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Changes in Brain Electrical Activity According to Post-traumatic Stress Symptoms in Survivors of the Sewol Ferry Disaster: A 1-year Longitudinal Study

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Objective: The pathology of post-traumatic stress disorder (PTSD) is associated with changes in brain structure and function, especially in the amygdala, medial prefrontal cortex, hippocampus, and insula. Survivors of tragic accidents often experience psychological stress and develop post-traumatic stress symptoms (PTSS), regardless of the diagnosis of PTSD. This study aimed to evaluate electroencephalographic changes according to PTSS in victims of a single traumatic event.
Methods: This study enrolled 60 survivors of the Sewol ferry disaster that occurred in 2014 from Danwon High School and collected electroencephalographic data through 19 channels twice for each person in 2014 and 2015 (mean 451.88 [standard deviation 25.77] days of follow-up). PTSS was assessed using the PTSD Checklist-Civilian Version (PCL-C) and the participants were divided into two groups according to the differences in PCL-C scores between 2014 and 2015. Electroencephalographic data were converted to three-dimensional data to perform low-resolution electrical tomographic analysis.
Results: Significant electroencephalographic changes over time were observed. The group of participants with worsened PCL-C score showed an increased change of delta slow waves in Brodmann areas 13 and 44, with the largest difference in the insula region, compared to those with improved PCL-C scores.
Conclusion: Our findings suggests that the electrophysiological changes in the insula are associated with PTSS changes.

KEY WORDS: Post-traumatic stress disorder; Post-traumatic stress symptoms; Electroencephalography; Insula.

INTRODUCTION

Post-traumatic stress disorder (PTSD) is defined as an exposure to significant traumatic events resulting in four clustered symptoms observed for at least 1 month after the event (intrusions, avoidance of trauma-related thoughts and activities, negative alteration in cognition and mood, and changes in arousal) based on the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) criteria [1]. PTSD is a clinically important psychiatric disorder, with a lifetime prevalence of approximately 8% in the general population of United State and 2% of South Korea, and imposes a large psychological burden [2-4].

In South Korea, on April 16, 2014, a tragic accident named the Sewol ferry disaster occurred. The ferry, carrying 475 passengers, sank at the southwestern tip of Korea, killing more than 300 people. Of the 325 high school students on board, 250 drowned, leaving only 75 survivors. The surviving students experienced fears of death from a human disaster and sadness after losing close friends. Previous studies have reported an increased incidence of post-traumatic stress symptoms (PTSS) in adolescents who have experienced a difficult disaster, which they were unable to overcome [5-7].

About 70% of people experience at least one traumatic

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event in their lifetime [8]. Although exposure to traumatic events may increase the risk of PTSD, only fractions of trauma-exposed individuals develop PTSD [9]. Previous studies have identified biological changes in people with PTSS and have shown that the pathology of PTSD is associated with changes in brain structure and function, especially in the amygdala, medial prefrontal cortex, hippocampus, anterior cingulate cortex, and insula [10-12]. However, most of these studies have limitations in that they were cross-sectional studies, compared the patient group to the non-exposed control group, or targeted individuals who had experienced various types of traumatic events. Therefore, there is a need to identify objective changes through longitudinal studies in a homogeneous group that had experienced a single kind of trauma.

Electroencephalography (EEG) is often employed to measure electrical brain signals because of its advantages such as easy handling, non-invasiveness, excellent temporal resolution, and localization of signals within the brain [13]. However, EEG is known to have the disadvantage of having poor spatial resolution in generally, which makes it difficult to infer the location of the brain regions that generate neuronal activity measured on the scalp. In the standardized low-resolution brain electromagnetic tomography (sLORETA) software, EEG of the scalp is calculated and reconstructed three-dimensionally [14]. sLORETA have the benefit of superior time resolution of EEG measurements of milliseconds, and also have spatial resolution of approximately 7 mm, which is similar to that of functional magnetic resonance imaging (fMRI) [15,16]. Because sLORETA is a tool that provides highly accurate localization, it is effective at identifying which cortical areas show changes in activity.

The existing EEG studies including sLORETA studies did not show absolute or consistent results in patients with post-traumatic stress symptoms. A quantitative EEG study showed low theta power in developed PTSD group compared to resilient group, but the other study showed increased theta power on central brain regions and beta activity in frontal, central, and occipital regions [17,18]. A study comparing the resting EEG of PTSD patient with control group with no history of the trauma showed no significant difference on any of the spectral bands between two groups [19]. Lower activity of the low theta band (4−5 Hz) was observed in the right temporal lobe and in both frontal lobes in the PTSD patient group compared to the control group in a sLORETA study [20]. The other sLORETA study showed a widespread increase of theta activity (4.5−7.5 Hz) in parietal lobes and in frontal lobes in PTSD patients compared to the control group. The present study aimed to determine which biophysiologic changes were associated with PTSS and localize them through longitudinal observations in a group of participants who had experienced the same trauma.

