[UCI]I804:11046-000000520245

Structural brain and resting state brain activity alterations in trauma-exposed firefighters

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Structural brain and resting state brain activity alterations in trauma-exposed firefighters

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The Doctoral Dissertation
submitted to the Department of Medicine,
the Graduate School of Yonsei University
in partial fulfillment of the requirements for the degree of
Doctor of Philosophy

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June 2019

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Acknowledgements

I would like to express my special thanks of gratitude to Professor Seung-Koo Lee, who has always guided me throughout the Graduate School. Thank you for all your support and patience. You are the greatest boss of all in the Severance neuroradiology department!

Also, I thank my family for their everlasting love and support. I couldn’t have endured without you.

Sumin, the love of my life, thank you most of all. Your tears and laughter give me warmth and energy. I sincerely hope that you will grow up to be a thoughtful, warm human being who loves to seek wisdom and intelligence

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Structural brain and resting state brain activity alterations in trauma-exposed firefighters

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INTRODUCTION: To analyze the altered brain regions and intrinsic brain activity patterns in trauma-exposed firefighters without posttraumatic stress disorder (PTSD).

MATERIALS AND METHODS: This study received institutional review board approval, and all subjects underwent informed consent and resting-state functional MRI (rsfMRI). Thirty-one firefighters over 40 years old without PTSD (31 men, mean age, 49.8 ± 4.7 years) were included. Twenty-six non-traumatized healthy controls (HCs) (26 men, mean age, 65.3 ± 7.84 years) were also included. Voxel-based morphometric analysis was examined to investigate focal differences in brain anatomy. Seed-based functional connectivity analysis, integrated local correlation, and fractional amplitude of low-frequency fluctuations were employed to investigate differences in spontaneous brain characteristics.

RESULTS: The Seoul Verbal Learning Test mean z-scores on immediate recall, delayed recall, Controlled Oral Word Association Test (COWAT) animal, COWAT phonemic were significantly lower in the firefighters group than the HCs, indicating decreased neurocognitive function. Firefighters showed reduced gray matter volume at the left superior parietal gyrus and left inferior temporal gyrus compared with HCs. Firefighters showed alterations in rsfMRI values in multiple regions, including the fusiform gyrus, anterior cingulate gyrus, and cerebellum relative to HCs.

CONCLUSION: Structural brain and resting-state functional abnormalities may be useful imaging biomarkers for identifying alterations in trauma-exposed firefighters without PTSD.

Key words: firefighters, fractional amplitude of low-frequency fluctuation, integrated local correlation, voxel-based morphometry

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I. INTRODUCTION

The extremely stressful (traumatic) events in the firefighting duty can increase the risk for posttraumatic stress disorder (PTSD) symptoms in firefighters [1,2]. According to previous literature, [2-4] the prevalence rate of PTSD is two times greater in firefighters (18–37%) than general population (7–9%). Previous neuroimaging studies showed various abnormalities in brain structure [5-7] and function [8,9] in patients with PTSD. However, the firefighters that fail to satisfy the criteria of PTSD that frequently experience extremely stressful (traumatic) experiences have been understudied, although this population may provide a unique opportunity to examine the neural system related to work-related traumatic stressors. These individuals may be resilient people who have avoided the development of PTSD. Emerging evidence suggests that traumatic stress itself may have a substantial impact on brain structure and function even in the absence of PTSD symptoms. [10,11] Also, disturbances in brain function have already been suggested to contribute to cognitive impairments in patients with psychiatric disorders including PTSD. [12,13] However, the consequences of trauma on neurocognitive function in firefighters without PTSD remain unclear.

Previous studies have shown that human brain structure and function can be explored *in vivo* by neuroimaging techniques, such as voxel-based morphometry (VBM) and resting-state fMRI (rsfMRI). VBM allows a whole-brain regional specific assessment of deep gray matter and the brain cortex, which consists of neuronal cell bodies generating and processing nerve signals underlying brain function. [14] On the other hand, resting-state fMRI (rsfMRI) examines spontaneous fluctuations in blood oxygen level-dependent signals in the absence of a stimulus or task and enables the investigation of regional neural activity and functional connectivity. [15] Hypothesis-driven seed-based resting state functional connectivity (RSFC) analysis performs temporal cross-correlation and intuitive interpretation, whereas data-driven approaches such as integrated local correlation (ILC) and amplitude of fractional ALFF (fALFF) and are useful when studying subjects without any underlying hypothesis and has demonstrated high test-retest reliability. [15-17] Study on trauma-exposed firefighters without PTSD using these methods can inform the field’s understanding of the neural correlates of stress exposure.

The purpose of this study was to analyze the altered brain regions and intrinsic brain activity patterns in trauma-exposed firefighters without PTSD.

