Original article

Brain metabolism in patients with vegetative state after post-resuscitated hypoxic-ischemic brain injury: statistical parametric mapping analysis of F-18 fluorodeoxyglucose positron emission tomography

Yong Wook Kim, Hyoung Seop Kim and Young-Sil An

Keywords: *hypoxic-ischemic brain injury; vegetative state; brain metabolism*

Background Hypoxic-ischemic brain injury (HIBI) after cardiopulmonary resuscitation is one of the most devastating neurological conditions that causing the impaired consciousness. However, there were few studies investigated the changes of brain metabolism in patients with vegetative state (VS) after post-resuscitated HIBI. This study aimed to analyze the change of overall brain metabolism and elucidated the brain area correlated with the level of consciousness (LOC) in patients with VS after post-resuscitated HIBI.

Methods We consecutively enrolled 17 patients with VS after HIBI, who experienced cardiopulmonary resuscitation. Overall brain metabolism was measured by F-18 fluorodeoxyglucose positron emission tomography (F-18 FDG PET) and we compared regional brain metabolic patterns from 17 patients with those from 15 normal controls using voxel-by-voxel based statistical parametric mapping analysis. Additionally, we correlated the LOC measured by the JFK-coma recovery scale-revised of each patient with brain metabolism by covariance analysis.

Results Compared with normal controls, the patients with VS after post-resuscitated HIBI revealed significantly decreased brain metabolism in bilateral precuneus, bilateral posterior cingulate gyrus, bilateral middle frontal gyri, bilateral superior parietal gyri, bilateral middle occipital gyri, bilateral precentral gyri ($P_{FEW\ correctecd}$ <0.0001), and increased brain metabolism in bilateral insula, bilateral cerebella, and the brainstem ($P_{FEW\ correctecd}$ <0.0001). In covariance analysis, the LOC was significantly correlated with brain metabolism in bilateral fusiform and superior temporal gyri ($P_{uncorrected}$ <0.005).

Conclusions Our study demonstrated that the precuneus, the posterior cingulate area and the frontoparietal cortex, which is a component of neural correlate for consciousness, may be relevant structure for impaired consciousness in patient with VS after post-resuscitated HIBI. In post-resuscitated HIBI, measurement of brain metabolism using PET images may be helpful for investigating the brain function that cannot be obtained by morphological imaging and can be used to assess the brain area responsible for consciousness.

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Hypoxic-ischemic brain injury (HIBI) after cardiopulmonary resuscitation is one of the most devastating neurological conditions causing the impairment of consciousness among adult brain injuries.[1] The pathophysiology of HIBI is a multi-factorial processes comprising of hypoxia, ischemia, anoxia, cytotoxicity or combination of these. Common etiologies include cardiopulmonary arrest, respiratory failure, and carbon monoxide poisoning.[2] For the survivors from HIBI, 30%–60% will develop long-standing cognitive, behavioral, or other neurological problems.[3] These problems may be functionally debilitating and severely affect the quality of life for patients and their families.

After post-resuscitated HIBI, most patients remain in a comatose state at least temporally, and when patients recover from coma the process follows a typical progression through various states of diminished consciousness. Clinically, patients in coma are unresponsive, usually with closed eyes and absent sleep-wake cycles, and do not response to various stimulations. Although there may be purposeless or reflexive behaviors in some cases, goal-directed motor activity is absent. Unlikely coma, the vegetative state (VS) is characterized by recovery of spontaneous eye opening and the restoration of sleep-wake cycles, but the

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Department and Research Institute of Rehabilitation Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea (Kim YW)
Department of Physical Medicine and Rehabilitation, National Health Insurance Corporation Ilsan Hospital, Gyonggi-do, Republic of Korea (Kim HS)
Department of Nuclear Medicine, Ajou University School of Medicine, Suwon, Republic of Korea (An YS)
Correspondence to: Yong Wook Kim, Department of Rehabilitation Medicine, Yonsei University College of Medicine, 250 Seongsanno, Seodaemungu, Seoul 120-752, Republic of Korea (Tel: 82-2-22287316. Fax: 82-2-3632795. Email: ywkim1@yuhs.ac)
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absence of any meaningful behavioral response to stimuli.