METHODS

Participants

This study enrolled survivors of the Sewol ferry disaster who agreed to participate in the psychiatric approach. All participants were same-grade students of Danwon High School. They had been hospitalized at Korea University Ansan Hospital to receive care for psychological trauma in April 2014, where self-reported questionnaires, such as PTSD Checklist-Civilian Version (PCL-C), Patient Health Questionnaire-9 (PHQ-9), Brief Resilience Scale (BRS), Athens Insomnia Scale (AIS), were administered and initial EEG recordings were obtained. From July to August 2015, 1 year after the initial evaluation, we followed up the participants to evaluate changes in psychological stress through the same questionnaires and EEG measurements. The average of the follow-up duration is 451.88 (standard deviation [SD] 25.77) days. This study was performed retrospectively using the results of clinical scales and EEG recordings, which are routine psychiatric examinations of our hospital. Fourteen subjects were excluded for refusal to respond to the self-reported questionnaires and undergo EEG measurements; thus, a total of 60 medical records were included in the analyses. The research protocol was approved by the Institutional Review Board of Korea University Ansan Hospital for research involving human subjects (No. 2014AS0290).

EEG Recordings and Data Analysis

EEG was performed for 10 minutes under an eyes-closed resting state in a comfortable and quiet room. The participants were kept awake and were not disturbed in a sitting position. EEG was performed using the Neuronics 32 system (Intermed Co., Ltd., Seoul, Korea) with 19 Ag/AgCl scalp electrodes arranged on a head cap according to the International 10-20 system [21]. The amplifier bandwidths varied from 1 to 50 Hz, with a 60 Hz notch filter,

and the EEGs were digitized at 200 Hz per epoch. The impedances at all electrodes were maintained below 10 kΩ during the measurements.

Artifact-free epochs were selected with > 90% split-half reliability and > 90% test-retest reliability, with a total epoch duration of 60 seconds. The statistical properties of the segments were calculated using NeuroGuide software (https://appliedneuroscience.com/). Artifacts were eliminated using the artifact rejection toolbox in the NeuroGuide software and visual inspection. The selected EEG data were quantified using fast Fourier transform and split into seven frequency bands: delta (1.5−6.0 Hz), theta (6.5−8.0 Hz), alpha1 (8.5−10.0 Hz), alpha2 (10.5−12.0 Hz), beta1 (12.5−18.0 Hz), beta2 (18.5−21.0 Hz), and beta3 (21.5−30.0 Hz).

For source localization, the EEG data were converted to three-dimensional data and analyzed using standardized low-resolution brain electromagnetic tomography (sLORETA), which is a tomographic method to map EEG data from sensor space to cortical source (also known as EEG source modeling) and is based on images of standardized current density [14,16,22]. Independent t tests was performed to compare baseline (2014) EEG power of each band between PLC-C and improved PLC-C score groups based on the threshold for statistical significance ($p < 0.05$). Independent t test was also conducted to compare the changes of sLORETA current densities from 2014 to 2025 between the two groups. The nonparametric permutation was used to correct for multiple comparisons tests performed for each picture contrast between the two groups [23].

PTSD Checklist-Civilian Version (PCL-C)

PTSS was assessed using the PTSD Checklist (PCL). Among the three versions of the PCL (military, civilian, and specific), we used the civilian version. This self-reported rating scale for PTSD comprises 17 items reflecting the DSM-IV symptoms of PTSD. The participants indicated their frequencies of experiencing PTSD symptoms in the past month on a 5-level scale from "not at all" (1) to "extremely" (5). The sum of the scores served as the total PTSS severity score.

An ideal cutoff for the PCL-C score has not been reported. Depending on the prevalence and setting characteristics, a wide range of PCL-C scores have been proposed as cutoffs for PTSD screening or to aid the diagnostic assessment of PTSD. The present study focused on the changes in PCL-C scores between 2014 and 2015 rather than a cutoff score or the diagnosis of PTSD. In real-world practice, 80% of individuals who are exposed to extreme trauma do not develop PTSD [24]. Hence, it is more common for psychiatrists to care for patients with PTS who do not meet the criteria for PTSD. Thus, we classified the participants into two groups according to the difference in PCL-C scores between 2014 and 2015 to determine the changes in EEG recordings according to changes in PTSS: worsened and improved PCL-C score groups. The worsened group comprised 34 survivors with the same score or a positive difference in PCL-C score in 2015 compared to that in 2014, whereas the improved group comprised 26 patients with a negative difference in PCL-C scores between 2015 and 2014.