II. MATERIALS AND METHODS

1. Participants

This study was approved by the Yonsei University Heath System institutional review board, and all participants provided signed informed consent forms after receiving a complete description of the study. A total of 35 retired firefighters and incumbents over 40 years old were prospectively included in this study. Participants underwent comprehensive medical and psychiatric interviews. According to the Structural Clinical Interview for DSM-IV Axis I Disorders (SCID-IP), none of the participants were diagnosed with PTSD. The Psychometric Qualities of the Korean Version of the Post-traumatic Diagnosis Scale (PDS) [18] was also performed. The PDS is a 17-item self-report instrument that can provide both a diagnosis of PTSD and measures of overall and subscale symptom severity. [19] Respondents rate each item on a 4-point scale (0 = not at all to 3 = very much) over a period of the past month. A symptom is counted as present if a score of 1 or higher is selected. These frequency scores are summed to produce a severity score. The Seoul Neuropsychological Screening Battery (SNSB) was performed to determine the cognitive status by trained clinical neuropsychologists [20]. The Seoul Verbal Learning Test recall test (memory), the Seoul Verbal Learning Test delayed recall test (memory), Rey Complex Figure delayed recall test (memory), Korean-Boston Naming Test (language), Rey Complex Figure copy test (visuospatial), Controlled Oral Word Association Test (COWAT) animal (frontal/executive), COWAT phonemic (frontal/executive), Stroop Test (frontal/executive), Korean-Trail Making Test-Elderly’s version (frontal/executive), and Digit Symbol Coding correct (frontal/executive) was performed. The Beck anxiety inventory

(BAI) [21], Center for Epidemiologic Studies Depression scale (CES-D) [22], Alcohol Use Disorders Identification Test (AUDIT) [23] and the Pittsburgh Sleep Quality Index (PSQI) [24] test were also performed. The exclusion criteria are as follows: 1) history of traumatic brain injury, 2) presence of comorbid medical conditions, 3) history of psychiatric disorder (e.g., psychotic or mood disorders), 4) history of substance abuse, and 5) absence of imaging sequences. A total of 31 firefighters (31 men, 49.8 ± 4.7 years) were enrolled. We also recruited 26 healthy controls (HC) (26 men, 65.3 ± 7.8 years) who were sex-matched, serving as a general non-traumatized group. In the HC group, only the SNSB test was performed.

2. Image acquisition

MRI scanning was conducted on a 3T scanner (Achieva; Philips Healthcare, Best, the Netherlands or Ingenia CX; Philips Healthcare, Best, the Netherlands) with a 32-channel head coil. T2*-weighted functional neuroimaging data were collected with a single shot echo-planar imaging (EPI) sequence, allowing for full-brain coverage collected axially (repetition time [TR] = 2000 ms, echo time [TE] = 40 ms, field of view [FOV]= 220 × 220 mm^2, number of slices = 31 (interleaved), number of axial volumes = 165, voxel size = = 2.75 × 2.75 × 4.5 mm^3, flip angle [FA] = 90°, and total acquisition time = 5 min 38 sec). Participants were instructed to rest and keep their eyes closed, lie still, and think of nothing in particular. For anatomical imaging, a 3D-T1-turbo field echo sequence was used with following parameters: TR = 9.9 ms, TE = 4.6 ms, FOV = 220 × 220 mm^2, section gap = 0 mm, voxel size = 0.859 × 0.859 × 1.0 mm^3, FA = 15°, total acquisition time = 5 min 29 sec. Head motion was minimized with restraining foam pads provided by the manufacturer.

3. Image analysis

A. Anatomical data preprocessing and VBM

All images were processed and analyzed using the CAT12 toolbox (C. Gaser, Structural Brain Mapping Group, Jena University Hospital, Jena, Germany; http://dbm.neuro.uni-jena.de/cat/) implemented in SPM12 (Wellcome Trust Centre for Neuroimaging; http://www.fil.ion.ucl.ac. uk/spm/software/spm12/). CAT12 served as the platform for all the analyses, as it offers processing pipelines for voxel-based morphometry (VBM) allowing us to perform all analysis with this software package. For processing- and analysis-steps, pre-set parameters in accordance with standard protocol (http://www.neuro.uni-jena.de/cat12/CAT12-Manual.pdf) were used, applying default settings unless indicated otherwise. Pre-processing included correction for bias-field inhomogeneities, normalization using the DARTEL-algorithm [25] and segmentation into grey matter (GM), white matter (WM) and cerebrospinal fluid (CSF). [26] The segmentation was followed by accounting for partial volume effects. [27] Data were smoothed with a 8 mm full-width at half-maximum (FWHM) Gaussian kernel. Processing also included a two-step quality assurance: first, all images were visually inspected for artefacts (prior to pre-processing); secondly, all underwent a statistical quality control for inter-subject homogeneity and overall image quality as included in the CAT12 toolbox (“check homogeneity” function) after segmentation. This second step again included a visual inspection procedure for potential newly introduced artefacts.

