의학박사 학위논문

The early cerebral hemodynamic changes in mild traumatic brain injury

- Voxel based morphometric study using perfusion CT scanned within 24 hours after injury -

경도 외상성 뇌손상 환자의 초기 대뇌 혈류역학 변화

- 수상 당일 촬영한 뇌 관류 전산화 단층 촬영을 이용한 복셀 기반의 형태 계측 방법을 이용한 연구 -

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서울대학교 의과대학원
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정 상 봉

A thesis of the Degree of Doctor of Philosophy

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August 2012
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Abstract

Objective

Only a few studies have investigated the changes associated with cerebral perfusion in mild traumatic brain injury (mTBI). Moreover, these studies were conducted on several cerebral lobes (frontal, temporal, and occipital) regardless of the differentiation between white and gray matter as regions of interest. The present study was conducted to test the hypothesis that cerebral hemodynamic change in mTBI patients could be detected early on perfusion computed tomography (pCT) by comparative voxel-wise mapping and to evaluate which network is mostly affected.

Methods

Admission pCT scans of 21 consecutive mTBI patients who visited our hospital between January 2017 and July 2017 were compared to scans from 15 normal controls. The image files were converted to an analyzable file format and then processed for spatial normalization with statistical parameter mapping (SPM) analysis. The pCT data of all patients with mTBI were then compared to those of normal controls.

Results

SPM analysis of pCT imaging from mTBI patients demonstrated significantly decreased cerebral blood flow (CBF) in the area involving mainly the left angular gyrus, the left supramarginal gyrus, and the area surrounding the cerebral white matter (p = 0.002; family-wise error[FEW] corrected). Other

perfusion parameters, including cerebral blood volume (CBV), mean transit time (MTT) and time to peak (TTP) were also significantly decreased in the same areas (CBV, p = 0.032; MTT, p = 0.002~0.021, and TTP, p = 0.002~0.006, all FWE corrected).

Conclusions

The results of the present study support the presence of early cerebral hemodynamic changes following mTBI, as detected by voxel-wise mapping. Our data further suggest that the location of such perfusion deficits are in a multisensory association area, which includes the angular gyrus, one of the most consistent resting state networks.

Keywords: mild traumatic brain injury, cerebral hemodynamic change, perfusion CT, voxel-based morphometry, angular gyrus, resting state network

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Introduction

Mild traumatic brain injury (mTBI) is a significant public health concern as it is a very common cause of cognitive impairment in socially active populations. Most patients with mTBI recover fully; however, some continue to report not only different subjective symptoms, such as headaches, dizziness, but also neurocognitive dysfunction with attention, memory or concentration impairments. Such prolonged post-mTBI symptoms significantly affect the quality of life for patients by interfering with their ability to return to work (1, 2).

One of most widely used imaging techniques in the acute phase of head injury including mTBI is non-contrast computed tomography (CT) for its merits of accessibility and rapidity. However, approximately 20% of the patients who sustain mild-to-moderate head injury have been reported to experience problems with resuming work due to neurobehavioral sequelae even though no abnormalities on admission non-contrast CT could be detected (3). Magnetic resonance imaging (MRI) is more sensitive for detecting smaller lesions or non-hemorrhagic contusions compared to CT scanning (4, 5). Early, routine MRI scanning, however, is seldom performed in trauma patients (6). Moreover, quantification of perfusion parameters in MRI is possible but not practical.

Perfusion CT (pCT) is a recently introduced and widely available modality that makes use of the dynamics of intravenous-injected contrast material distribution. In an increasing number of hospitals, pCT is applicable even in the emergency setting of TBI. It provides absolute quantitative values of the cerebral perfusion parameters, including cerebral blood flow (CBF), cerebral

