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 (Brodsky 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 (= 34.0 and 48.5, respectively): the low CTQ group (lower 25%, $n = 44$, 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 pre-stimulus 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).

2.3.1. Go/Nogo experiment

Subjects were seated approximately 60 cm away from a computer screen (Mitsubishi, 22-inch CRT monitor). Stimuli for Go/Nogo task, which consisted of numbers 1–8, were presented randomly on the screen. The subjects were instructed to press a space bar as accurately and quickly as possible when Go stimuli (even numbers: 2, 4, 6, 8) appeared at the center of the screen, and not to respond when Nogo stimuli (odd numbers: 1, 3, 5, 7) were displayed. There were 300 trials. The Go condition appeared with an 80% probability, whereas the Nogo condition appeared with a 20% probability. On each task trial, a fixation cross was presented for 100 ms. Following intervals of 700–1000 ms, Go or Nogo targets appeared for 500 ms. In between trials, there was a 500 ms interval. The stimuli were generated by *E-Prime* (Psychology Software Tools, Pittsburgh, PA, USA). Time windows for N2 and P3 extraction during Go and Nogo trials were based on previous studies (Bokura et al., 2001; Sehlmeyer et al., 2010) and visual inspection of the grand-averaged waveforms at the 4 electrodes of interest (Fz, FCz, Cz, and Pz), all of which were located on the midline (Omura and Kusumoto, 2015). The N2 and P3 peaks were defined as the most negative and positive points of the grand-averaged waveforms at these 4 electrodes of interest in each condition (Go-N2: 150–350 ms; Go-P3: 250–500 ms; Nogo-N2: 150–350 ms, Nogo-P3: 300–550 ms). In addition, N2d (Nogo-N2 minus Go-N2) and P3d (Nogo-P3 minus Go-P3) components were analyzed.

2.3.2. Source imaging

EEG has been regarded as the most appropriate neuroimaging modality for investigating fast changes in brain activity due to its superior temporal resolution. However, EEG has some intrinsic limitations. First, sensor-level EEG has low spatial resolution originating from volume conduction. That is, the signals might not reflect brain activities right below the recording electrodes (Nolte et al., 2004; van den Broek et al., 1998). Second, EEG data might have poor signal-to-noise ratios as they can be severely contaminated by various noises and artifacts (Lange and Inbar, 1996; Lemm et al., 2006). One of the cost-effective options to enhance spatial and temporal resolution is to use EEG source-imaging methods. The spatial resolution of EEG can be substantially improved by mapping the scalp potential distribution onto the underlying cortical source space using source-imaging methods. Standardized low-resolution brain electromagnetic tomography (sLORETA) is a well-established source-imaging method (Pascual-Marqui, 2002) and has been comparable to results from intracranial recording (Lantz et al., 1997).

sLORETA was used to compute the cortical distribution of the standardized source current density of each ERP component. sLORETA is a representative source-imaging method for solving the EEG inverse problem (Pascual-Marqui, 2002), which assumes that the source activation of a voxel is similar to that of the surrounding voxels for calculating a particular solution, and applies an appropriate standardization of the current density. The lead field matrix was computed using a realistic head model segmented based on the Montreal Neurological Institute (MNI) 152 standard template, wherein the three-dimensional solution space was restricted only to the cortical gray matter and hippocampus (Fuchs et al., 2002). The solution space is composed of 6239 voxels with a 5-mm resolution. Anatomical labels, such as the Brodmann areas, were provided by using an appropriate transformation from MNI to Talairach space (Brett et al., 2002).

The source images of N2 and P3 were analyzed in the Nogo condition, and the periods were defined between 150 and 350 ms and 300 and 550 ms after stimulus onset, respectively. Previous neuroimaging and ERP source-localization studies have found that the response-inhibitory action in the Go/Nogo task is observed predominantly in the frontal cortex. Thus the regions of interest of Nogo-N2 and P3 source activities in this study were selected as follows: Nogo-N2—ACC (Bekker et al., 2005), OFC (Bokura et al., 2001), DLPFC (Lavric et al., 2004), MFC (Bekker et al., 2005), and IFC (Pliszka et al., 2000); and Nogo-

P3—ACC (Beste et al., 2008; Kim and Jung, 2014), OFC (Bokura et al., 2001), DLPFC (Banaschewski and Brandeis, 2007), IFC (Bokura et al., 2001), MFC (Tian and Yao, 2008), middle frontal cortex (Beste et al., 2008), superior frontal gyrus (SFG) (Kim and Jung, 2014), precentral gyrus (PG) (Kim and Jung, 2014), and inferior parietal lobule (IPL) (Kim and Jung, 2014).