B. Functional data preprocessing

Standard image pre-processing methods were conducted employing the SPM12 software (http://www.fil.ion.ucl.ac.uk/spm/) with the CONN toolbox (http://www.nitrc.org/projects/conn) for functional connectivity analysis in MATLAB R2017b (MathWorks Inc., Natick, Massachusetts, US) environment. The functional images were corrected for slice time and motion, co-registered with a high-resolution anatomical scan, normalized into the MNI space, resampled at 3 mm^3 and smoothed with a Gaussian kernel of 8 mm^3 FWHM. In addition, the ARtifact detection Tools (ART: http://www.nitro.org/projects/artifact_detect) were used to measure motion artefacts in all individuals in both groups. We controlled for motion artefacts using 32 parameters: 12 realignment parameters with 1^{st} order temporal derivatives, ten WM-related artefacts with 1^{st} order temporal derivatives, and ten CSF-related artefacts with 1^{st} order temporal derivatives by realignment parameters detected with ART.

C. Regions-of-interests (ROIs) definition

We identified the brain regions which showed significant (false discovery rate [FDR]-corrected $P < .05$) grey-matter volume difference in the VBM analysis and used the automated anatomical labeling (AAL) to define the ROI. As a result, the following two brain regions were selected: the left superior parietal gyrus and left inferior temporal gyrus.

D. RSFC analysis

Following the pre-processing steps outlined above, the blood oxygenated level-dependent (BOLD) signal data were passed through a band pass filter (0.009–0.08 Hz) within the CONN toolbox in SPM12 for further data correction. The mean BOLD signal time course was then extracted from each of the predefined ROIs. The time course for each ROI was then correlated with the time course of the whole-brain voxels, allowing for the calculation of a correlation coefficient for each ROI by Pearson’s product–moment calculation.

E. ILC and fALFF analyses

Local coherence carries information regarding localized synchrony among neighboring neuronal units and is dependent on the physical proximity (i.e., anatomic structure). Regional homogeneity (ReHo) measure [28] is one method to investigate the local coherence. However, as ReHo is derived using Kendall's coefficient of concordance (KCC) [29,30] which is dependent on the number of voxels in the neighborhood, and inherently dependent on the spatial resolution. [16] On the other hand, this dependence on the spatial resolution is negligible for integrated local correlation (ILC), which is the integration of the entire spatial correlation function for each voxel and does not require the specification of a finite neighborhood. [16] Therefore, the present study used ILC measure to investigate the local coherence.

The amplitude of the low frequency fluctuations (ALFF) measures local activity of a given region. [31] ALFF values are calculated by applying a fast Fourier transformation to the BOLD time series of each voxel, giving the power of each frequency over time.

The square root of the power of frequencies between .01 and .08 Hz is proportional to the amplitudes of the BOLD signal and the changes in these amplitudes are considered the fluctuations of the BOLD signal. Dividing the low frequency band (.01–.08 Hz) by all frequencies measured proved more specific and sensitive to BOLD signal within gray matter as compared to CSF. [32] This measure is termed fractional ALFF (fALFF) and is considered to be a more GM-specific measure of local spontaneous brain activity than ALFF. [32,33] Both fALFF and ILC were calculated within the CONN toolbox.

4. Statistical analysis

To analyze demographic data and neuropsychological test scores, assumptions of normal distribution were tested with the Kolmogorov-Smirnov test. For neuropsychological performance, z-scores according to age- and education -specific norms were compared between groups. Student's t-test and Mann-Whitney test were performed according to normality. Multiple comparisons were corrected using false discovery rate (FDR) approach and a FDR corrected P value < 0.05 was considered statistically significant.

Independent t test was performed on each pair of the group's statistical images such as fALFF maps and ILC maps by using the SPM12 toolbox. The assumptions of unequal variance and independence among all groups was made on t tests. For VBM analysis, to allow more exploratory examination, the threshold for statistical analysis was first set to an uncorrected P < .001, and among the regions found from the uncorrected threshold, a voxel-level false discovery rate (FDR)-corrected P < .05 and a cluster-level uncorrected P < .05 were applied to reduce the potential Type I error. For RSFC, ILC, and fALFF analyses, the threshold for statistical analysis was first set to an uncorrected $P < .001$, and among the regions found from the uncorrected threshold, a cluster-level uncorrected $P < .05$ were applied.

III. RESULTS

There were 31 subjects identified as the trauma-exposed firefighter group without PTSD (all male, mean age 49.8 ± 4.7 years), and 26 HC subjects (all male, mean age 65.3 ±.7.8 years). The demographic and clinical characteristics of each group are provided in Table 1. There were no differences in the years of educations ($P = .22$). The group was sex-matched, but the age was significantly different between 2 groups ($P < .001$). The firefighters showed BAI, CES-D, AUDIT, PDS, and PSQI scores of 5.10 ± 5.58, 7.61 ± 3.72, 8.03 ± 5.5, 4.35 ± 5.5, and 6.55 ± 3.06, respectively.

Table 1. Demographic and Clinical Characteristics

	Trauma-exposed Firefighters (n = 31)	Healthy controls (n = 26)	P value*
Age	49.77 ± 4.70	65.31 ± 7.84	< .001
Sex			
Male	31 (100)	26 (100)	na
Education duration (years)	13.84 ± 2.35	12.65 ± 4.60	.22

Data are expressed as mean with standard deviation in parentheses or number with percentage in parentheses.

* Calculated from Student t test for continuous variables and Chi-square test for categorical variables, to compare the patient characteristics of firefighters and the healthy controls.

