Journal of Psychiatric Research 47 (2013) 1492–1498

Contents lists available at SciVerse ScienceDirect

Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/psychires

Evoked potential correlates of Post-Traumatic Stress Disorder in refugees with history of exposure to torture☆

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ARTICLE INFO

Article history:
Received 1 May 2013
Received in revised form
12 June 2013
Accepted 14 June 2013

Keywords:
Post-Traumatic Stress Disorder
PTSD
Evoked potentials
Sensory gating
Visual
Auditory

ABSTRACT

The presence and magnitude of information processing deviations associated with Post-Traumatic Stress Disorder (PTSD) are far from being well-characterized. In this study we assessed the auditory and visually evoked cerebral responses in a group of Iraqi refugees who were exposed to torture and developed PTSD ($N = 20$), Iraqi refugees who had been exposed to similar trauma but did not develop PTSD ($N = 20$), and non-traumatized controls matched for age, gender, and ethnicity ($N = 20$). We utilized two paired-stimulus paradigms in auditory and visual sensory modalities, respectively. We found significantly smaller amplitudes of both the auditory P50 and the visual N75 responses in PTSD patients compared to controls, reflecting decreased response to simple sensory input during a relatively early phase of information processing (interval 50–75 ms post stimulus). In addition, deficient suppression of the P50/N75 response to repeating stimuli at this early stage in both modalities is indicative of difficulty in filtering out irrelevant sensory input. Among associations between electrophysiological and clinical measures, a significant positive correlation was found between dissociation score and P50 S1 amplitudes ($p = 0.024$), as well as stronger auditory P50 gating correlated with higher quality-of-life index scores ($p = 0.013$). In addition, smaller amplitudes of N150 visual evoked response to S1 showed a significant association with higher avoidance scores ($p = 0.015$). The results of this study highlight the importance of early automatic auditory and visual evoked responses in probing the information processing and neural mechanisms underlying symptomatology in PTSD.

1. Introduction

Information processing (IP) deviations associated with PTSD have not yet been fully explored utilizing evoked potential (EP) techniques. Evidence from the limited available literature is suggestive of IP deviation in PTSD (Javanbakht et al., 2011). These abnormalities are clinically presented as difficulties in encoding information, inhibiting distracting stimuli, as well as deficits in attention, emotional processing and working memory (Liberzon and Martis, 2006; Vasterling et al., 1998, 2002; Tso et al., 2011).

Sensory gating is a filtering mechanism which protects higher cortical centers from flooding by irrelevant sensory information (Venables, 1964). Healthy individuals can efficiently filter out repeating irrelevant auditory and visual information (Adler et al., 1982; Gjini et al., 2008), which reflects the brain's capability to selectively regulate its sensitivity to incoming sensory stimuli and thus direct processing resources to perceptually more important or salient environmental stimuli (Cromwell et al., 2008; Davies et al., 2009). Three auditory evoked potential (EP) components are commonly used to examine sensory gating during the mid-latency phases of IP as part of the paired-click protocol (Boutros et al., 2004): P50, N100, and the P200. P50 is a positive deflection with a latency of about 50 ms from the onset of auditory stimuli, N100 is a negative deflection peaking at about 100 ms and P200 waveform is a positive deflection peaking about 200 ms post stimulus presentation. Paired-click paradigms consist of two identical clicks (S1 = S2) presented in pairs with a short inter-stimulus interval of 500 ms and an inter-pair interval of 8–10 s. The longer inter-pair interval is necessary to assure that the effects of one pair of

☆ Data were collected at the Clinical Electrophysiology Laboratory, Wayne State University, Detroit, MI, USA.

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http://dx.doi.org/10.1016/j.jpsychires.2013.06.007

stimuli do not carry over to the next pair (Zouridakis and Boutros, 1992). A significant reduction in the amplitudes of P50, N100, and P200 response to the second stimulus (S2) in the pair compared to the first one (S1) is observed in healthy participants reflecting an effective filtering mechanism of repeating irrelevant auditory information.

A sensory gating dysfunction during the early and pre-attentive P50 phase of auditory IP has been reported in the literature in association with PTSD (Hunter et al., 2011; Ghisolfi et al., 2004; Metzger et al., 2002; Gillette et al., 1997; Neylan et al., 1999; Skinner et al., 1999; Holstein et al., 2010). In addition to sensory gating deficits, a concurrent deficiency in stimulus encoding might be present in PTSD. Most of the previous studies did not reveal a difference in the auditory P50 response to S1 (Neylan et al., 1999; Morgan and Grillon, 1999), while one found a reduced response in PTSD patients in the right hemisphere correlating with clinical symptomatology (Hunter et al., 2011). Sensory gating of repeating irrelevant visual information has not been examined in PTSD. Visually evoked potentials (VEPs) reflect neural transient events related to sensory transmission of visual stimuli, such as light flashes or visual patterns. Early VEPs consist of N75 (or C1), P100 (or P1), and N150 (or N1) waveforms, which are consecutive negative (N) or positive (P) deflections of the averaged electric potentials peaking at about 75, 100 and 150 ms from the visual stimulus presentation onset. These are exogenous responses to visual stimuli and their amplitudes are dependent on the physical characteristics of the stimuli. A previous study in released prisoners of war (POWs) showed increased responses as well as delayed latencies during several stages of visual processing represented by visual components P50-N75-P100-N145 of VEPs (Vrca and Malinar, 1996). In another study, significant differences were found in the latencies of P100 and N145 responses (Vrca et al., 1997).

