis I disorders, assessed using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I), are presented in Table 1. All participants were free of neurological or other major medical conditions. Two PTSD participants and two trauma-exposed controls had a history of mild traumatic brain injury according to standard criteria (Kay et al., 1993). No participant had substance dependence except for two PTSD participants who had suffered from alcohol dependence two and 15 years ago. Seven PTSD participants and one trauma-exposed control were currently medicated with antidepressants, including selective serotonin or noradrenaline reuptake inhibitors. Six PTSD participants were taking medication as follows: a non-opioid analgesic ($N = 1$), an antiretroviral ($N = 1$), thyroid substitutes ($N = 2$), a calcium channel blocker ($N = 1$), and an anti-asthmatic ($N = 1$). One trauma-exposed control took an angiotensin II receptor antagonist.

Participants with PTSD were recruited from the psychiatric outpatient department of the University Hospital of Zurich and the Psychiatric Services of the County of St. Gallen-North, Switzerland, from individual local psychotherapists, and by advertisement. Trauma-exposed controls were recruited by advertisement.

Prior to scanning, participants completed the CTQ (Bernstein et al., 2003), Multidimensional Inventory of Dissociation (MID) (Dell, 2006), the trait portion of the State-Trait Anxiety Inventory (STAI) (Spielberger et al., 1970) and the Beck Depression Inventory (BDI) (Beck et al., 1961). Standard cognitive tests were administered using Hogrefe Test System 4 software (Hogrefe, 2006) and included the Viennese Matrices Test (Formann and Piswanger, 1979), an adapted version of the Raven Progressive Matrices (Raven, 1947), the Test of Word Power (Schmidt and Metzler, 1992), and the d2 Test of Attention (Brickenkamp and Zillmer, 1998). Immediately prior to scanning, participants completed the state portion of the STAI (Spielberger et al., 1970). All measures were German-adapted and validated versions. Socio-demographic and clinical data are presented in Table 1. The study protocol was approved by the Institutional Review Board of the County of Zurich, Switzerland. This study was carried out in accordance with the Declaration of Helsinki, and all participants provided written informed consent after full explanation of the procedures.

2.2. Task procedures

The participants engaged in a picture viewing task in which they were instructed to press a button when a picture containing a human being or human body part was shown. This response requirement was included only to direct the participant's attention to the presented pictures and to prevent behavioral avoidance such as eye closing. The task was not designed to investigate cognitive performance; consequently, response speed was not emphasized in the participants' instructions. Using images containing humans or human body parts as targets was motivated by practical reasons, because these targets could be unambiguously and easily categorized.

A total of 48 IAPS pictures spanning a range of emotional content (valence: mean = 4.8, SD = 2.1, range = 1.7–8.3; arousal: mean = 4.8, SD = 1.8, range = 1.7–7.3) were presented. Each of three identical sessions consisted of two sequences comprising non-repeating IAPS pictures with comparable normative ratings for valence and arousal. Each sequence consisted of three 30 s blocks containing neutral, positive, or negative pictures, with each block separated by a 30 s fixation point. In each block, 8 different pictures were presented for 400 ms with each picture presented twice in rapid succession (inter-stimulus interval = 400 ms) to make the stimulus more "salient", followed by a variable inter-trial-interval of 2300–2800 ms. Thus, even though we utilized homogeneous stimulus blocks, the subsequent statistical modeling was consistent with rapid event related designs.

At the end of each sequence, cognitive and emotional self-reports referencing the previous task were collected using a 5-point Likert scale ("not at all" to "very much so") with one item each for hypervigilance ("I felt vigilant"), numbing ("I felt emotional numb"), re-experiencing ("I experienced a flashback"), depersonalization ("My body felt vague, indefinite, strange"), derealization ("I felt far away from what was happening around me") and somatoform dissociation ("I was unusually weak or paralyzed in one or more of my muscles"). The hypervigilance and numbing items were constructed according to DSM-IV PTSD criteria; the remaining four items were selected and adapted from the State Scale of Dissociation (Krüger et al., 2002), a 56-item scale that measures distinct dimensions of state dissociation, according to the results of a validation study of the German adaptation of the scale (Mueller-Pfeiffer and Wittmann, 2013). In contrast to the SSD, which uses a 10-point scale, we used a 5-point scale in order to allow collection of responses in the scanner using a 5-digit response unit (Fiber Optic Button Response System, Psychology Software Tools, Inc., Pittsburgh, PA).

After the picture viewing fMRI session, the IAPS pictures were again presented to the participants outside the scanner and they were asked to rate the emotional valence and arousal of each picture using the Self-Assessment Manikin, a 9-point, non-verbal pictorial assessment technique for measuring affective reactions to stimuli (Bradley and

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