1. Neuropsychological test results

The results of neuropsychological tests presented as group mean z-scores based on age, education, and gender specific information in the firefighters and HC groups are summarized in Table 2. The Seoul Verbal Learning Test on immediate recall, delayed recall, and COWAT animal were significantly lower in the firefighters group than the HCs (FDR-corrected P = .004, < .001, and < .001, respectively). The Rey Complex Figure copy test were significantly higher in the firefighters group than the controls (P = .003). There was no significant difference in the Rey Complex Figure copy test copy test (P = .329), Korean-Boston Naming Test (P = .204), COWAT phonemic (P = .128) or Stroop color-word test (P = .251).

Table 2. Neuropsychological test results presented as group mean z-scores based on age, education, and gender specific normative information.

	Trauma-exposed Firefighters	Healthy controls (n = 26)	FDR-corrected

	(n = 31)		P value*
SVLT recall test	-0.53 ± 0.90	0.19 ± 0.85	.004
SVLT delayed recall test	-0.51 ± 0.92	0.36 ± 0.69	< .001
RCF delayed recall test	0.59 ± 1.12	0.74 ± 0.92	.329
Naming K BNT	0.54 ± 0.83	0.41 ± 0.66	.204
RCF copy test	0.76 ± 0.60	0.13 ± 0.68	.003
COWAT animal	-0.62 ± 0.95	0.42 ±1.00	< .001
COWAT phonemic	-0.20 ± 0.89	0.18 ± 0.67	0.128
Stroop Test - color reading correct	0.08 ± 0.71	0.33 ± 0.83	.251

FDR, false discovery rate; SVLT, Seoul Verbal Learning Test; RCF, Rey Complex Figure; K BNT, Korean-Boston Naming Test; COWAT, Controlled Oral Word Association Test

2. Group comparison of gray matter volumes

Compared with the HCs, the firefighters showed lower gray matter volumes at the left superior parietal (P < .05, FDR-corrected) and left inferior temporal gyrus (P < .05, FDR-corrected) relative to the HCs (Figure 1, Table 3). No gray matter increase was found in firefighters compared with HCs. These significantly different areas on VBM were used as seeds to perform seed-based functional connectivity analyses.

Left superior parietal gyrus Left inferior temporal gyrus

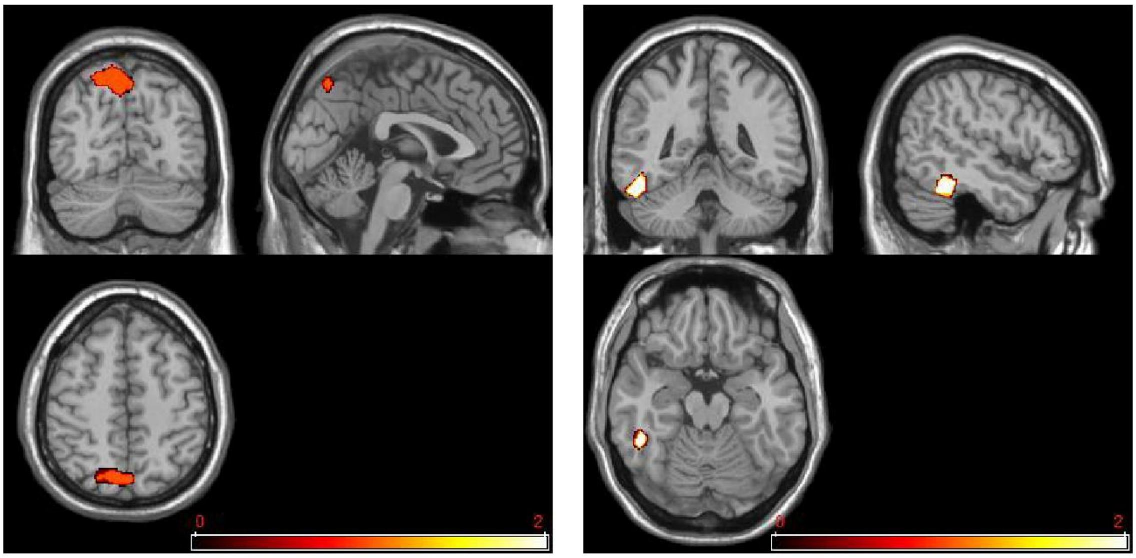


Figure 1. Brain regions showing less gray matter volume in trauma-exposed firefighters than in HCs (p < .05, FDR-corrected).

Table 3. Decreased gray matter volumes in the trauma-exposed firefighters relative to the healthy controls

Brain regions	Peak MNI coordinates			No. of voxels	Peak *t* value
	x	y	z		
Left superior parietal gyrus	-12	-69	54	1104	5.76
Left inferior temporal gyrus	-49.5	-45	-19.5	450	4.47

The regions that survived a whole-brain FDR-corrected threshold of p < 0.05, cluster size > 20.