blood volume (CBV), mean transit time (MTT), and time to peak (TTP). The advantage of pCT over MRI is the possibility for data quantification. Therefore, early pCT has the potential of being used to understand the pathophysiology and clinical outcome of mTBI. So far, there have been only a few reports on the use of pCT during the acute mTBI phase, investigating various cerebral hemodynamic parameters and clinical outcomes (7–9). Metting et al. showed that disturbed cerebral perfusion in mTBI patients with normal non-contrast CT correlates with severity of injury and outcome (8). They also conducted another study trying to establish an association between regional cerebral hypoperfusion and neuropsychological deficits (9). However, these studies were conducted on only two axial slabs for several cerebral lobes (frontal, temporal, and occipital) regardless of differentiating white and gray matter as regions of interest (ROI). A ROI is a form of annotation, often associated with categorical or quantitative information. Each ROI is manually drawn even in anatomically ill-definable locations; therefore, manually driven ROI-based studies are limited by intra-observer and inter-observer reliability and bias. The present study was conducted to test the hypothesis that cerebral hemodynamic changes occur in the early phase of mTBI, which can be detected by pCT through comparative voxel-wise mapping. The image files were compared after the normalization-process on standard stereotaxic space. We also evaluated which network would be mainly associated with such cerebral hemodynamic changes.

2. Materials and Methods

2.1. Patient and control groups

Consecutive patients presented in our emergency department within 24 hours after acute mTBI between January 2017 and July 2017 were prospectively identified for enrolment. In our study, mTBI was defined as an initial Glasgow coma scale (GCS) of 13–15 without consciousness alteration or with it lasting less than 30 minutes, and post-traumatic amnesia lasting less than 1 hour (10). Exclusion criteria were: age (below 20 or above 70), history of neurologic disorders, such as stroke or brain tumor, or psychiatric morbidity, history of previous hospitalization for head injury, addiction to alcohol or drugs or pregnancy. Patients with a history of diabetes, nephropathy and contrast allergy were also excluded to prevent interference from non-specific white matter lesions or to avoid complications during pCT scanning.

Fifteen subjects who visited our Neuroscience Center for headaches only were used as the control group. The control subjects fulfilled the same exclusion criteria with the patient group and were not significantly different from them in respect to age (p = 0.574, Mann–Whitney U test) or sex (p = 0.561, Fisher's exact test).

Informed consent for pCT and general clinical research was obtained from patients and control individuals before enrollment. Permission to perform this study was provided by the Institutional Review Board of the National Medical Center, Korea (IRB number, 2016-09-062).

2.2. Perfusion computed tomography and image meta-analysis

Perfusion CT was performed in all patients within 24 hours after admission with a 128-channel multi-detector CT scanner, SOMATOM Definition Flash (Siemens Healthcare, Erlangen, Germany). After standard non-contrast brain CT scanning, pCT was performed in adaptive 4D spiral mode, based on a constant periodic bi-directional table movement. It was vertically imaged with scanning coverage of 100 mm in the Z axis. Axial slices with a thickness of 10 mm and an increment of 4 mm were continuously acquired. The pCT imaging parameters were as follows: tube voltage 80 kV, tube current 200 mAs, 30 spiral images with a travel time of 1.5 second per spiral, and a total acquisition time of 45 seconds. A total of 35 ml of highly iodinated contrast medium (Xenetix 350, Guerbet, Roissy, France) was injected at a rate of 4 ml/s followed by 20 ml of saline solution at 4 ml/s. The scanning delay time was 6 seconds after contrast injection.

Brain perfusion maps of CBV, CBF, MTT, and TTP were obtained from the pCT datasets. Data were processed on a dedicated workstation with commercially available 3D perfusion software (Syngo Volume Perfusion CT Neuro, Siemens Healthcare, Forchheim, Germany), including a 3D rigid motion correction, adaptive 4D noise reduction, and automatic exclusion of non-parenchymal voxels. The arterial input function was automatically placed in the anterior cerebral artery and the venous outflow in the superior sagittal sinus for the correction. For all datasets, we performed perfusion analysis with the vendor given software using a semi-automated deconvolution-based algorithm (11, 12). For each of the aforementioned perfusion parameters a set

of 23 color-coded slices was reconstructed. The colored slices were stored in Digital Imaging and Communications in Medicine (DICOM) format.