Brain positron emission tomography (PET) imaging has long been performed for the measurement of brain function in the VS state after acquired brain injury. However, in adult HIBI, the application of PET has been severely limited. Although the several studies using PET images for the evaluation of brain function in patients following post-cardiac arrest have been reported, most of them enrolled small numbers of patients and measured regional brain metabolism using visual analysis or the region of interest method.[4,5] In this study, we analyzed the changes of overall brain metabolism and investigated the brain areas correlated with the level of consciousness (LOC) in patients with VS after post-resuscitated HIBI using voxel-by-voxel based statistical parametric mapping (SPM) analysis with localization by automated anatomic labeling.[6]

METHODS

Subjects

We consecutively enrolled 17 patients with VS after post-resuscitated HIBI and 15 normal controls. The diagnosis of VS was performed according to the clinical rating scale for measurement for the LOC by JFK Coma Recovery Scale-Revised (JFK CRS-R).[7] The JFK CRS-R, initially described by Giacino et al,[7] has been used to investigate the LOC measuring by neurobehavioral response of the patients following brain injury. The JFK CRS-R consists of 6 subscales addressing auditory, visual, motor, oromotor, communication, and arousal processes. Scoring is based on the presence or absence of specific behavioral responses to sensory stimuli administered in a standardized manner. For each subscale, the lowest value represents reflexive activity, whereas the highest values represent cognitively mediated behaviors for auditory function (0–4 points), visual function (0–5 points), motor function (0–6 points), oromotor function (0–3 points), communication (0–2 points), and arousal (0–3 points). The summation of scores for the six subscales gives the total JFK CRS-R score. The families of all participants gave informed consents and all procedures were performed with the approval of the Institutional Review Board for Clinical Studies.

Imaging and SPM analysis of F-18 fluorodeoxyglucose positron emission tomography (F-18 FDG PET)

Brain metabolism using F-18 FDG PET were acquired on a GE Advance PET scanner (GE, USA). After fasting for at least 8 hours, subjects received 15 mCi (555 MBq) of F-18 FDG intravenously. All subjects were kept in unstimulated for 20 minutes with closed eye and unplugged ears, and then emission of scanning started and continued for 15 minutes. To reduce head movement during scanning, the subjects were positioned and maintained using an individually molded head holder. The in-plane and axial resolution of the scanner were 4.8 mm full width at half maximum (FWHM), respectively. F-18 FDG PET images were reconstructed using a trans-axial 8.5 mm Hanning filter and an 8.5 mm axial Ramp filter and displayed in a 128×128×35 matrix with a pixel size of 1.95 mm×1.95 mm×4.25 mm.

PET images were analyzed using SPM2 (Wellcome Department of Cognitive Neurology, Institute of Neurology, University College London, UK). Prior to the statistical analysis, the PET images for all subjects were created by averaging all images and were spatially normalized with the Montreal Neurological Institute standard PET template (MNI, McGill University, USA) using a nonlinear transformation of SPM2. Spatially normalized images were then smoothed by convolution using an isotropic Gaussian kernel with a 12-mm FWHM to increase the signal-to-noise ratio and to accommodate the variation in subtle anatomical structures. The effects of global metabolism were removed by normalizing the count of each voxel to the mean count of the brain (proportional scaling in SPM).

Statistical analysis

After spatial normalization, groups analysis (comparison between normal control and all patients with VS, normal control and short course VS patients, normal control and patients with VS after cardiac arrest induced HIBI, and normal control and patients with VS after respiratory failure induced HIBI) were performed on a voxel-by-voxel basis using two sample *t*-test. Statistical significance was determined using an extent threshold of 50 voxels. Correction for multiple comparisons was applied using familywise error (FEW) approaches and the corrected threshold was set at $P < 0.0001$. In addition, using single covariance analysis model, we searched for significant brain areas in which brain metabolism correlated with the LOC in all patients. Regions reaching an uncorrected P value of 0.005 were considered significant in the covariance analysis with 50 continuous voxels in cluster size. For visualization of the *t*-score statistics, the significant voxels were projected onto the 3D-rendered brain or a standard high-resolution MRI template provided by SPM2, thus allowing for anatomic identification. Anatomic labeling of significant voxels was performed using the automated anatomic labeling SPM toolbox[6] which was based on anatomy provided by the MNI.