Patient Health Questionnaire-9 (PHQ-9)

The PHQ-9 is a self-administered scale derived from the full PHQ, which is a 3-page questionnaire. The PHQ-9 comprises nine items and is designed to measure the severity of depression. It focuses exclusively on the nine diagnostic criteria for DSM-IV depressive disorder. Each item is rated from 0 (not at all) to 3 (nearly every day). Thus, the total score ranges from 0 to 27 [25].

Brief Resilience Scale (BRS)

The BRS is a simple scale consisting of six questions assessing the ability to "bounce back" or recover from stress. Three questions (Questions 1, 3, and 5) are positively worded, while three (Questions 2, 4, and 6) are negatively worded. One to five points are given for each question and scores for the negative questions are reversed and summed. The higher the total score, the higher the resilience [26].

Athens Insomnia Scale (AIS)

The AIS is a self-report questionnaire used to measure the intensity of sleep difficulties. The AIS comprises eight questions: five assess nocturnal sleep problems and three estimate the next-day consequences of insomnia. Each item is scored from 0 (no problem at all) to 3 (very serious problem), with the total score ranging from 0 to 24. Higher AIS scores indicate the presence of clinically significant insomnia symptoms.

Table 1. Clinical characteristics of the participants

Variable	Improved PCL-C score group	Worsened PCL-C score group	p value
Sex			
Male	16	11	0.024*
Female	10	23	
Age (yr)	16.12 ± 0.33	16.29 ± 0.46	0.099
Scale scores in 2014			
PCL-C	35.42 ± 13.62	25.09 ± 9.33	0.001*
PHQ-9	5.23 ± 5.94	2.85 ± 3.51	0.077
AIS	5.62 ± 4.62	3.24 ± 3.21	0.022*
BRPS	19.58 ± 5.78	19.65 ± 4.87	0.960
IQ	101.54 ± 10.82	103.15 ± 12.44	0.602
Scale scores in 2015			
PCL-C	26.69 ± 12.41	35.53 ± 13.01	0.010*
PHQ-9	4.50 ± 5.13	6.50 ± 5.45	0.154
AIS	5.69 ± 4.02	5.44 ± 3.78	0.805
Changes in clinical scale scores[a]			
ΔPLC-C	−8.73 ± 9.04	10.44 ± 9.82	-
ΔPHQ-9	−0.73 ± 2.78	3.65 ± 4.28	< 0.001*
ΔAIS	0.23 ± 3.45	2.21 ± 3.26	0.027*

Values are presented as number only or mean ± standard deviation.
PCL-C, post-traumatic stress disorder checklist-civilian version; PHQ-9, patient health questionnaire-9; AIS, athens insomnia scale; BRPS, brief psychiatric rating scale; IQ, intelligence quotient.
[a]Scale scores in 2015 − scale scores in 2014.
*$p < 0.05$.

Statistical Analyses

All data in this study are expressed as arithmetic means ± SDs, where appropriate. Descriptive analyses were performed to evaluate the baseline characteristics of the participants. We used chi-square and Student's t tests for categorical and continuous variables, respectively. Data analyses and descriptive statistics were performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA). The results were considered statistically significant if the p value was < 0.05 (two-tailed).

RESULTS

Clinical Characteristics

Although the data of 74 participants were collected initially, 14 participants were excluded due to the absence of completed questionnaires and EEG results. Finally, this study enrolled 60 patients. The clinical characteristics of the participants are provided in Table 1. Of the participants, 45.9% were male and the mean age of the participants was 16.2 ± 0.4 years. The mean PCL-C scores in 2014 and 2015 were 29.36 ± 12.41 and 31.95 ± 13.32, respectively. There was no significant difference in age, intelligence quotient, or BRS scores between the groups. There were more male participants in the improved PCL-C score group and more female participants in the worsened PCL-C score group.

The changes in the clinical scale scores after 1 year are also provided in Table 1. There was a significant difference in the changes in PHQ-9 scores over a 1-year period between the worsened and improved PCL-C score groups ($p < 0.001$). The mean change in AIS score also was significantly different between the two groups ($p = 0.027$).

EEG Recordings

We observed no significant differences between the worsened and improved PCL-C score groups for any band of baseline activity in 2014 ($p = 0.821$).