2.4. Statistical analysis

For statistical analysis, one-way analysis of variance (ANOVA) was used to compare the scores of the psychological and behavioral data among the three groups. In addition, multivariate ANOVA was conducted to compare the amplitude and latency of ERP components, and the source activity among the three groups. STAI and BDI were entered as covariates. The variables showing significant differences were further analyzed with post-hoc pairwise comparisons using least significant difference (LSD).

In addition, the relationships among variables were analyzed by Spearman's correlation. A 5000 bootstrap resampling technique was applied to correct for multiple correlations (Kim et al., 2016; Pernet et al., 2013; Ruscio, 2008). The significant level was set at $p < 0.05$ (two-tailed). Statistical analyses were performed using SPSS 21 (SPSS, Inc., Chicago, IL, USA).

3. Results

3.1. Psychological and behavioral measures

Table 1 shows the comparison of the demographic and psychological characteristics among the low CTQ, middle CTQ, and high CTQ groups. The scores of the BIS (attentional impulsivity), STAI, BDI, and CTQ (physical, emotional, sexual abuse, physical, and emotional neglect) were significantly higher in the high CTQ group than in the low CTQ group (attentional impulsivity: 15.39 ± 3.21 vs. 17.77 ± 3.67, $p = 0.002$; SAI: 32.45 ± 7.26 vs. 42.18 ± 7.61, $p < 0.001$; TAI: 34.27 ± 9.88 vs. 46.49 ± 9.06, $p < 0.001$; BDI: 5.39 ± 3.50 vs. 12.33 ± 7.60, $p < 0.001$). However, there was no significant difference among the 3 groups in Nogo false-alarm rate (0.12 ± 0.11 vs. 0.12 ± 0.08 vs. 0.14 ± 0.12, $p = 0.512$).

3.2. Electroencephalography data

Fig. 1a shows the N2d and P3d waveforms at Fz, FCz, Cz, and Pz electrodes in the low CTQ, middle CTQ, and high CTQ groups. Fig. 1b presents the scalp topographies of N2d and P3d components for low CTQ, high CTQ, and low-minus-high CTQ groups. There was no significant difference in the amplitude and latency of Nogo-N2 and P3 among the three groups. However, there were trending effects in P3d amplitudes at the Fz electrode ($F = 2.841$, $df = 2$, $p = 0.061$) and FCz electrode ($F = 2.513$, $df = 2$, $p = 0.084$). P3d amplitudes appeared to be higher in the low CTQ group than in the high CTQ group.

3.3. Source analysis of Nogo condition

Table 2 displays the comparisons of source activities in brain regions that show significant differences in Nogo-P3 among the low CTQ, middle CTQ, and high CTQ groups with STAI and BDI as covariates. The right ACC, bilateral MFC, bilateral SFG, and right PG were significantly lower in the high CTQ group than in the low CTQ group (right ACC: 8.68 ± 7.24 vs. 6.06 ± 3.66, $p = 0.045$; left MFC: 13.19 ± 11.83 vs. 7.92 ± 5.03, $p = 0.006$; right MFC: 13.17 ± 13.12 vs. 7.86 ± 4.40, $p = 0.003$; left SFG: 14.38 ± 11.70 vs. 9.31 ± 5.90, $p = 0.012$; right SFG: 13.65 ± 12.85 vs. 9.12 ± 5.23, $p = 0.006$; right PG: 3.83 ± 5.20 vs. 2.50 ± 1.66, $p = 0.016$).