RESULTS

Patients clinical data

The patients group consisted of nine males and eight females with a mean age of 40.5 years (range 21–64 years). The normal control group consisted of seven males and eight females with mean age 39.3 years (range 24–59 years). There was no significant difference between the two groups with respect to sex (P=0.51) or age (P=0.81).

Table 1 shows the demographics of 17 patients including sex, age, etiology of HIBI, duration from injury, and the score of JFK CRS-R. Among 17 patients with VS after

post-resuscitated HIBI, the causative injury was cardiac arrest in nine patients, respiratory failure in seven patients, and circulatory hypovolemia in one patient. The mean duration from injury was 13.1 months (range 1–60 months) with 13 patients with short course within 7 months after injury and the mean score of total JFK CRS-R was 4.9 points (range 3–6 points).

Changes of brain metabolism in 17 patients with VS after post-resuscitated HIBI

Table 2, Figure 1, and Figure 2 showed the differences in brain metabolism between the control subjects and patients with VS after HIBI. SPM analysis of F-18 FDG PET images showed that, compared to normal controls, patients with VS following HIBI showed significantly decreased brain metabolism in bilateral precuneus, bilateral posterior cingulated gyri, bilateral middle occipital gyri, bilateral superior parietal gyri, the right superior frontal gyrus, the right angular gyrus, the right supramarginal gyrus, both middle frontal gyri, and bilateral precentral gyri ($P_{FEW\ correctecd}$ <0.0001, κ=50; Table 2; Figure 1). In contrast, bilateral insular cortices, bilateral cerebella, the right inferior frontal gyrus, and the brainstem showed a significant increase in brain metabolism in patients with VS following HIBI compared with normal controls ($P_{FEW\ correctecd}$ < 0.0001, κ=50; Table 2; Figure 2).

Changes of brain metabolism in short course patients (13 cases within 7 months after injury) with VS after post-resuscitated HIBI

Table 3, Figure 3, and Figure 4 showed the differences in

Table 1. Demographics of patients with VS following HIBI

No.	Sex	Age (years)	Etiology of HIBI	Duration (months)	JFK CRS-R	
					A/V/M/O/C/A	Total (*n*)
1	Male	44	Cardiac arrest	1	A0/V0/M2/O0/C0/A2	4
2	Male	46	Cardiac arrest	2	A1/V1/M2/O0/C0/A2	6
3	Female	52	Hypovolemia	2	A1/V1/M1/O1/C0/A2	6
4	Male	64	Cardiac arrest	4	A1/V1/M1/O1/C0/A2	6
5	Male	30	Cardiac arrest	5	A1/V0/M1/O1/C0/A2	5
6	Female	53	Respiratory failure	5	A1/V0/M1/O1/C0/A2	5
7	Female	54	Cardiac arrest	5	A1/V0/M2/O1/C0/A2	6
8	Male	36	Cardiac arrest	6	A0/V0/M2/O1/C0/A2	5
9	Male	21	Respiratory failure	6	A0/V0/M1/O1/C0/A2	4
10	Male	48	Respiratory failure	7	A1/V0/M1/O1/C0/A2	5
11	Female	34	Respiratory failure	5	A1/V0/M1/O0/C0/A2	4
12	Female	59	Respiratory failure	10	A1/V0/M1/O1/C0/A2	5
13	Female	30	Respiratory failure	4	A0/V0/M1/O1/C0/A2	5
14	Female	24	Cardiac arrest	5	A1/V0/M2/O1/C0/A2	6
15	Male	27	Cardiac arrest	36	A1/V0/M1/O0/C0/A2	4
16	Male	41	Respiratory failure	60	A0/V0/M1/O0/C0/A2	3
17	Male	25	Cardiac arrest	59	A1/V0/M1/O1/C0/A2	5

HIBI: Hypoxic-ischemic brain injury; JFK CRS-R: JKF coma recovery scale-revised; A/V/M/O/C/A: Auditory/Visual/Motor/Oromotor/Communication/Arousal function scale.