2.3. Statistical parametric mapping analysis

Firstly, the gray scale image files of each perfusion map were downloaded as a DICOM file format. The files were then converted to analyzable file formats after separating the header and image information with the MRIcro software. Image analysis was conducted by statistical parametric mapping (SPM12, Wellcome Department, University College of London, London, England) which operated under the MATLAB (The MathWorks®, Sherbom, Massachusetts) software. We installed MATLAB (R2017a) to run SPM12. Secondly, the spatial normalization process was performed. Spatial normalization refers to an automated process for warping the orientation, size, and shape of an individual's brain scan to match a standard stereotaxic space (13). This process is useful for conducting group statistics, where tests can be applied to a group of images registered in uniform space. Contemporary spatial normalization algorithms are guided by Montreal Neurological Institute (MNI) template images, derived from a population of neurologically healthy individuals. With this method, the normalization warps each individual's brain to approximately match the shape and size of the template image. The normalized images were smoothed using an 8-mm (full width at half maximum) isotropic Gaussian kernel. Meanwhile, we used the open-source skull stripped CT template (https://github.com/neurolabusc/clinical/blob/master).

Contrasts were defined to compare the perfusion parameters of mTBI patients to normal controls. A t−statistic image denoting the contrast condition effect was constructed. The resulting set of t values for each group comparison constitutes the SPM (t).

In multiple comparisons like in brain imaging, multiple testing correction is required that recalculates probabilities obtained from a statistical test, which has been repeated multiple times. We observed a statistically significant result by controlling the inflation of type I error (α) level with family−wise error (FWE) correction. The probability of making one or more type I errors in the family of tests is controlled within the level α. We analyzed only the areas that had at least 50 active voxels. The anatomical location corresponding to the above results was presented with SPM12. Statistically significant areas were also overlaid on the MRI standard atlas.

3. Results

3.1. Patient characteristics

A total of 32 patients were screened for inclusion. Of those, 8 patients had to be excluded for one of the previously mentioned reasons. The raw pCT scan data in 3 patients were discarded due to storage error. Therefore, the data from 21 patients qualified for final analysis. Further demographics about these 21 patients are summarized in Table 1. No evidence of litigation from the patient group was observed during this study. None of the patients were severely disabled and no patient required neurosurgical intervention. There were no significant differences in terms of gender or age between the groups.

All participants were classified as right-handed according to the Edinburgh handedness inventory (14).

The mean time between admission and pCT scanning was 6.9 hours (standard deviation, 2.2 hours). Perfusion CT scanning was always completed without complications, and no adverse reactions to the contrast material occurred.

Table 1. Patient demographics and clinical findings

Age	46.28 ± 15.97
Male : Female	12 : 9
Mode of injury	
Traffic accident	12 (57.1%)
Slip down	3 (14.2%)
Direct impact	4 (19.0%)
Other	1 (4.7%)
Glasgow coma scale	14.8 ± 0.4
15	18 (85.7%)
14	2 (9.5%)
13	1 (4.7%)

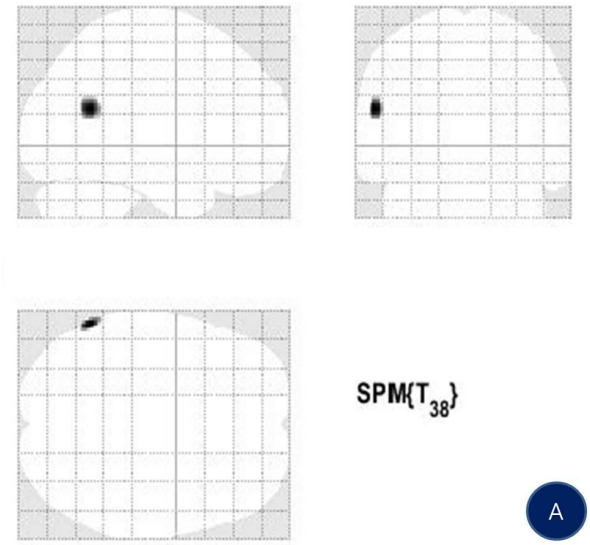
3.2. Differences in pCT mapping between mTBI and control patients

When comparing pCT parameters in mTBI to those of normal controls, decreased CBF was detected in an area mainly including the left angular gyrus (AG), the left supramarginal gyrus (SMG), and the left cerebral white matter (p = 0.002, FWE corrected). Other perfusion parameters were also significantly decreased in the nearby areas (CBV, p = 0.032; MTT, p = 0.002~0.021, and TTP, p = 0.002~0.006, all FWE corrected).