3. rsfMRI results

A. Seed-based RSFC results

(A) Group comparison of RSFC by using the left superior parietal gyrus as seed

Compared with the HC, the firefighters showed decreased RSFC in the right superior frontal gyrus, right precentral gyrus, right fusiform gyrus, left superior frontal gyrus, left inferior orbital gyrus, and left superior frontal gyrus (uncorrected voxel-wise $P < .001$, uncorrected cluster-wise $P < .05$). The firefighters showed increased RSFC in the right cerebellum lobule VIII, left parahipppocampal gyrus, right fusiform gyrus, and right cerebellum lobules IV and V (uncorrected voxel-wise $P < .001$, uncorrected cluster-wise $P < .05$).

(B) Group comparison of RSFC by using the left inferior temporal gyrus as seed

Compared with the HC, the firefighters showed decreased RSFC in the left superior temporal gyrus, rigiht precentral gyrus, and left middle temporal gyrus (uncorrected voxel-wise $P < .001$, uncorrected cluster-wise $P < .05$). The firefighters showed increased RSFC in the right cerebellum lobules VI and IX (uncorrected voxel-wise $P < .001$, uncorrected cluster-wise $P < .05$). The results of RSFC using the left superior parietal gyrus and left inferior temporal gyrus is summarized in Figure 2 and Table 4.

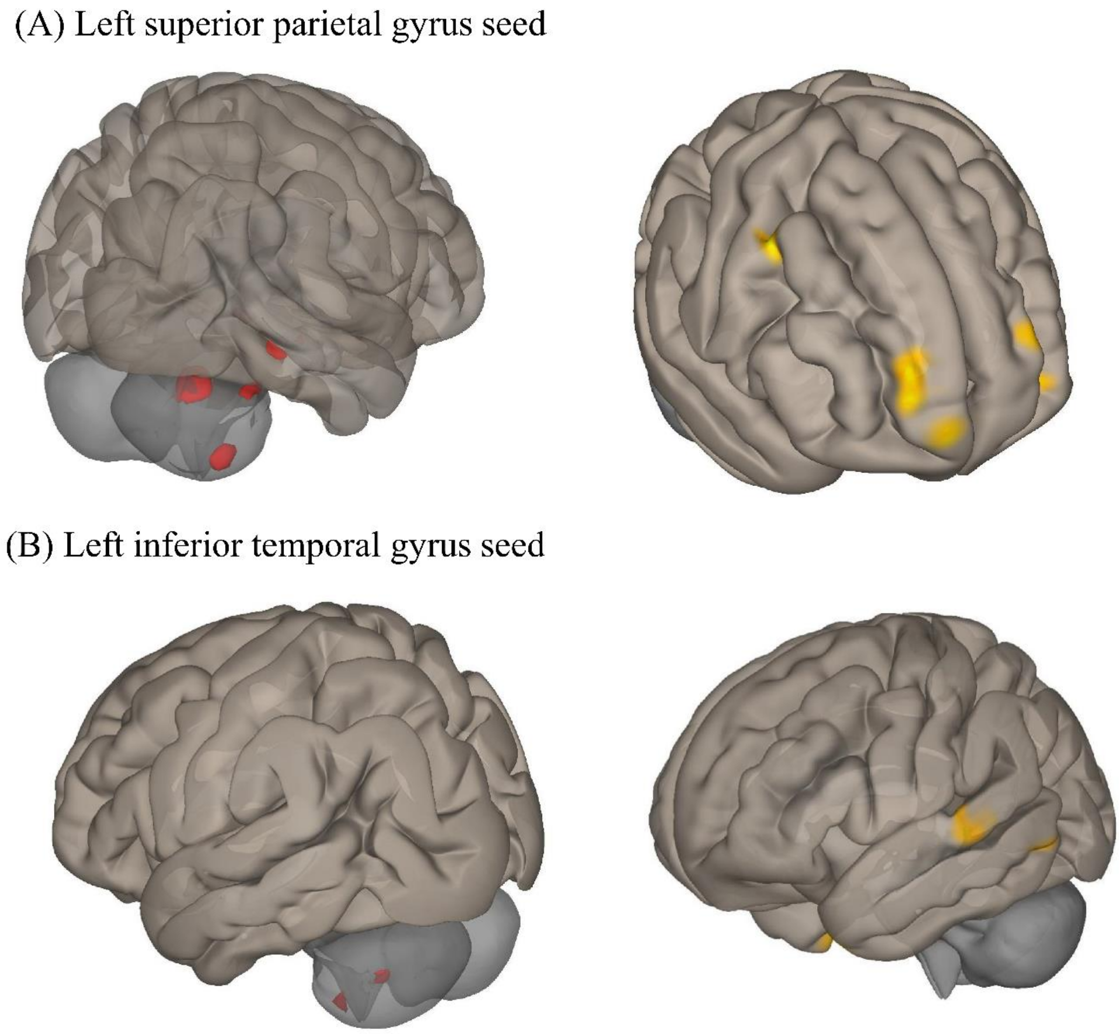


Figure 2. Seed-based functional connectivity analysis in the firefighters using the left superior parietal gyrus and left inferior temporal gyrus as a seed. Red colors indicate increased connectivity, and yellow colors indicated decreased connectivity in the firefighter group compared with the healthy controls (uncorrected voxel-wise P < .001, uncorrected cluster-wise

P <0.05). (a) Results by using left superior parietal gyrus as seed. (b) Results by using left inferior temporal gyrus as seed.