Table 2. Brain metabolism in all patients (17 cases) with VS following HIBI compared with normal controls ($P_{FEW\ corrected}$ <0.0001, κ=50)

Brain metabolism	Area	Coordinate			*t* score	Cluster
		x	*y*	*z*		
Decrease						
Right side	Precuneus	6	–66	30	16.48	2214
Left side	Middle occipital gyrus	–48	–78	14	15.99	2162
Left side	Middle cingulum	–4	–52	38	15.73	2214
Left side	Precuneus	–14	–74	58	15.07	2162
Left side	Superior parietal gyrus	–28	–58	58	14.83	2162
Right side	Middle cingulum	4	–45	35	14.53	2214
Right side	Superior parietal gyrus	30	–56	66	14.29	110
Right side	Middle occipital gyrus	38	–90	–6	13.67	1166
Right side	Superior frontal gyrus	22	12	68	13.36	100
Right side	Middle temporal gyrus	62	–64	10	13.34	391
Right side	Middle frontal gyrus	50	6	52	12.55	303
Right side	Precentral gyrus	38	–15	70	12.12	303
Right side	Angular gyrus	56	–70	32	12.07	391
Left side	Middle frontal gyrus	–42	6	56	11.58	192
Right side	Supramarginal gyrus	55	–54	30	11.45	391
Left side	Precentral gyrus	–35	–5	55	10.27	192
Increase						
Right side	Insula	38	–6	24	12.41	146
Right side	Cerebellum	22	–48	–46	11.61	2430
Left side	Cerebellum	–22	–50	–50	10.99	2430
Left side	Insula	–36	–10	24	10.34	80
Right side	Inferior frontal gyrus	26	38	–2	10.19	92
Mid	Brainstem	–	–	–	–	–

brain metabolism between the normal controls and short course patients with VS after HIBI. SPM analysis showed that, compared to control subjects, short course patients showed significantly decreased brain metabolism in the right precuneus, the left middle occipital gyrus, the right inferior occipital gyrus, bilateral middle frontal gyri, the right superior frontal gyrus, and bilateral precentral gyri ($P_{FEW\ correctecd}$ <0.0001, κ=50; Table 2). In contrast, bilateral insular cortices, bilateral cerebella, and the brainstem showed a significant increase in brain metabolism in short course patients with VS following HIBI compared with normal controls ($P_{FEW\ correctecd}$ < 0.0001, κ=50; Table 3).

Changes of brain metabolism in patients with VS after post-resuscitated HIBI according to the etiologies (cardiac arrest and respiratory failure)

SPM analysis showed that, compared to normal controls, patients with VS after cardiac arrest induced HIBI showed significantly decreased brain metabolism in bilateral superior parietal gyri, bilateral precuneus, bilateral middle and inferior occipital gyri, the right middle temporal gyrus, and the left superior occipital gyrus ($P_{FEW\ correctecd}$ <0.0001, κ=50; Table 4). In contrast, the right insular cortex, both cerebella, and the brainstem showed a significant increase in brain metabolism in patients with VS following cardiac arrest induced HIBI compared with normal controls ($P_{FEW\ correctecd}$ <0.0001, κ=50; Table 4). In addition, compared to normal controls, SPM analysis in patients with VS after respiratory failure induced HIBI showed significantly decreased brain metabolism in bilateral middle occipital gyri, the left precuneus, bilateral middle frontal gyri, the right superior frontal gyri, and the bilateral precentral gyri ($P_{FEW\ correctecd}$ <0.0001, κ=50; Table 4). In contrast, bilateral cerebella, bilateral insular cortices, the right inferior