However, significantly different changes of activity in the delta band were observed between 2014 and 2015 in the worsened PCL-C score group compared to those in the improved PCL-C score group (Fig. 1). The group with worsened PCL-C score showed a increased change in delta power, and the region with the largest difference was localized to Brodmann area 13 of the left sublobar insular gyrus (X = −35, Y = −5, Z = 20, t = 4.15, $p = 0.017$). Increased change of delta activity was additionally observed in Brodmann area 44 of the left precentral gyrus (X =

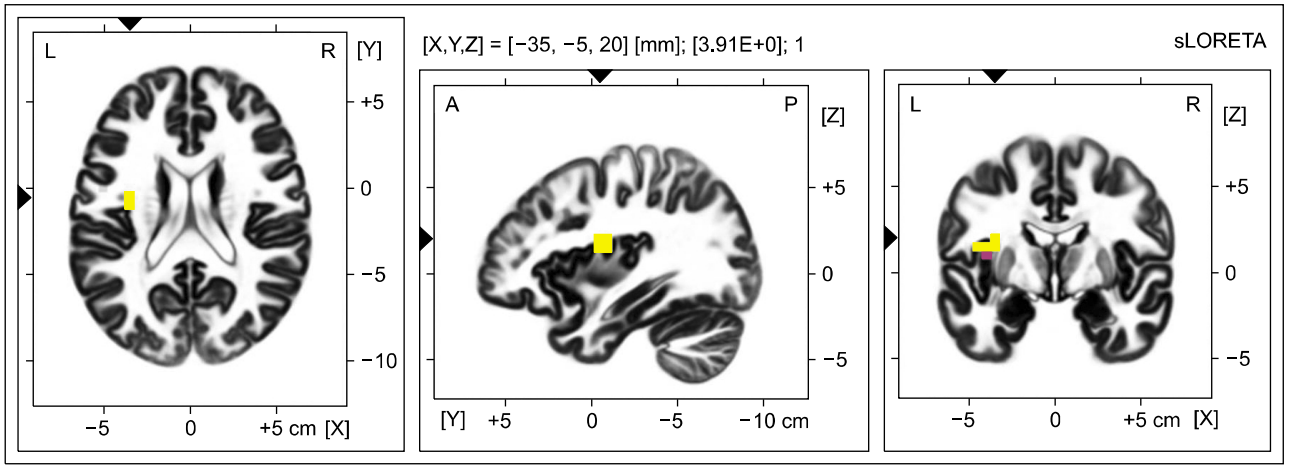

Fig. 1. A significant increase in the delta power spectra was detected on electroencephalography between 2014 and 2015 in the worsened group compared to that in the improved group. The red and yellow colors indicate increased cortical activity. The maximal difference was found in the left sublobar insular gyrus. The statistical significance was set at $p < 0.05$.

−45, Y = 0, Z = 10, t = 3.89, $p < 0.05$). The threshold for significance was t = 3.801, corresponding to a p value of < 0.05. We did not observe significant differences of EEG changes in the other frequency bands.

DISCUSSION

In this study, sLORETA revealed a significant difference between the groups with worsened and improved PCL-C scores, with higher changes of delta power in the left sublobar insular gyrus and prefrontal gyrus in the group with worsened scores. Increased changes of delta activity in insula means relatively enhanced slow wave activity in insula, indicating altered functioning, possibly left insular dysfunction, in PTSS psychopathology.

The insula is a triangular area of the brain located beneath the Sylvian fissure. It is covered by the opercula of the frontal, parietal, and temporal lobes [27,28]. Neurons in the insular cortex exhibit broad and dense interconnections; thus, the insula is involved in emotion; attention; and verbal, motor, visual, olfactory, gustatory, and somatosensory data processing [29,30]. The role of the insula in psychiatric disorders, including PTSD, has received much attention [28,31].

A previous voxel-based analysis using magnetoencephalograms showed focally enhanced slow wave (1−4 Hz) activity in the insula region of the PTSD group compared to that in the control group [32]. Furthermore, in several neuroimaging studies, PTSD patients showed a reduction in the gray matter volume of the insula compared to that in controls [33-35]. Structural brain magnetic resonance imaging (MRI) studies of combat-exposed US military veterans showed smaller volumes of the left insula, subgenual anterior cingulate cortex, caudate, and hypothalamus in the PTSD group compared to those in the trauma-exposed healthy control group [36]. The regional cerebral metabolic rate of glucose in the (right) anterior insula and adjacent prefrontal and striatal areas was lower in the PTSD group than that in the recovery group in an 18fluoro-2-deoxyglucose positron emission tomography (FDG-PET) study of trauma-exposed individuals [37]. Based on these results, the study suggested that glucose metabolism in the anterior insula might be related to resilience after trauma and vulnerability to PTSD development. A long-term FDG-PET study on PTSD (20 years after trauma experience) reported relatively diminished activity in the insular region [38].