Table 4. Regions showing significant differences in functional connectivity when using left superior parietal gyrus and left inferior temporal gyrus as seeds

Brain regions	Peak MNI coordinates (x, y, z)			No. of voxels	Peak t value
	x	y	z		
Seed: Left superior parietal gyrus					
HC > firefighter					
Right superior frontal	24	68	12	383	5.41
Right precentral gyrus	42	2	48	108	5.02
Right fusiform gyrus	32	12	-44	100	4.97
Left superior frontal gyrus	-24	60	22	53	4.37
Left inferior orbital gyrus	-24	28	-22	50	4.34
Left superior frontal gyrus	-30	54	0	42	4.12
Firefighter >HC					
Right lobule VIII of cerebellar hemisphere	26	-50	-54	150	7.85
Left parahippocampal gyrus	-12	-2	-20	95	4.66
Right fusiform gyrus	36	-38	-16	66	4.37
Right lobule IV, V of cerebellar hemisphere	30	-38	-28	76	3.97

Seed: Left inferior temporal gyrus					
HC> firefighter					
Left superior temporal gyrus	-60	-24	2	74	4.31
Right precentral gyrus	52	0	34	104	4.20
Left middle temporal gyrus	-48	-58	-4	53	4.16
Firefighter>HC					
Left lobule IX of cerebellar hemisphere	-2	-25	-46	64	4.51
Right lobule VI of cerebellar hemisphere	30	-52	-32	53	4.17

MNI = Montreal Neurological Institute

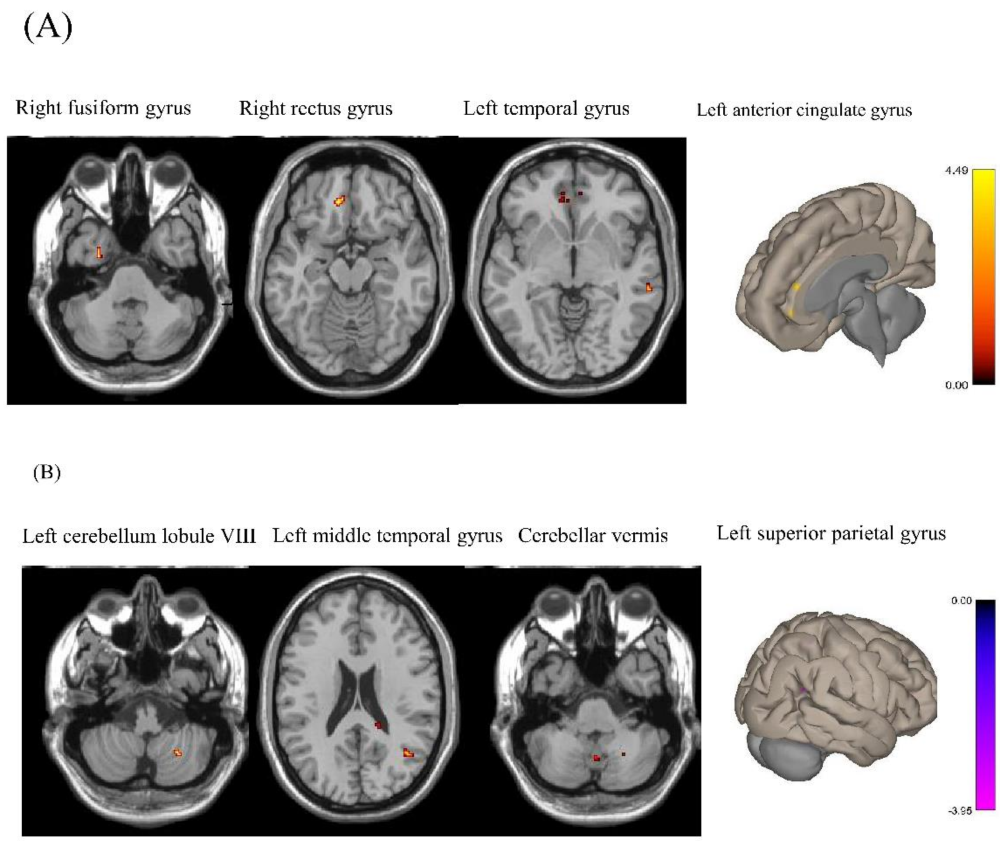
The regions that survived a threshold of uncorrected voxel-wise P < .001, uncorrected cluster-wise P <0.05

B. ILC

The firefighters showed decreased ILC in the right fusiform gyrus, right rectus gyrus, left middle temporal gyrus, right superior parietal gyrus, and left anterior cingulate gyrus than the HCs (uncorrected voxel-wise P < .001, uncorrected cluster-wise P <0.05). The ILC significantly increased in the left cerebellum lobule VIII, cerebellar vermis, bilateral crus cerebellum, right cerebellum lobule VI, right precentral gyrus, left superior parietal gyrus, left middle temporal gyrus. n the firefighters than the HCs (uncorrected voxel-wise P < .001, uncorrected cluster-wise P <0.05). (Figure 3a and 3b)