Fig. 2 shows the regions that were significantly different between the low CTQ and high CTQ groups. The color of each region indicates

Table 1

Comparison of baseline demographic, psychological, and behavioral characteristics in participants with low, middle, and high childhood trauma questionnaire (CTQ) scores.[b]

|	Low CTQ (N = 44)	Middle CTQ (N = 74)	High CTQ (N = 39)	P	Pairwise test, p[a]
	Mean ± SD or N (%)				Low vs. high
Age (years)	26.14 ± 5.92	28.50 ± 6.65	28.33 ± 6.13	0.124	
Sex					
Male	20 (45.5)	25 (33.8)	12 (30.8)	0.315	
Female	24 (54.5)	49 (66.2)	27 (69.2)		
Education (years)	13.91 ± 1.88	14.59 ± 1.74	14.67 ± 1.61	0.075	
Nogo false alarm rate	0.12 ± 0.11	0.12 ± 0.08	0.14 ± 0.12	0.521	
Barratt Impulsivity Scale (BIS)	58.07 ± 10.17	58.82 ± 8.52	62.87 ± 9.23	0.037	0.019
Attentional impulsivity	15.39 ± 3.21	15.76 ± 3.30	17.77 ± 3.67	0.003	0.002
Motor impulsivity	23.91 ± 4.98	25.35 ± 4.42	26.26 ± 4.45	0.063	
Non-planning impulsivity	18.77 ± 4.19	17.72 ± 3.45	18.85 ± 3.78	0.193	
State Anxiety Inventory (SAI)	32.45 ± 7.26	36.12 ± 7.05	42.18 ± 7.61	< 0.001	< 0.001
Trait Anxiety Inventory (TAI)	34.27 ± 9.88	39.24 ± 8.13	46.49 ± 9.06	< 0.001	< 0.001
Beck Depression Inventory (BDI)	5.39 ± 3.50	6.91 ± 4.30	12.33 ± 7.60	< 0.001	< 0.001
Childhood Trauma Questionnaire	31.41 ± 2.06	40.53 ± 3.64	60.00 ± 9.94	< 0.001	< 0.001
Physical abuse	5.66 ± 1.10	6.54 ± 1.80	10.05 ± 3.93	< 0.001	< 0.001
Emotional abuse	5.07 ± 0.26	5.80 ± 1.33	9.21 ± 3.67	< 0.001	< 0.001
Sexual abuse	5.16 ± 0.65	5.45 ± 0.98	7.44 ± 3.39	< 0.001	< 0.001
Physical neglect	5.55 ± 1.25	6.38 ± 1.96	7.82 ± 2.97	< 0.001	< 0.001
Emotional neglect	9.98 ± 1.89	16.36 ± 3.85	25.49 ± 4.27	< 0.001	< 0.001

[a] p-Values represent statistically significant differences between the low and high CTQ groups with post-hoc test using LSD.

[b] The participants were divided into 3 subgroups based on the 25% and 75% quartiles of the total CTQ score (= 34.0 and 48.5, respectively): the low CTQ group (lower 25%), the middle CTQ group (25–75%), and the high CTQ group (upper 25%).

the p-value from post-hoc test using LSD. The red color denotes decreased source activity in the regions related to Nogo-P3 for the high CTQ group.

