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Increased anticipatory contingent negative variation in posttraumatic stress disorder

Hongxia Duan [a,c,d], Li Wang [b], Guillén Fernández [d], Kan Zhang [a], Jianhui Wu [a,*]

[a] Key Laboratory of Behavioral Science, Institute of Psychology, Chinese Academy of Sciences, Beijing, China
[b] Key Laboratory of Mental Health, Institute of Psychology, Chinese Academy of Sciences, Beijing, China
[c] University of Chinese Academy of Sciences, Beijing, China
[d] Donders Institute for Brain, Cognition and Behavior, Department for Cognitive Neuroscience, Radboud University Medical Centre, Nijmegen, The Netherlands, The Netherlands

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ABSTRACT

Altered anticipation processes are implicated across various clinical samples, but few studies focused on the posttraumatic stress disorder (PTSD). We measured contingent negative variation (CNV) in a choice reaction paradigm among 58 survivors of the Wenchuan earthquake, including 28 individuals who were diagnosed with PTSD and 30 without PTSD. Compared to the non-PTSD group, the PTSD group had significantly larger CNV amplitude. On the behavioral level, although the reaction times were comparable between groups, the PTSD group committed more errors than the non-PTSD group. Furthermore, the total PTSD symptom severity score as well as the re-experiencing symptom score were positively related to CNV amplitude. These results suggested that individuals with PTSD might be more alerted to and anticipate more to upcoming events in their environment, yet still have degraded performance in response to the stimulus.

1. Introduction

Posttraumatic stress disorder (PTSD) is a severe and complex mental disorder associated with exposure to traumatic events (American Psychiatric Association, 1994). According to the newly released DSM-5, PTSD comprises four symptom clusters, namely re-experiencing, avoidance, negative alterations in cognition and mood, and alterations in arousal and reactivity (American Psychiatric Association, 2013). PTSD is associated with impairment in several cognitive domains, such as attention, learning and memory (for reviews, see Horner & Hamner, 2002; Pittenger, 2013). These cognitive dysfunctions are viewed as important pathogenetic factors in PTSD development (Parsons & Ressler, 2013).

Anticipation to upcoming stimuli/events in the environment is an essential adaption in human beings. Numerous studies have demonstrated that individuals can prepare efficiently for an upcoming event with the aid of a warning stimulus preceding this significant event (Leuthold, Sommer, & Ulrich, 2004; Wynn, Horan, Kring, Simons, & Green, 2010). However, excessive anticipation and preparation for future events as well as the underlying neural circuitry is at the heart of anxious pathology (for reviews, see Grillon, 2008; Grupe & Nitschke, 2013). With the method of functional magnetic resonance imaging (fMRI), previous studies had begun to explore the anticipation-relevant brain areas in PTSD. The evidence showed that individuals with PTSD had exaggerated activation in the anterior insula during anticipation of aversive stimuli compared to the control individuals (Aupperle et al., 2012; Simmons et al., 2008; Simmons et al., 2013), whereas the striatum was less activated in PTSD during reward anticipation (Elman, Lowen, Frederick, Chi, Becerra, & Pitman, 2009).

As a direct cortical measure to anticipatory process, event-related potentials (ERP) are a useful tool with time precision of milliseconds. Contingent Negative Variation (CNV), the slow negative brain potential, is the most extensively studied anticipatory ERP. It can be observed between a warning stimulus (S1) and an imperative stimulus (S2) which requires a motor response (Walter, 1967). The CNV reflects the activation of multiple areas, mainly distributed over frontal-parietal regions (Cui, Egkher, Huter, Lang, Lindinger, & Deecke, 2000; Fischer, Langner, Diers, Brocke, & Birbaumer, 2010; Gómez and Flores, 2011). Generally, literature considered CNV linked with at least two distinct associative processes: attentive orientation to the warning stimulus and

* Corresponding author at: Institute of Psychology, Chinese Academy of Sciences, 16 Lincui Road, Chaoyang District, Beijing, 100101, China. Fax: +86 10 64836047.
E-mail address: wujh@psych.ac.cn (J. Wu).

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anticipatory attention during executive control (Tecce 1972; Cui et al., 2000).

Previous results have suggested that larger CNV amplitude was associated with relatively higher stress and arousal levels among healthy participants (Brown, Fenwick, & Howard, 1989; Nagai et al., 2004; Tecce, 1972). Siniatchkin and colleagues (2006) found that healthy women had larger CNV amplitude under experimental achievement stress compared to control condition. Duan, Yuan, Yang, Zhang, Zhang, and Wu, 2015 found that the CNV was more negative in individuals under long-term stress than a control group. The results from two other studies revealed that individuals with high-trait anxiety had a greater CNV than individuals with low-trait anxiety who performed at comparable levels (Ansari & Derakshan, 2011; Glanzmann & Froehlich, 1984). Ansari and Derakshan (2011) proposed that anxious individuals use more mental resources to prevent performance degradation at the cost of processing efficiency.

