Dysfunctional frontal lobe activity during inhibitory tasks in individuals with childhood trauma: An event-related potential study

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ABSTRACT

Background: Individuals who experience childhood trauma are vulnerable to various psychological and behavioral problems throughout their lifetime. This study aimed to investigate whether individuals with childhood trauma show altered frontal lobe activity during response inhibition tasks.

Methods: In total, 157 healthy individuals were recruited and instructed to perform a Go/Nogo task during electroencephalography recording. Source activities of N2 and P3 of Nogo event-related potentials (ERP) were analyzed. The Childhood Trauma Questionnaire (CTQ) and Barratt Impulsivity Scale (BIS) were applied. Individuals were divided into three groups based on their total CTQ score: low CTQ, middle CTQ, and high CTQ groups.

Results: The high CTQ group exhibited significantly higher BIS scores than the low CTQ group. P3 amplitudes of the differences between Nogo and Go ERP waves exhibited higher mean values in the low CTQ than the high CTQ group, with trending effects. In Nogo-P3, the source activities of the right anterior cingulate cortex, bilateral medial frontal cortex (MFC), bilateral superior frontal gyrus (SFG), and right precentral gyrus were significantly lower in the high CTQ than the low CTQ group. Motor impulsivity showed a significant negative correlation with activities of the bilateral MFC and SFG in Nogo-P3 conditions.

Conclusions: Our study revealed that individuals with childhood trauma have inhibitory failure and frontal lobe dysfunction in regions related to Nogo-P3.

1. Introduction

Childhood trauma appears to be a crucial etiological factor in the development of many serious psychological and behavioral disorders across the lifespan (Terr, 1991). Epidemiological studies have indicated that children exposed to early adverse experiences are more susceptible to developing depression and/or anxiety disorders (Heim and Nemeroff, 2001). In addition, childhood trauma may play a role in the development of impulsivity, which has been associated with maladaptive behaviors such as substance abuse and suicide (Brody et al., 2001; Tucci et al., 2010).

Furthermore, childhood trauma can produce long-term changes in brain development (Kaufman et al., 2000). Neuroimaging studies have suggested that traumatic experiences in early life may lead to structural and functional changes in the brain (Bremner, 2006). Additionally, reports have associated childhood adversity to structural changes in areas of the frontal regions and areas connected to the frontal regions such as the orbitofrontal cortex (OFC) (Hanson et al., 2010), dorsolateral prefrontal cortex (DLPFC) (Tomoda et al., 2009), and anterior cingulate cortex (ACC) (Cohen et al., 2006). These brain regions have been associated with emotional regulation (Kim and Lee, 2016). Meanwhile, impulsivity, a manifestation of emotional dysregulation, has been identified to significantly correlate with frontal lobe dysfunction (Miyake et al., 2000).

Traditionally, response inhibition has been explored using several tasks such as the Go/Nogo task and antisaccade task (Bokura et al., 2001; Nieuwenhuis et al., 2001). In the Go/Nogo task, individuals are instructed to respond to Go trials and not to respond (inhibit) to Nogo trials (Bokura et al., 2001). The Go/Nogo event-related potentials (ERP) have been used as an informative measure to evaluate inhibitory
capacity (Eimer, 1993; Messerotti Benvenuti et al., 2015). Typically, the N2 and P3 components of ERPs are analyzed in Go/Nogo task. These two components generally appear in sequence, and are associated with the early and late phases of response inhibition, respectively (Ramautar et al., 2004). An increased Nogo-N2 amplitude may reflect increased efforts to facilitate response inhibition and to inhibit false responses (Geczy et al., 1999). On the other hand, the Nogo-P3 component has been recognized to reflect later inhibitory processes, such as response evaluation or successful response inhibition (Munro et al., 2007). Moreover, it has been suggested that the difference between Nogo and Go ERP waves would represent the reliable Nogo effect (Guan et al., 2015; Kiehl et al., 2000). The N2d (Nogo-N2 minus Go-N2) reflects conflict monitoring, whereas the P3d (Nogo-P3 minus Go-P3) indicates response inhibition (Kiehl et al., 2000). The N2d and P3d components are indices of the Nogo effect and mirror frontal inhibitory function (Guan et al., 2015).

It has been reported that response-inhibitory action particularly activates the frontal cortex. Functional magnetic resonance imaging (fMRI) analyses of the Go/Nogo task have shown that successful inhibition trials are associated with increased activation predominantly in the frontal cortex, including the ACC, DLPFC, medial OFC, and inferior frontal cortex (IFC) (Braver et al., 2001; Goghari and MacDonald 3rd, 2009; Menon et al., 2001). ERP source analysis has also revealed that Nogo-N2 and P3 activities were observed in the frontal cortex such as the ACC, OFC, and medial frontal cortex (MFC) (Bokura et al., 2001; Tian and Yao, 2008). Interestingly, the activity of the aforementioned regions has been identified to be critical for emotional regulation and can be altered through childhood trauma (Hart and Rubia, 2012). Despite this possible association between childhood trauma and frontal lobe activity, there have been no previous studies evaluating the cortical source activity of electroencephalography (EEG) signals using an inhibitory paradigm (i.e., Go/Nogo task) in individuals with traumatic childhood experiences.

We hypothesized that individuals with childhood traumas would show an altered amplitude and latency of Nogo ERP. Moreover, the source activity of Nogo ERP could reflect the inhibitory function of the frontal lobe, and individuals with traumatic childhood experiences would show altered frontal lobe activity in the regions related to Nogo ERP.