Areas with significantly reduced perfusion parameters are summarized in Table 2. The overlay of significantly reduced parameters during standard MRI and 3D volume-rendering imaging is displayed in Fig. 1, 2, 3, and 4.

Table 2. Areas with significantly reduced perfusion in patients with mTBI compared to healthy individuals.

	MNI coordinates : x, y, z (mm)			Corresponding anatomical area	
	x	y	z		
CBF	−58	−56	20	Left angular gyrus	23.0%
				Left supramarginal gyrus	15.6%
				Left superior temporal gyrus	21.2%
				Left middle temporal gyrus	9.0%
				Left cerebral white matter	7.4%
				Unknown	23.0%
CBV	−48	−60	40	Left angular gyrus	69.7%
				Left cerebral white matter	16.6%
				Left supramarginal gyrus	3.6%
				Unknown	10.1%
MTT	−52	−68	20	Left angular gyrus	44.3%
				Left middle temporal gyrus	26.0%
				Left cerebral white matter	2.3%
				Unknown	27.3%
	−56	−60	14	Left middle temporal gyrus	39.3%
				Left angular gyrus	21.3%
				Left supramarginal gyrus	15.1%
				Left cerebral white matter	3.1%
				Unknown	20.2%
TTP	−52	−66	20	Left angular gyrus	53.5%
				Left middle temporal gyrus	22.5%
				Left cerebral white matter	2.3%
				Unknown	21.2%
	−58	−52	40	Left middle temporal gyrus	74.6%
				Left superior temporal gyrus	10.9%
				Left cerebral white matter	10.5%
				Unknown	4.0%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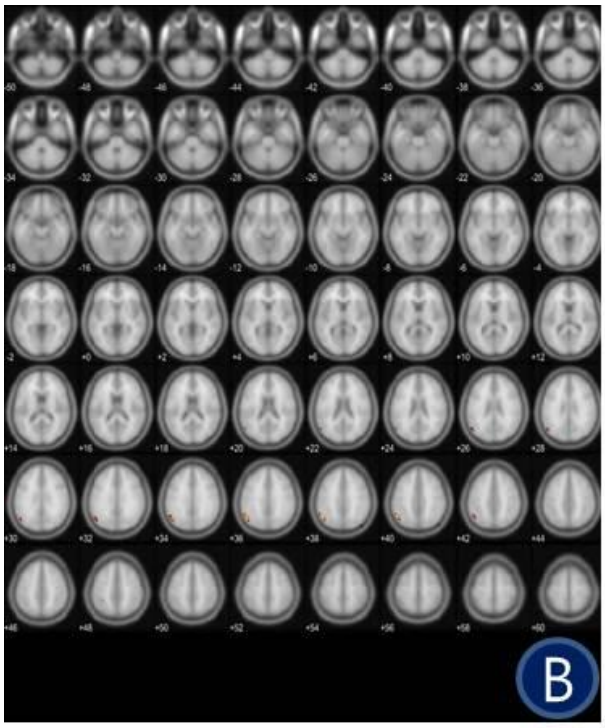
A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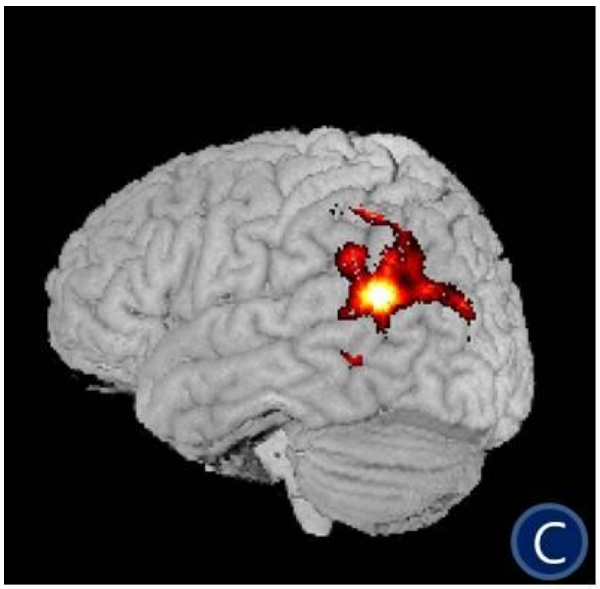
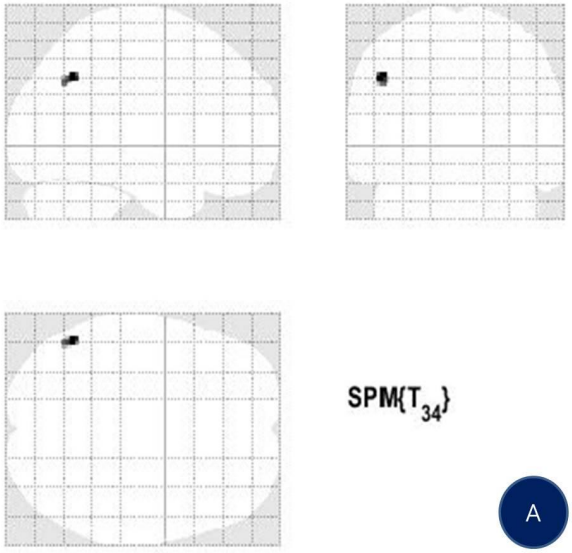