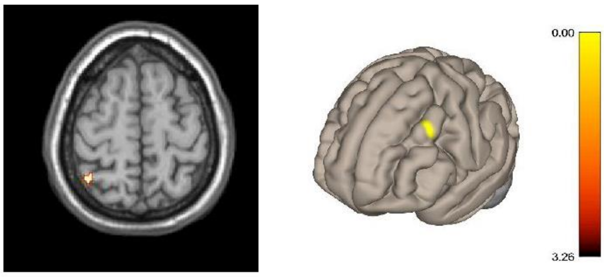
C. fALFF

In comparison with the HCs, the firefighters showed decreased fALFF in the right crus cerebellum and right frontal middle gyrus (uncorrected voxel-wise P < .001, uncorrected cluster-wise P <0.05). The fALFF significantly increased in the right precentral gyrus and left superior parietal gyrus in the firefighters than the HCs (uncorrected voxel-wise P < .001, uncorrected cluster-wise P <0.05). (Figure 3c and 3d)



(C)

Right frontal middle gyrus



(D)

Right precentral gyrus Left superior parietal gyrus

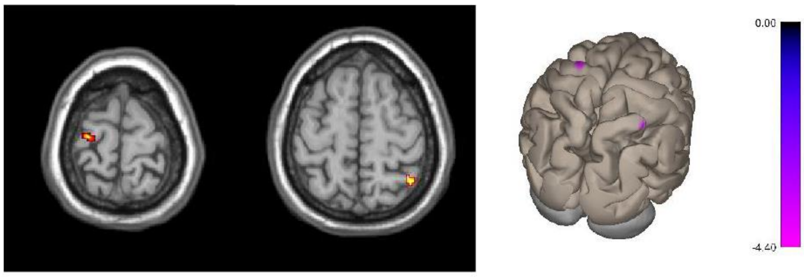


Figure 3. Two-sample t-test results for ILC and fALFF (uncorrected voxel-wise P < .001, uncorrected cluster-wise P <0.05). (A) The firefighters showed decreased ILC in the right fusiform gyrus, right rectus gyrus, left middle temporal gyrus, right superior parietal gyrus, and left anterior cingulate gyrus than the HCs. (B) The ILC significantly increased in the left cerebellum lobule VIII, cerebellar vermis, bilateral crus cerebellum, right cerebellum lobule VI, right precentral gyrus, left superior parietal gyrus, and left middle temporal gyrus in firefighters than in HCs. (C) The firefighters showed decreased fALFF in the right crus cerebellum and right frontal middle gyrus than HCs. (D) The fALFF significantly increased in the right precentral gyrus and left superior parietal gyrus in the firefighters than the HCs.

IV. DISCUSSION

Our study evaluated structural brain and resting state functional activity alterations to determine difference between trauma-exposed firefighters and HCs. The firefighters showed lower mean z-scores on neurocognitive abilities compared to the HCs. The VBM results revealed trauma-exposed structural abnormalities in left superior frontal gyrus and left inferior temporal gyrus. Also, trauma-exposed alterations in rsfMRI values were noted in multiple regions, including the fusiform gyrus, anterior cingulate gyrus, and cerebellum.

Disturbances in intrinsic brain function have already been suggested to contribute to neurocognitive impairments in patients with psychiatric disorders, including PTSD. [34,35] Previous studies on childhood trauma has shown that traumatized patients show poor performance on measures of executive function, processing speed, and working memory. [36,37] However, the neurocognitive function and the relationships between neurocognitive function and resting state functional activity alterations has not been clear in trauma-exposed firefighters. Our study results suggest that exposure to traumatic stress events in firefighters might adversely impact the cognitive systems that support executive functioning, even in firefighters without PTSD.

In our study, the VBM results showed trauma-exposed structural abnormalities in left superior parietal gyrus and left inferior temporal gyrus. Caution is indicated in interpreting the VBM results because there may be partially overlapping clusters in the superior parietal gyrus. The superior parietal gyrus is divided into two subareas; the lateral superior parietal gyrus is defined as the superior parietal lobule, whereas the medial superior parietal gyrus is defined as the precuneus. The left superior parietal lobule is known to contribute to spatial orientation and working memory processing. [38,39] The precuneus not only plays a pivotal role in the default mode network, [40] but is also involved in a variety of complex functions, which include recollection and memory, integration of information relating to the perception of environment, cue reactivity, episodic memory retrieval, and affective response to pain. [41,42] The superior parietal lobule and precuneus may whereas the inferior temporal gyrus is critical for working and recognition memory. [43] The decreased volume of the left superior parietal gyrus and left inferior temporal gyrus in firefighters may partially account for the fact of decreased neurocognitive test results. In a previous meta-analysis of structural changes in PTSD, [5] only a handful of VBM studies compared trauma-exposed non-PTSD subjects and HCs with variable results; few studies reported lack of statistically significant findings between the trauma-exposed non PTSD subjects and HCs, [44,45] while other studies showed either gray matter reductions at the left pallidum and pulvinar of the right thalamus [46] or bilateral insula, hippocampus, left caudate, and putamen. [47] One plausible explanation for these discrepant results may be due to different trauma exposure and subjects; firefighters constantly experience multiple work-related traumatic events, whereas the aforementioned studies were performed in subjects exposed with a single trauma event. Further longitudinal studies with larger population are warranted to determine structural changes in trauma-exposed subjects without PTSD.