3.4. Correlation analysis

The bilateral MFC and SFG, and right PG of Nogo-P3 were significantly correlated with emotional neglect (left MFC: $r = -0.215$, $p = 0.007$; right MFC: $r = -0.198$, $p = 0.013$; left SFG: $r = -0.195$,
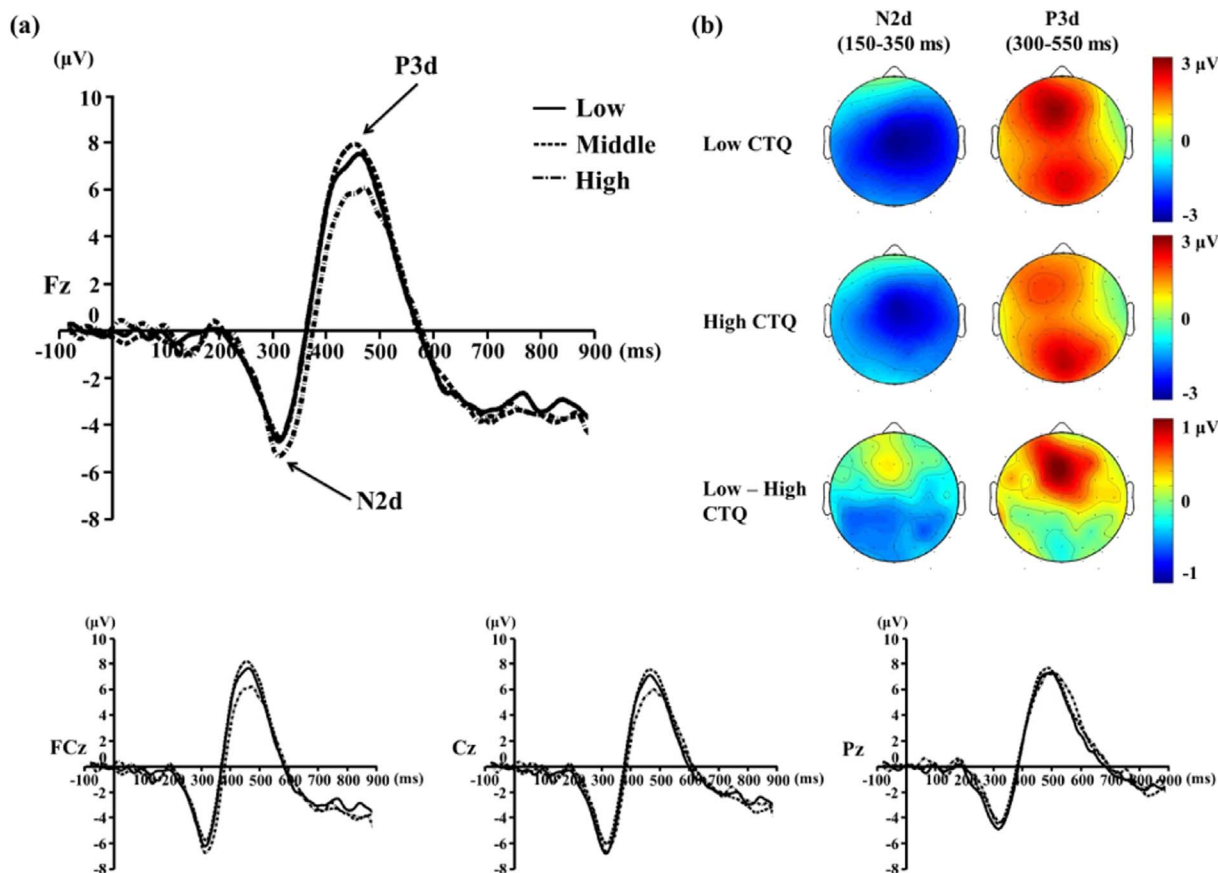
Fig. 1. Grand averages and topographies of N2d and P3d for three CTQ groups (a) Grand averages of N2d and P3d (Nogo minus Go) at the Fz, FCz, Cz, and Pz electrodes for the low, middle, and high childhood trauma questionnaire (CTQ) groups. (b) Scalp topographies of N2d and P3d components for the low, high, and low minus high CTQ groups.

Table 2
Brain regions showing significant differences in source activities of Nogo-P3 among low, middle, and high childhood trauma questionnaire (CTQ) groups. State-Trait Anxiety Inventory and Beck Depression Inventory were used as covariates.

	Low CTQ (N = 44)	Middle CTQ (N = 74)	High CTQ (N = 39)	P	Pairwise test, p^{a}
	Mean ± SD				Low vs. high
Nogo-P3					
Anterior cingulate cortex (Rt)	8.68 ± 7.24	5.91 ± 4.18	6.06 ± 3.66	0.028	0.045
Medial frontal cortex (Lt)	13.19 ± 11.83	8.39 ± 4.54	7.92 ± 5.03	0.003	0.006
Medial frontal cortex (Rt)	13.17 ± 13.12	8.32 ± 4.20	7.86 ± 4.40	0.002	0.003
Superior frontal gyrus (Lt)	14.38 ± 11.70	9.71 ± 5.00	9.31 ± 5.90	0.007	0.012
Superior frontal gyrus (Rt)	13.65 ± 12.85	9.35 ± 4.84	9.12 ± 5.23	0.015	0.006
Precentral gyrus (Rt)	3.83 ± 5.20	3.05 ± 1.93	2.50 ± 1.66	0.048	0.016

[a] p-Values represent statistically significant differences between the low and high CTQ groups with post-hoc test using LSD. Lt: left, Rt: right.

$p = 0.014$; right SFG: $r = -0.169$, $p = 0.034$; right PG: $r = -0.202$, $p = 0.011$). Moreover, the left MFC of Nogo-P3 was significantly correlated with the total CTQ score ($r = -0.191$, $p = 0.017$, respectively).