Fig. 1 Statistical parametric mapping (SPM) analysis reveals cerebral blood flow (CBF) alteration in brain areas of mild traumatic brain injury (mTBI) patients (A). Significantly decreased CBF with a cluster of more than 50 voxel was detected in mTBI scans (p < 0.05 family-wise error corrected for multiple comparisons). The changes are overlaid on a standard MRI template (B) and on a 3D volume-rendering image (C).



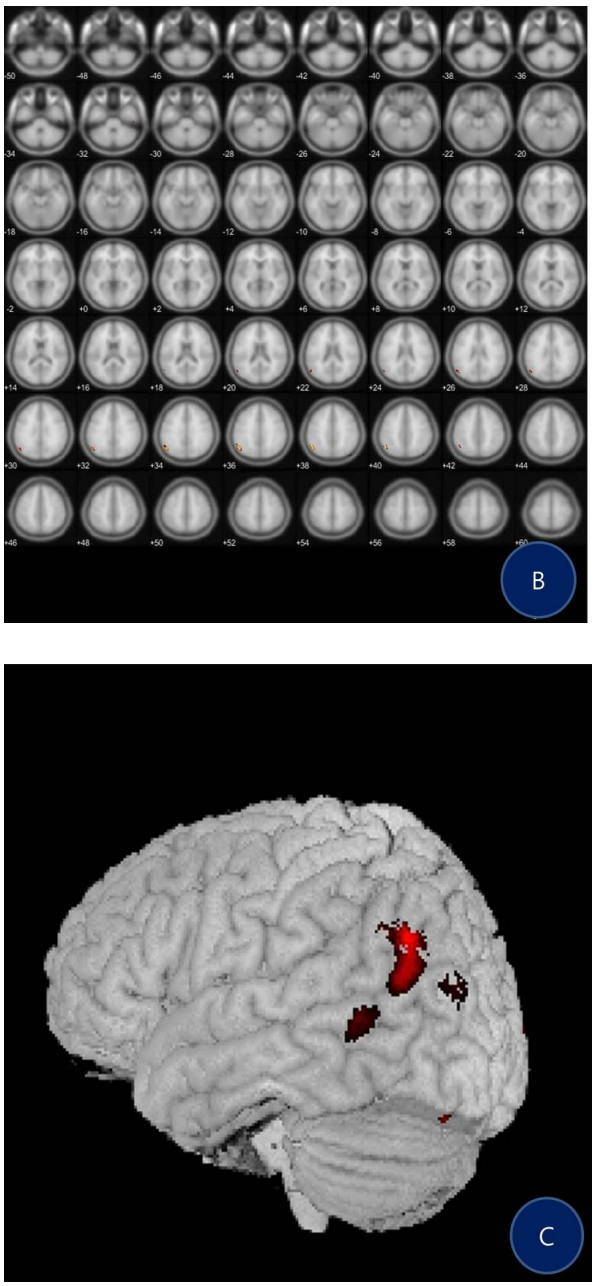
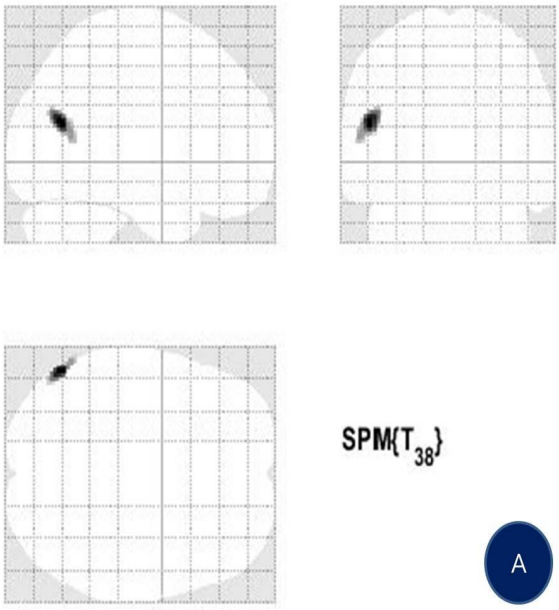