Also, firefighters differ from other trauma-exposed subjects in the aspect that they are exposed to hazardous conditions including chemicals, fumes, and particulates. [48] Previous epidemiological studies have linked acute and chronic effects of these exposures such as higher risks of cancers and cardiovascular disease, [49,50] and recent study shows that particulate matters may cause adverse neurologic outcomes by triggering cognitive decline and accelerated brain aging. [51,52] Therefore, there might be a synergic effect between exposure to hazardous conditions as well as exposure to trauma. Further studies are warranted to confirm our results.

Although there are ample studies focusing either on the brain structural or functional differences of PTSD compared to either a non-trauma or a trauma-exposed control groups, there is limited literature focusing in the differences between a trauma-exposed group to HCs. A previous study that performed a subgroup analysis of the trauma-exposed group with the HCs in a PTSD study suggested that ReHo changes in the salience network including the anterior cingulate gyrus, irrespective of the development of PTSD. [53] In our study, the firefighters showed decreased ILC in the anterior cingulate gyrus, which is consistent with results of the previous study. Also, multiple previous studies have demonstrated impaired fusiform activity and connectivity in PTSD; decreased ILC was also seen in firefighters from our studies. [54,55] These impairments in connectivity may underline symptoms of trauma-exposed subjects. We also found altered ILC and fALFF values the cerebellum in firefighters. There is a growing body of evidence indicating that disrupted cerebellar activity may contribute to psychiatric illness; a previous meta-analysis of rsfMRI in PTSD showed altered activities in the cerebellar hemisphere (cerebellar pyramis) in PTSD patients, [56] which may be related to our results. [56] Another recent study demonstrated that the right anterior insula could be a core region of the network undergoing changes after experiencing a traumatic or painful event, but may not be specifically involved in the development of PTSD, but this finding was not noted in this study. [57]

The study has several limitations. First, this is a retrospective study with a relatively small sample size. Our results should be considered preliminary until confirmed in larger samples. Second, the age was not matched between the firefighters and HCs. However, we performed regression analysis to compensate for the age difference. Third, liberal statistical thresholds were applied in the rsfMRI results, which could increase the risk of false positive results. Fourth, because none of the firefighters were diagnosed with PTSD, no PTSD cases were included.

V. CONCLUSION

In conclusion, structural brain and resting-state functional abnormalities may be useful imaging biomarkers for identifying alterations in trauma-exposed firefighters without PTSD.

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ABSTRACT (IN KOREAN)

외상에 노출된 소방관들의 뇌 구조 및 휴식기 뇌기능 변화

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INTRODUCTION: 외상 후 스트레스 장애 (PTSD)가 없는 외상에 노출된 소방관들에서 뇌 구조의 변화와 휴식기 뇌기능 변화를 연구하고자 한다.

MATERIALS AND METHOD: 본 연구는 기관 검토위원회의 승인을 얻었으며, 모든 피험자는 정보에 입각 한 동의와 휴식기 기능 뇌자기공명영상 (rsfMRI) 검사를 받았다. PTSD가 없는 40 세 이상의 31 명의 소방관 (31 명, 평균 연령, 49.8 ± 4.7 세)이 포함되었다. 26 명의 외상을 받지 않은 건강한 대조군 (26 명, 평균 연령, 65.3 ± 7.84 세)도 포함되었다. Voxel-based morphometry 분석을 시행하여 뇌 해부학상의 국소적 차이를 조사하였으며, 휴식기 뇌기능의 차이를 조사하기 위해 seed-based functional connectivity analysis, integrated local correlation, 그리고 fractional amplitude of low-frequency fluctuations 분석을 시행하였다.

RESULTS: Seoul Verbal Learning Test의 평균 z값을 비교 시 소방관은 건강한 대조군에 비해 immediate recall, delayed recall, Controlled Oral Word

Association Test (COWAT) animal, COWAT phonemic 항목에서 점수가 유의하게 낮았으며, 신경인지 기능이 감소한 것으로 나타났다. 소방관은 left superior parietal gyrus와 left inferior temporal gyrus의 회색질 부피가 건강한 대조군에 비해 감소되어 있었다. 소방관은 fusiform gyrus, anterior cingulate gyrus, cerebellum 등을 포함한 여러 부위에서 건강한 대조군에 비해 rsfMRI 값의 변화를 보였다.

CONCLUSION: 구조적 뇌 및 휴식 상태 기능 이상은 PTSD가 없는 외상에 노출된 소방관의 변화를 확인하는 데 유용한 이미징 바이오 마커일 수 있다.

핵심되는 말: 소방관, fractional amplitude of low-frequency fluctuation, integrated local correlation, voxel-based morphometry