Bilateral MFC and bilateral SFG of Nogo-P3 showed significant negative correlation with a subscale of BIS, specifically, motor impulsivity (left MFC: $r = -0.195$, $p = 0.014$; right MFC: $r = -0.187$, $p = 0.019$; left SFG: $r = -0.168$, $p = 0.035$; right SFG: $r = -0.196$, $p = 0.014$). In addition, the left MFC of Nogo-P3 was significantly correlated with SAI ($r = -0.187$, $p = 0.019$) and TAI ($r = -0.168$, $p = 0.035$) (Fig. 3).

4. Discussion

This study aimed to determine whether individuals with higher CTQ scores show altered activity of the frontal lobe, which is associated with inhibitory function. Consistent with our hypothesis, the high CTQ group showed altered activity in frontal regions that are significantly correlated with anxiety, motor impulsivity, and the severity of traumatic childhood experiences. Childhood trauma was significantly related to decreased activity of the right ACC, bilateral MFC, bilateral SFG, and right PG in Nogo-P3. To our knowledge, this is the first study to evaluate the relationship between childhood trauma and frontal lobe dysfunction during an inhibitory-control task using ERP source activity in adults.

In the source activity of Nogo-P3, the right ACC, bilateral MFC, bilateral SFG, and right PG showed weaker activation in the high CTQ group than in the low CTQ group. Nogo-P3 is known to reflect the outcome of inhibitory processes and motor-inhibition (Guan et al., 2015). Moreover, Nogo-P3 was proposed as a possible psychophysiological marker for impulsivity (Nijs et al., 2007). Previous studies reported that diminished Nogo-P3 might be an