As a stress-related disorder, there are only two studies assessing the anticipatory change with CNV in PTSD to our knowledge, and the results were contradictory. In one study with the classic S1–S2 paradigm, PTSD patients had smaller frontal and central CNV amplitudes than healthy control participants, and the authors speculated that this might result from noradrenergic inefficiency on the one hand and a lack of motivational and emotional involvement in the experimental protocol on the other (Boudarene & Timsit-Berthier, 1997). Kimble, Ruddy, Deldin, & Kaufman (2004), however, found that veterans with PTSD had larger frontal CNV compared to non-PTSD veterans. They proposed that this exaggerated frontal CNV is representative of frontal dysfunction in PTSD individuals. In the conventional S1-S2CNV task, nothing happens during the interval and attention is easily diverted away from the task, and it is especially the case for psychiatric patients who suffer more often from loss of focused attention (Linssen, Sambeth, Riedel, & Vuurman, 2013). Characteristics of participants might also play a role. In the study by Kimble et al. (2004) participants were Vietnam veterans who were exposed to combat, and participants in the PTSD group were taking various psychotropic medications. However, in the study by Boudarene and Timsit-Berthier (1997), PTSD and control groups were selected based on traumatic life events, and there were no information about medication use. Thus, the question how anticipatory processes are affected in PTSD needs further exploration.

PTSD is a clinical syndrome with highly heterogeneous clinical syndrome composed of distinct symptom clusters with distinct biological and behavioral correlates (Asmundson et al., 2000; Pietrzak et al., 2013; Swick, Honzel, Larsen, Ashley, & Justus, 2012), which might explain the mixed effects of PTSD as a group on anticipatory processing. Since PTSD was first introduced in DSM-III (American Psychiatric Association, 1980), the diagnostic criteria have long been characterized by three distinct symptom clusters: re-experiencing, avoidance, and arousal. Previous studies explored the correlates of distinct symptom clusters in the tripartite model with information processing abnormalities, such as sensory gating, attention or memory as assessed by different ERP components in PTSD (for reviews, see Javanbakht, Liberzon, Amirsadri, Gjini, & Boutros, 2011; Lobo et al., 2015). However, it should be noted that several confirmatory factor analysis (CFA) studies have proven that the tripartite model fails to capture the underlying construct of posttraumatic stress symptomatology (Gentes et al., 2014; Gootzeit & Markon, 2011; Stein et al., 2013). The latest development in the literature is a hybrid 7-factor model (Armour et al., 2015; Pietrzak et al., 2015; Wang, Zhang et al., 2015), which is derived from the CFA and builds on the recently released DSM-5 (American Psychiatric Association, 2013). This 7-factor model is comprised of re-experiencing (B1–B5), avoidance (C1–C2), negative affect (D1–D4), anhedonia (D5–D7), externalizing behaviors (E1–E2), anxious arousal (E3–E4), and dysphoric arousal (E5–E6).

Thus, there were two aims of the current study. The first was to explore the anticipatory abnormality indexed by CNV in PTSD. For this purpose, CNV was assessed in traumatized participants with PTSD and without PTSD by using a choice reaction task adapted from other studies (Simons, Ohman, & Lang, 1979; Wynn et al., 2010). This task required participants to discriminate between two different warning stimuli and to respond accordingly followed by a corresponding emotional (negative or neutral) picture, to increase task difficulty as well as attention concentration of the patients. The secondary aim of this study was to explore the relationship between CNV amplitude and distinct symptom clusters of a newly proposed 7-factor model as a continuum that ranges from normal to pathological, as recommended by the Research Domain Criteria (RDoC) project (Craske, 2012).

2. Methods

2.1. Participants

Participants were recruited from one of the largest rebuilt communities located in Hanwang Town, which was almost completely wrecked in the 2008 Wenchuan earthquake. We excluded participants with (1) past or current head injury, (2) significant substance abuse, or (3) self-reported neurological disorder or other serious medical condition. Participants with the age range from 41 to 60 years were selected. We chose this middle age group based on the observation from cross-sectional as well as longitudinal findings in healthy population that brain tissue increase in young adulthood, plateau in middle age and precipitous decline in the old age (Bartzokis et al., 2001; Jernigan & Fennema-Notestine, 2004; Raz et al., 2005). Furthermore, Cardenas and colleagues (2011) explored brain volume changes in middle-aged PTSD patients, and found that PTSD patients did not show significant brain atrophy compared to trauma controls. On the other hand, this age selection is also consistent with previous studies with PTSD population (Cardenas et al., 2011; Gavrieli, Farr, Davis, Crowell, & Mantzoros, 2015; Hamner & Gold, 1998). Based on the DSM-5 diagnostic criteria (American Psychiatric Association, 2013), at least one intrusion symptom, one avoidance symptom, two negative alterations in cognitions and mood symptoms, and two arousal symptoms endorsed as 2 or greater were identified as probable PTSD cases. The study sample consisted of 30 participants who had a diagnosis of PTSD and 31 control participants matched in demographic variables like age, gender, education level and marital status (see Table 1). All the participants from both the PTSD group and non-PTSD group went through the same earthquake and participated in the study in one day. They didn't take any psychiatric medication for at least four weeks before the experiment, which was conducted from 13 to 31 December 2013, approximately five and a half years after the earthquake. All the participants reported normal hearing and normal or corrected-to-normal vision. There were four participants reporting left-hand dominance, with two from the PTSD group and two from the non-PTSD group.

Two participants (one in the PTSD group and one in the non-PTSD group) were excluded from the final analyses because they had less than four artifact-free trials (Kropp, Kiewitt, Göbel, Vetter, & Gerber, 2000). Another participant in the PTSD group was excluded due to the CNV amplitude out of normal range (±3 standard deviation). The final sample consisted of 28 participants in the PTSD group and 30 participants in the non-PTSD group. The demographic variables are shown in Table 1. They gave written informed consent and were paid for their participation. The experiment was