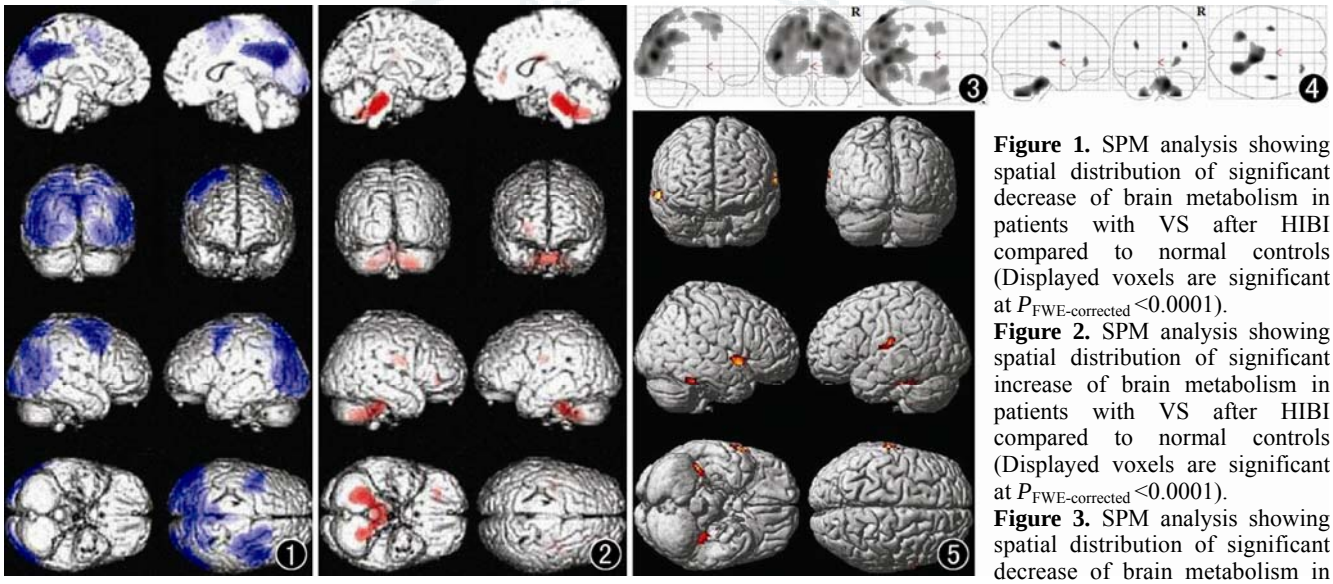

Figure 1. SPM analysis showing spatial distribution of significant decrease of brain metabolism in patients with VS after HIBI compared to normal controls (Displayed voxels are significant at $P_{FWE\text{-}corrected}$ <0.0001).

Figure 2. SPM analysis showing spatial distribution of significant increase of brain metabolism in patients with VS after HIBI compared to normal controls (Displayed voxels are significant at $P_{FWE\text{-}corrected}$ <0.0001).

Figure 3. SPM analysis showing spatial distribution of significant decrease of brain metabolism in short course VS patients after HIBI compared to normal controls (Displayed voxels are significant at $P_{FWE\text{-}corrected}$ <0.0001).

Figure 4. SPM analysis showing spatial distribution of significant increase of brain metabolism in short course VS patients after HIBI compared to normal controls (Displayed voxels are significant at $P_{FWE\text{-}corrected}$ <0.0001).

Figure 5. SPM analysis showing the brain areas in which brain metabolism correlates with the LOC measured by JFK coma recovery scale-revised in all patients with vegetative state after hypoxic-ischemic brain injury (Displayed voxels are significant at $P_{uncorrected}$ <0.005).

Table 3. Brain metabolism in short course patients (13 cases within 7 months after onset) of VS following HIBI compared with normal controls ($P_{FWE\ corrected}$ <0.0001, κ=50).

Brain metabolism	Area	Coordinate			*t* score	Cluster
		x	*y*	*z*		
Decrease						
Left side	Middle occipital gyrus	–48	–74	14	20.45	10197
Right side	Precuneus	8	–68	32	18.25	10197
Right side	Inferior occipital gyrus	42	–88	–6	16.79	10197
Right side	Middle frontal gyrus	48	14	52	13.13	1145
Right side	Superior frontal gyrus	24	10	68	13.11	1145
Right side	Precentral gyrus	30	–12	70	12.78	1145
Left side	Precentral gyrus	–38	–8	66	11.66	325
Left side	Middle frontal gyrus	–38	6	60	10.96	325
Increase						
Right side	Cerebellum	24	–58	–50	10.59	1602
Right side	Insula	38	–6	24	10.77	92
Left side	Cerebellum	–24	–52	–50	10.34	237
Left side	Insula	–34	–8	24	10.29	64
Right side	Inferior frontal gyrus	24	38	0	9.63	66
Mid	Brainstem	–	–	–	–	–

Table 4. Brain metabolism in patients with VS following HIBI according to the etiologies (cardiac arrest vs. respiratory failure) compared with normal controls ($P_{FEW\ corrected}$ <0.0001, κ=50)