Fig. 2 Statistical parametric mapping (SPM) analysis reveals changes in cerebral blood volume (CBV) in brain areas of patients with mild traumatic brain injury (mTBI) (A). Significantly decreased CBV with a cluster of more than 50 voxel was detected in certain mTBI brain regions ($p < 0.05$ family-wise error corrected for multiple comparisons). The changes are overlaid on a standard MRI template (B) and on a 3D volume-rendering image (C).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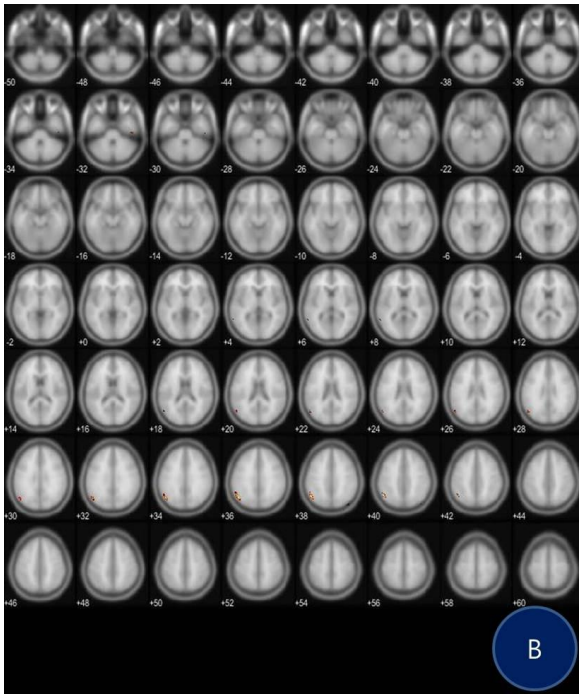
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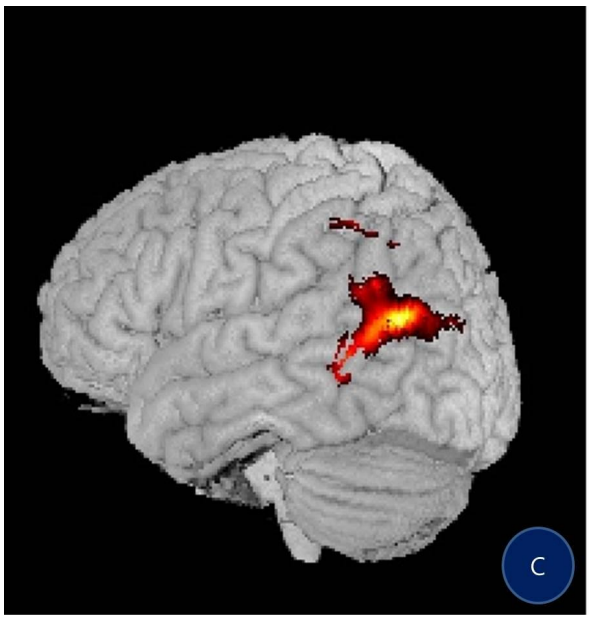
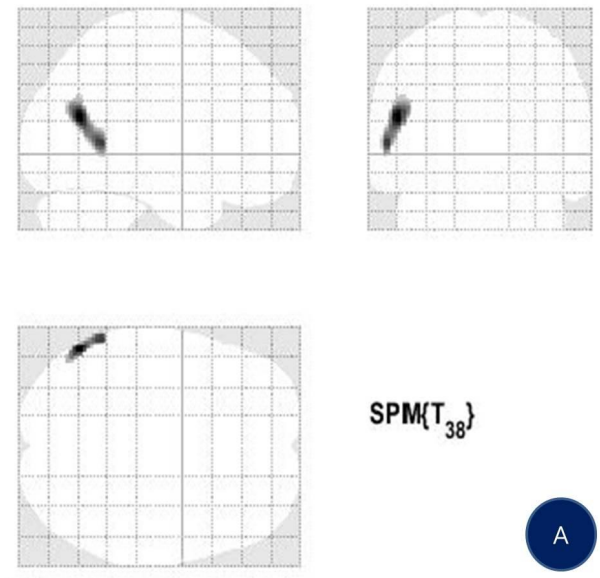
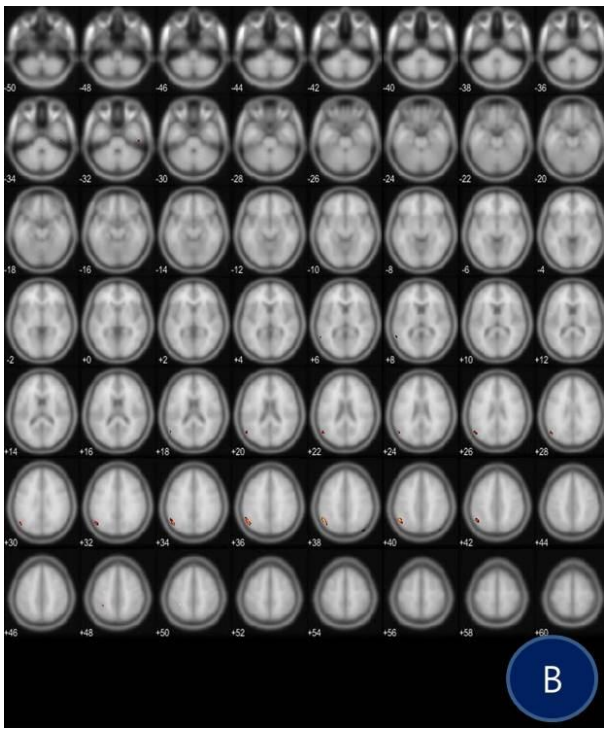