indicator of poor response inhibition (Buchmann et al., 2011; Hartmann et al., 2015). Anatomically, the ACC is known to be involved in conflict monitoring (Carter et al., 1998) and the allocation of attention associated with conflict resolution (Bob et al., 2006). ACC volume reduction was reported in adults with a history of adverse childhood events (Cohen et al., 2006). Our result of decreased activity of the ACC suggests that childhood trauma influences ACC activity related to response inhibition. For the MFC and SFG, previous studies reported that individuals with a history of childhood maltreatment showed a reduced size and function of the MFC (Gorka et al., 2014; Tomoda et al., 2009). Furthermore, poor
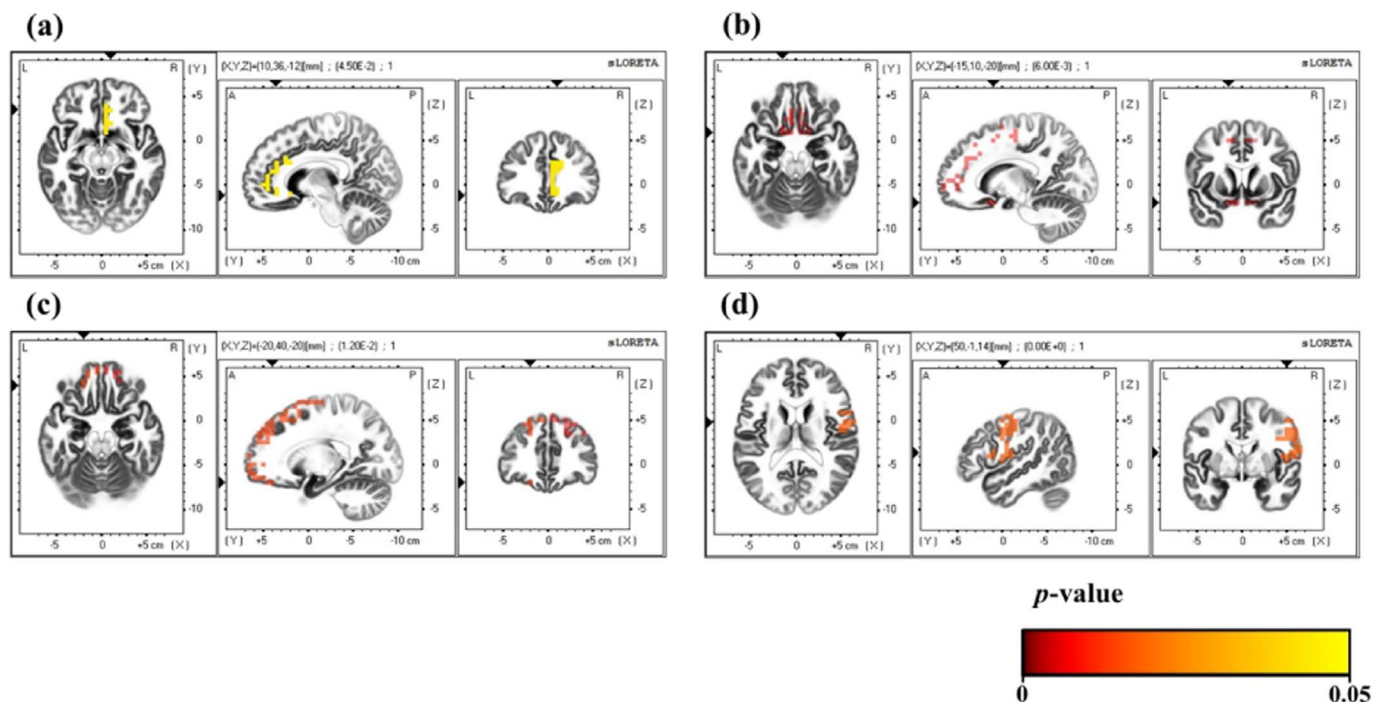
Fig. 2. Differences in the source activity of the Nogo-P3 component between the low and high childhood trauma questionnaire groups (a) right anterior cingulate cortex, (b) bilateral medial frontal cortex, (c) bilateral superior frontal gyrus, and (d) right precentral gyrus. The red color denotes the decreased source activity in the regions related to Nogo-P3 for the high CTQ group.
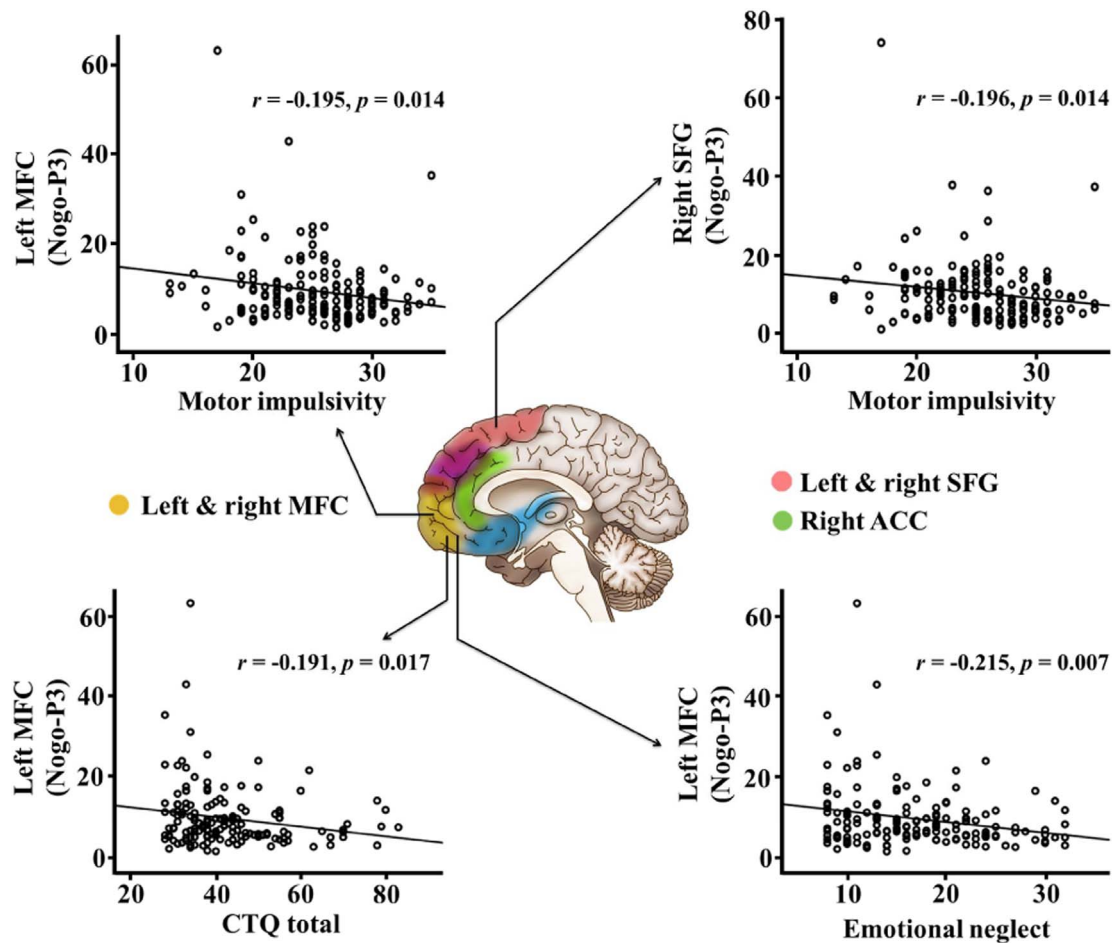
Fig. 3. Brain regional correlations with some critical psychological scores. The left medial frontal cortex and right superior frontal gyrus of Nogo-P3 showed a significant correlation with the motor impulsivity subscale score of the Barratt impulsivity scale. The left medial frontal cortex of Nogo-P3 showed significant correlation with the childhood trauma questionnaire (CTQ) and the emotional neglect subscale score of CTQ.