It should be noted that none of the reviewed studies examined all EP aspects including auditory and visual modalities in the same individuals. This is important in order to be able to define the extent of IP deviations in multiple sensory modalities in PTSD subjects, as well as to clarify the role of early and late sensory gating modules in the nature and severity of most common symptoms in this disorder.

Post-Traumatic Stress Disorder (PTSD) results from exposure to intense life-threatening trauma and is associated with perceptual and cognitive dysfunction (Vieweg et al., 2006; Sautter et al., 1999; Liberzon et al., 1999; Liberzon and Martis, 2006; Liberzon and Sripada, 2008). The lifetime prevalence of PTSD has been reported to be about 14% among displaced Iraqi refugees residing in the United States (Kira et al., 2007). During recent decades many individuals have fled horrendous conditions in Iraq, thirty percent of whom are estimated to have been victims of torture. Like other forms of severe traumatic exposure, not all subjects exposed to torture develop PTSD. There is a sizeable community of Iraqi refugees in Southeastern Michigan with history of exposure to torture, which constituted the population from which samples were selected in the current study. Furthermore, with the ever increasing number of war veterans and attended individuals with PTSD, further focused research in this area is both warranted and timely.

Based on the available literature, we hypothesized that the amplitudes and sensory gating of the mid-latency evoked responses, especially at early stages, are more impaired (i.e., decreased amplitude/gating) in the PTSD subjects as compared to the trauma-exposed subjects without a diagnosis of PTSD (non-PTSD TE) and healthy control groups, reflecting deficiencies in the IP as well as decreased ability to filter out irrelevant input. We aimed also to investigate associations of evoked potentials with symptom clusters obtained from a PTSD self-report measure, hypothesizing that deficits in early and late phases of mid-latency IP would be associated with intrusive and avoidance symptom clusters of PTSD, respectively. Taking into account the limited information regarding IP in PTSD individuals with history of exposure to torture, our specific interest stemmed from gathering information in an area in which there has been very little investigation.

2. Materials and methods

2.1. Subjects and clinical evaluation

Sixty individuals participated in this study, divided into three groups: 20 subjects with a diagnosis of PTSD, 20 subjects who experienced similar trauma but did not develop PTSD (non-PTSD TE), and 20 healthy controls. All subjects signed a consent form approved by Wayne State University Human Investigations Committee. Participants in each category were matched in age, gender and ethnicity. Subjects' demographics are presented in Table 1. The PTSD and non-PTSD TE participants were recruited from an Arab American Chaldean Council (AACC) clinic in Michigan, which also employs language interpreters in cases that require translation of subtle information during screening procedures. The healthy controls were recruited through flyers posted at AACC or word-of-mouth.

Clinical diagnosis was established via Structured Clinical Interview for DSM-IV-tr (SCID) and the Clinician Administered PTSD Scale (CAPS). The CAPS is a validated 'gold standard' 30-item structured interview that corresponds to the DSM-IV-tr criteria for PTSD (Blake et al., 1995; Weathers et al., 2001). Symptoms severity at the time of electrophysiological testing was evaluated by administering the Clinician Administered PTSD Scale-2 questionnaire (CAPS-2; (Blake et al., 1995)). This questionnaire includes 18 questions about PTSD symptoms using a 5-point Likert scale to indicate the frequency of symptoms in the past week on a scale from 0 (not at all), to 5 (more than once a day). CAPS-2 provides a total score indicating the number of PTSD symptoms in the past week. Subscores included re-experience (intrusiveness), avoidance, hypervigilance and the related construct of dissociative experiences. The Quality of Life Index (QLI) questionnaire was also administered (Ferrans and Powers, 1995). This questionnaire includes 33 questions about how satisfied one is with specific areas of life. It uses a 6-point Likert scale to answer the questions on a scale from 1 (very dissatisfied), to 6 (very satisfied).

The inclusion criteria for subjects exposed to trauma: (1) Outpatient Iraqi refugees who had been subject to torture and were

Table 1
Demographics information.

	N	Gender	Age (mean ± SD)	CAPS-2 (mean ± SD)	QCI (mean ± SD)	Depression
PTSD	20	10 males 10 females	46.7 ± 10.3	49.85 ± 19.91	85.95 ± 32.56	9 subjects (co-morbidity)
Non-PTSD TE	20	10 males 10 females	46.6 ± 11.2	28.4 ± 23	101.2 ± 39.9	12 subjects (primary diagnosis)
Control	20	10 males 10 females	45.5 ± 10.6	5.6 ± 6.38	156.9 ± 23.2	0