Altered functional connectivity between the insula and dorsal anterior cingulate cortex or amygdala was observed in PTSD patients [38,39]. The insula is engaged in anticipation processes and fear conditioning, and studies have suggested that changes in insular activity may be related to the hyperarousal symptoms of PTSD. The anterior insula is a key area involved in interoceptive awareness, integrating emotionally potent stimuli with body arousal, and providing a representation of subjective feeling states [40].

The anterior insula has been suggested to interfere with the integration of fragmented somatic sensation and emo-

tional states into declarative memories, which may lead to dissociative phenomena [41]. A fMRI study using script-driven imagery responses showed a negative correlation between dissociative symptoms in the PTSD group and anterior insula activation [42]. Decreased functional connectivity of the vestibular nuclei with the parieto-insular vestibular cortex was observed in dissociative subtype PTSD in resting-state fMRI studies, suggesting that dysregulation of this integration contributes to dissociative symptoms [43].

Emotional face processing in PTSD patients showed that childhood maltreatment was negatively correlated with amygdala-insular connectivity and activation of the insula and dorsal anterior cingulate cortex during the processing of fear and anger [44]. Individuals who recovered from PTSD after prolonged exposure therapy showed increased functional connectivity between the insular and cingulate regions and changes in functional activation, especially in the left anterior insula, in an fMRI study [45]. In a resting-state fMRI study comparing PTSD patients and individuals who had experienced trauma without PTSD using the amplitude of low-frequency fluctuation (ALFF) to reflect the intrinsic functional baseline activity of the brain, PTSD patients showed decreased ALFF in the insula, right lingual gyrus, cuneus, middle occipital gyrus, and cerebellum [46].

Delta power is generally associated with decreased sleep and alertness [47]. However, it is also related to the situation in which the person is awake but the body is at rest. It is known that there is a strong correlation between power of delta wave and the default mode network (DMN) in previous studies. The parahippocampal gyrus and the delta power within the DMN showed highly significant correlation in a simultaneous fMRI-EEG study [48]. Less delta power was observed in individuals experiencing greater psychological distress in adults who had experienced depression [49]. A greater change in the delta waves, generated in the insula in the worsened PTSS group than in the improved PTSS group in this study, may mean that the worsened PTSS group needs more DMN activity for recovery. This is contrary to the previous results in which a decrease in DMN activity was observed in a study of PTSD patients [50]. Since this study was not conducted in clinical PTSD patients, results may differ from those in PTSD patients. However, this is consistent with the result of increased functional connectivity of DMN in depressed patients with ruminations [51].

We speculate that people experiencing acute trauma who do not meet the criteria for PTSD may still experience psychological stress and require medical intervention. However, most previous studies have focused on patients with confirmed PTSD. Thus, more attention to symptoms and changes irrespective of diagnosis is needed in clinical practice settings. By identifying differences in objective measurements such as EEG between the PTSS groups with improved and worsened scale scores, we may proactively prevent symptom aggravation.

Our study has several limitations in terms of the generalizability of the findings. The first is the comorbidity of depression. Because of the common comorbidity of depression in patients who suffer from PTSD [52-54], the findings of this study may have resulted from neurophysiological changes in depression. Second, since this study employed a retrospective design, selection bias was possible. To generalize our results, a prospective study is needed. Third, we classified the participants into two groups according to the change of PCL-C scores which reflect PTSS between 2014 and 2015, however, did not consider the cut off value dividing the severity of symptoms.

Despite these limitations, our study had the unique strength of homogeneity of study participants. The population of this study, who had the same educational experience of the same grade, controlled for the diversity of traumatic events and population differences, which may be confounding factors in PTSD studies. Based on electrophysiological data obtained immediately and 1 year after the accident, we could speculate the knowledge of longitudinal neurophysiological changes. In this study, we observed an enhanced change of delta wave in the insula region in the group with worsened PTSS scale scores. This finding suggests that the electrophysiological changes in the insula are associated with PTSS changes.

■ Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

■ Author Contributions

Conceptualization: Young-Hoon Ko, Changsu Han. Data acquisition: Sehee Jin, Sang Won Jeon, Seung-Hoon Lee, Cheolmin Shin. Formal analysis: Sehee Jin, Cheolmin Shin. Supervision: Young-Hoon Ko, Yong-Ku Kim, Jongha Lee. Writing−original draft: Sehee Jin, Cheolmin Shin.

Writing—review & editing: Cheolmin Shin, Jongha Lee, Young-Hoon Ko. All authors have read and approved the final manuscript.

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