medial frontal activation might be related to poor control over limbic responses since the medial frontal lobe is strongly connected with the amygdala (Price, 1999). Additionally, children who experienced maltreatment showed reduced cortical thickness in the SFG (Kelly et al., 2013). Previous studies have also reported that childhood maltreatment was associated with cortical thinning and volumetric reduction in the right precentral gyrus (Brooks et al., 2014; Whittle et al., 2013). Taken together, this evidence suggests that the regions considered in this study would be highly related to childhood trauma, and the decreased frontal lobe activity of Nogo-P3 might imply inefficient cognitive control in the high CTQ group. In addition, activities of the bilateral MFC and SFG of Nogo-P3 were negatively correlated with motor impulsivity in the present study. Previous studies demonstrated a decreased activation in the MFC and SFG during response inhibition in individuals with high impulsivity (Chen et al., 2007; Soloff et al., 2003). Our study provides additional evidence that childhood trauma represents an environmental risk factor for the development of impulsivity even in the nonclinical general population.

In contrast with our results, an EEG study reported that healthy subjects with childhood physical and sexual abuse showed a positive relationship between symptom severity and Nogo-P3 amplitude (Howells et al., 2012). In that study, however, Nogo-P3 amplitude was extracted from the parietal region (P3 and P4 electrodes), and cortical source activation was not investigated. Additionally, previous fMRI-based studies reported increased activity of the ACC (Carrion et al., 2008; Lim et al., 2015) and MFC (Carrion et al., 2008) during Go/Nogo tasks in subjects with childhood trauma. However, the subjects in the

Carrion et al.'s study (Carrion et al., 2008) did not represent a healthy population; instead, they were individuals with post-traumatic stress symptoms. Lim et al.'s study (Lim et al., 2015) focused on regions related to error processing and the results were obtained only during failed inhibition. Moreover, there was no significant group difference between childhood trauma and healthy control groups in activation for successful inhibition. In addition, the sample size of our study was larger than that of the above two studies.

There are some limitations in this study. First, although the CTQ has been widely used in research for clinical and nonclinical subjects (Grassi-Oliveira et al., 2014), the CTQ may not precisely reflect the participants' traumatic childhood experience because it is a subjective and retrospective self-report. Second, our results may not extrapolate clinical subjects. Third, our results only showed trending effects of Nogo ERP and were limited to source activities of Nogo ERP.

However, the differences of source activities between low and high CTQ groups were obvious and the source activities showed significant correlations with psychological measures such as childhood trauma and impulsivity. Despite the above limitations, our study showed the relationship between cortical source activation related to inhibitory control and childhood traumatic experiences. It suggests that the nonclinical population with childhood trauma might develop poor impulse control conditions regarding changes of frontal lobe activity.

5. Conclusions

In conclusion, our ERP source localization method detected

decreased activity of associated brain regions in Nogo-P3, which reflects impulsive behavior, in individuals with childhood trauma. Moreover, the significant correlation between frontal regional source activities and symptom severity scores strongly supported the validity of our results. To the best of our knowledge, this is the first study that implemented sLORETA to examine the cortical source activation in a population with childhood trauma during the Go/Nogo task for inhibitory control. This study suggests that traumatic experiences in childhood might lead to frontal lobe dysfunction causing poor impulse control throughout the lifespan.

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Author contributions

S.K. and J.S.K. are co-first authors and equally contributed to this study. S.K. and J.S.K. analyzed the data and wrote the paper. S.H.L. designed the study and wrote the paper. M.J.J and S.H.L collected the data. S.H.L. and C.H.I. reviewed and revised the paper.

Conflict of interest

None.

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