Etiology of HIBI	Area	Coordinate			*t* score	Cluster
		x	*y*	*z*		
Cardiac arrest						
Decrease						
Right side	Superior parietal gyrus	30	–51	68	18.57	137
Left side	Middle occipital gyrus	–48	–76	14	15.92	214
Right side	Precuneus	6	–64	32	15.41	947
Left side	Precuneus	–6	–50	44	14.44	947
Left side	Superior parietal gyrus	–28	–72	56	14.10	382
Right side	Middle occipital gyrus	30	–96	8	14.04	155
Right side	Inferior occipital gyrus	36	–94	–2	13.87	155
Right side	Middle temporal gyrus	60	–66	12	12.42	52
Left side	Inferior occipital gyrus	–46	–82	–6	11.56	214
Left side	Superior occipital gyrus	–16	–86	42	11.69	382
Increase						
Right side	Insula	38	–4	24	12.43	76
Left side	Cerebellum	–10	–38	–38	10.73	503
Right side	Cerebellum	26	–48	–48	9.79	503
Mid side	Brainstem	–	–	–	–	–
Respiratory failure						
Decrease						
Left side	Middle occipital gyrus	–48	–74	14	20.45	10197
Right side	Precuneus	8	–68	32	18.25	10197
Right side	Middle occipital gyrus	42	–88	6	16.79	10197
Right side	Middle frontal gyrus	48	14	52	13.13	1145
Right side	Superior frontal gyrus	24	10	68	13.11	1145
Right side	Precentral gyrus	30	–12	70	12.78	1145
Left side	Precentral gyrus	–38	–8	66	11.66	325
Left side	Middle frontal gyrus	–38	–6	60	10.96	325
Increase						
Right side	Cerebellum	24	–58	–50	10.59	1602
Right side	Insula	38	–6	24	10.77	92
Left side	Cerebellum	–24	–52	–50	10.34	237
Left side	Insula	–34	–8	24	10.29	64
Right side	Inferior frontal gyrus	24	38	0	9.63	66
Mid	Brainstem	–	–	–	–	–

frontal gyrus, and the brainstem showed significant increased brain metabolism in patients with VS following respiratory failure induced HIBI compared with normal controls ($P_{FEW\ corrected}$ <0.0001, κ=50; Table 4).

Correlation analysis between the level of consciousness and brain area

Table 3 and figure 5 show the results of SPM correlation analysis between the regional brain metabolism and LOC measured by JFK CRS-R in each patient of 17 cases. The JFK CRS-R score was positively correlated with brain metabolism in bilateral fusiform gyri and superior temporal gyri ($P_{uncorrected}$ <0.005, κ=50).

Table 5. Correlations between brain metabolism and JFK CRS-R score in all patients ($P_{uncorrected}$ <0.005, κ=50)

Side	Area	Coordinate			*t* score	Cluster
		x	*y*	*z*		
Right	Fusiform gyrus	36	–44	–22	7.07	644
Right	Superior temporal gyrus	62	8	–6	5.23	101
Left	Fusiform gyrus	–30	–44	–20	4.24	403
Left	Superior temporal gyrus	–66	–20	16	4.01	67

DISCUSSION

In our study, patients with VS after post-resuscitated HIBI showed widespread brain hypometabolism in the bilateral frontal, parietal including the precuneus and the posterior cingulate gyrus, and occipital areas. Also, the hypermetabolic brain areas were detected in the bilateral insular, cerebellum and brainstem.

Recent development in neuroimaging methods has allowed better estimation of the effects of HIBI on the brain. The magnetic resonance imaging (MRI), single photon emission computed tomography (SPECT), and PET images have become increasingly valuable in the work-up of patients with HIBI. As more effective treatment strategies developed, brain imaging tools have the significant role in diagnosis and intervention since they provide information on the severity and extent of HIBI and can be helpful in predicting long-term outcome.[8,9] However, the results of neuroimaging in patients with HIBI are highly variable depending on a number of factors, including the type of injury, the duration of insult and timing of imaging studies.[8]

According to the definition by the Multi-Society Task Force[1] and the Royal College of Physicians,[10] patients in VS are fully aroused, but are short of awareness for themselves and environment. The reticular activating system in the brainstem which normally modulates wakefulness is preserved to allow the maintenance of an

arousal state in the VS.[11] From the SPM analysis, our findings also demonstrated that, compared to normal controls, patients with VS after post-resuscitated HIBI showed increased brain metabolism in the brainstem which suggest the maintenance of arousal state.