2. Material and methods

2.1. Participants

The study was performed on 157 non-smoking healthy volunteers (57 men and 100 women) with a mean age of 27.80 ± 6.37 years. They were recruited from the local community through local newspapers and posters. The screening interview was conducted by one researcher in a face to face, semi-structured fashion. Participants with any treatment history of neurological (subjective cognitive decline, history of head trauma, loss of consciousness, and any central nervous system illness) or psychiatric (treatment history of depressive disorder, anxiety disorder, and any psychotic episodes) diseases were excluded. Individuals with a family history of any psychiatric disorder were excluded as well. Each participant had normal or corrected-to-normal vision, which was determined by checking visual acuity with the Snellen chart (Lovie-Kitchin, 1988). The participants were divided into 3 subgroups based on the 25% and 75% quartiles of the Childhood Trauma Questionnaire (CTQ) (Bernstein et al., 2003) total score (n = 44, 31.41 ± 2.06), the middle CTQ group (25–75%, n = 74, 40.53 ± 3.64), and the high CTQ group (upper 25%, n = 39, 60.00 ± 9.94). After an explanation of the study, informed consent was obtained from all individual participants. This study was approved by the Institutional Review Board at Inje University Ilsan Paik Hospital (2015-07-026-001).

2.2. Psychological measures

The State-Trait Anxiety Inventory (STAI) (Kim and Shin, 1978; Spielberger et al., 1983) and Beck Depression Inventory (BDI) (Rhee et al., 1995) were administered to evaluate anxiety and depression. The STAI is a self-rating scale of state and trait anxiety (Spielberger et al., 1983). It consists of a state anxiety inventory (SAI) and trait anxiety inventory (TAI); each inventory consists of 20 items (Kim and Shin, 1978). The cut-off score for moderate to high anxiety is > 30 whereas the cut-off score for low to no anxiety is ≤ 30 (Glozman, 2004). The BDI is a self-rating scale composed of 21 items to measure the severity of depression symptoms (Rhee et al., 1995). In general, a cut-off score of ≥ 13 is appropriate for identifying clinically significant depression (Beck and Beamesderfer, 1974).

The Barratt Impulsiveness Scale (BIS) (Lee et al., 2012; Patton et al., 1995) was used to assess impulsivity-related traits. The BIS consists of 30 items, and is designed to assess the personality/behavioral construct of impulsiveness. It has 3 sub-factors: attentional, motor, and non-planning impulsivity (Patton et al., 1995). A total score of ≥ 72 on the BIS indicates high levels of impulsivity (Stanford et al., 2009). The CTQ (Bernstein et al., 2003) was used to assess traumatic childhood experiences. The CTQ consists of 28 items (25 clinical and 3 validity items) that comprise 5 categories of childhood maltreatment including physical, emotional, and sexual abuse and physical and emotional neglect. Each subscale has 5 items rated on the 5-point Likert scale. A total score from 5 to 25 can be obtained. For clinical samples, researchers have usually used cut-off scores ≥ 10, ≥ 13, ≥ 8, ≥ 10, and ≥ 15 for physical abuse, emotional abuse, sexual abuse, physical neglect, and emotional neglect, respectively (≥ 56 for total score) (Bernstein and Fink, 1998; Heim et al., 2009). However, because the cut-offs were too high for the healthy participants of the present study, we used scores of the 25% and 75% quartiles to discriminate the levels of childhood trauma (= 34.0 and 48.5, respectively).

2.3. Recording and preprocessing of electroencephalography (EEG)

EEG was recorded using a NeuroScan SynAmps amplifier (Compumedics USA, Charlotte, NC, USA) with 64 Ag-AgCl electrodes mounted on a Quik-Cap using an extended 10–20 placement scheme. The ground electrode was placed on the forehead, and the reference electrodes were attached to both mastoids. The vertical electro-oculogram (EOG) channels were positioned above and below the left eye, and the horizontal EOG channels were recorded at the outer canthus of each eye. The impedance was maintained below 5 kΩ. All data were processed with a 0.1–100 Hz band pass filter and sampled at 1000 Hz.

The recorded EEG data were preprocessed using CURRY 7 (Compumedics USA, Charlotte, NC, USA). Gross artifacts such as movement artifacts were rejected based on visual inspection by a trained person with no prior information regarding the origin of the data. Artifacts related to eye movement or eye blinks were removed using a mathematical procedure implemented in the preprocessing software (Semlitsch et al., 1986) of CURRY 7. The data were filtered using a 0.1–30 Hz bandpass filter and epoched from 100 ms prestimulus to 900 ms post-stimulus. The epochs were subtracted from the average value of the pre-stimulus interval for baseline correction. If any remaining epochs contained significant physiological artifacts (amplitude exceeding ± 75 μV) in any of the 62 electrode sites, they were excluded from further analysis. Only artifact-free epochs were averaged across trials and subjects for ERP analysis. For the analysis of Go/No-go task, only correctly responded epochs were used. The number of epochs of Go/Nogo used for the analysis did not significantly differ among the low-CTQ, middle-CTQ, and high-CTQ groups (Go condition: 213.30 ± 19.53 vs. 207.26 ± 23.69 vs. 206.26 ± 21.81, p = 0.264; Nogo condition: 49.30 ± 7.04 vs. 48.20 ± 5.96 vs. 47.64 ± 7.81, p = 0.517, respectively).
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