The overall brain metabolism of comatose patients from HIBI is 50%–70% that of normal healthy subjects.[12] In VS, the global brain metabolic activity also decreases to 40%–50% of the normal healthy subjects.[13] Also, the frontoparietal cortex including the precuneus, posterior cingulate gyrus,[14,15] which is most active area in subject with conscious waking,[16] is known as a significantly impaired brain lesion in patients with VS. Our findings of widespread hypometabolic area in the precuneus, the posterior cingulum, and the frontoparietal area in all patients with VS after post-resuscitated HIBI is consistent with previous studies.[17-19] In addition, fourteen patients enrolled in this study failed to demonstrate a reflexive visual response from JFK CRS-R, which can explicate the significant hypometabolism in the occipital area regardless of the duration of insult. The mechanism of injury to the occipital cortex is unclear, however it can be postulated that the diffuse hypoxia affects the watershed region, a well-known border zone between arterial territories.[4,20] Also, the comparison of brain metabolism according to the etiologies showed that the HIBI from cardiac arrest was more involved in the parietal area, but the HIBI from respiratory failure more in the frontal cortex, which can be explained that the type of injury affects the different brain area.

Interestingly, we observed hypermetabolism not only in the brainstem, but also in the insular cortex and the cerebellum. The reciprocal connectivity of insular cortex with brainstem participates in the cardiovascular representation.[21] Benarroch[22] hypothesized the role of insular cortex as an internal regulatory system of the central autonomic network, and Oppenheimer et al[23] clarified the cardiovascular dysfunction induced by the injury to the insular cortex.[24] The research from Williamson et al[25] also reported that the insular cortex played a crucial role in cardiovascular adjustments within the central autonomic network. In addition, state-dependent regulation from insular area connected with subcortical structures may be involved in cardiovascular control.[26] Our findings of brain hypermetabolism in the insular cortex in patients with VS after HIBI could be suggested as the long-term maintenance of cardiovascular adjustment after resuscitation by regulation of the central autonomic network. The cerebellum receives mainly afferent inputs from the vestibular system, the sensory receptors of the extremities and the trunk. Rudolf et al[27] reported that the cerebellum is the brain area relatively spared from neuronal loss following HIBI. Beuthien-Baumann et al[28] hypothesized that relatively preserved input from the body, in contrast to decreased input from the cerebral hemispheres, could lead to a higher neuronal activity of the cerebellum in the VS. Our result of the preserved brain metabolism in the cerebellum is consistent with the previous studies.[14,27,28] Nevertheless, the underlying mechanism of increased metabolism and the precise role of the insular area and the cerebellum in patients with VS after post-resuscitated HIBI remain to be elucidated in the further study.

The reliable evaluation of the residual cognitive processing is of foremost importance for the appropriate management of patients with the VS. Objective assessment of LOC can be extremely difficult, as the response may be inconsistent, minimal, and difficult to document. However, the previous studies have indicated that functional neuroimaging may have an important role to play in the identification of residual cognition in the VS patients. The findings from Menon and Owen et al[29,30] and others[31,32] that visual stimulation by presenting photographs of a familiar face and meaningless picture to patient with VS activated the fusiform area, and auditory stimulation by meaningless sound activated the superior temporal cortex in patients with VS suggested the preserved cortical activity in VS. The results of our SPM analysis that the brain function in the fusiform and the superior temporal gyri is correlated with the LOC can be postulated the preserved cortical function in the temporal area in patients with VS after post-resuscitated HIBI.

Several limitations of the current study should be considered. First limitation relates to the lack of investigation of brain metabolism in the long course VS patients (more than 7 months after injury), which represents the change of brain metabolism according to the duration from injury. Second, it would be better and more clinically applicable if we were able to compare the changes of the LOC with initial PET image in each patient, which may provide the regional brain involvement associated with the recovery of consciousness from VS after post-resuscitated HIBI. However, we could not conduct the follow-up assessment of LOC in each patient.

In conclusion, our study suggests that the precuneus, the posterior cingulate area, and the frontoparietal cortex which is a component of neural correlate for consciousness, may be a relevant structure for impaired consciousness in patient with VS after post-resuscitated HIBI. In post-resuscitated HIBI, measurement of brain metabolism may be helpful for investigating the brain function that cannot be obtained by morphological imaging and can be used to assess the brain area responsible for consciousness. A better understanding of the underlying mechanism for impaired consciousness will contribute to optimizing therapeutic intervention for the HIBI.

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