Fig. 3 Statistical parametric mapping (SPM) analysis reveals brain areas with altered mean transit time (MTT) in patients with mild traumatic brain injury (mTBI) (A). Significantly decreased MTT with a cluster of more than 50 voxel was detected at certain mTBI brain regions ($p < 0.05$ family-wise error corrected for multiple comparisons). The changes are overlaid on a standard MRI template (B) and on a 3D volume-rendering image (C).





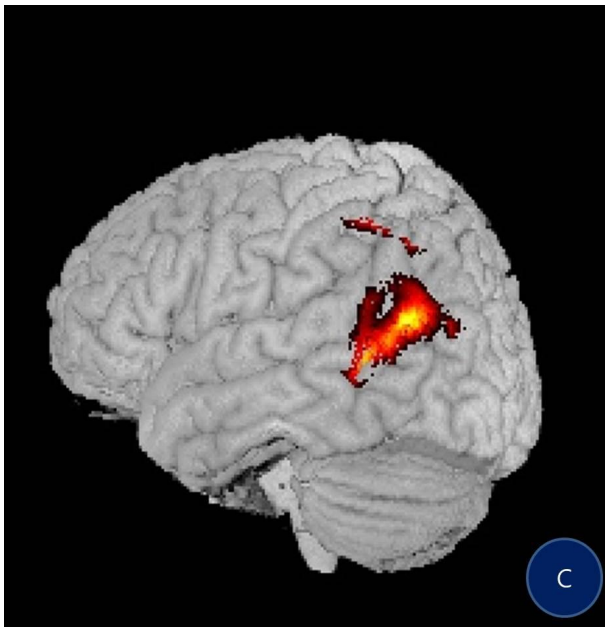


Fig. 4 Statistical parametric mapping (SPM) analysis reveals certain brain areas with altered time to peak (TTP) in patients with mild traumatic brain injury (mTBI) (A). Significantly decreased TTP with a cluster of more than 50 voxel was detected ($p < 0.05$ family-wise error corrected for multiple comparisons). The changes are overlaid on a standard MRI template (B) and on a 3D volume-rendering image (C).

Discussion

Although a significant number of patients sustaining mTBI exhibit long lasting cognitive impairment, the variable and subtle patient symptomatology is often not supported by objective neurological findings. This makes clinical detection and outcome prediction in the management of mTBI a challenge.

Following severe forms of TBI, there is an acute decrease in CBF in the first day (hypoperfusion phase), followed by a period of increased CBF (hyperemia phase lasting 1 to 3 days), and subsequently followed by another decrease in CBF that lasts from a few days to a few weeks (15). However, much less is known about CBF changes in mTBI. Mild TBI has been considered as a continuum of neurocognitive dysfunction, and the underlying pathophysiological mechanisms have attracted a lot of attention (16–18). The strongest outcome predictors in moderate to severe TBI, namely, duration of alteration of consciousness, initial GCS, and duration of post-traumatic amnesia, which are measures of injury severity have not been shown to be significant predictors of ongoing sequelae following mTBI (19–21). Recently, two studies with pCT during the acute phase after mTBI performed by Metting et al. reported that mTBI patients with impaired executive functioning had significantly different cerebral perfusion as compared to those with normal neuropsychological tests (8, 9). One of the major differences with the present study is that previous perfusion evaluation in most studies was limited to only specific brain area with a ROI approach. This method can only provide measures of predefined areas under presumed consideration. Additionally, smaller differences in volume may be overlooked. Since ROIs are usually

manually drawn, it results to not only time-consuming work but also to low reliability and bias in both the inter-observer and intra-observer level. We, instead, compared the hemodynamic changes of during early mTBI patient at the whole-brain level by scanning via voxel-based morphometry (VBM). This is a neuroimaging analysis technique that allows investigation of focal differences in brain anatomy, using the statistical approach of SPM. Compared to the ROI-based method, VBM registers every brain to a template, which eliminates of most of the large differences that exist among people. Following acquisition, the brain images are smoothed so that each voxel represents the average of itself and its neighboring voxels. Finally, the image volume is compared across brains at single voxel level. To the best of our knowledge, this is the first report of VBM using early pCT, which covers nearly the whole brain in the Z axis, for investigation of perfusion changes in mTBI patients. We encountered technical difficulties in applying VBM to our study together with pCT brain imaging. As our study was not based on MRI but CT images, which are inferior to MRI in terms of anatomical delineation (white and grey matter segmentation), segmentation and extraction of brain images are largely dependent on the bony structure, the skull. It is likely that VBM is sensitive to various artifacts, like the skull, which might lead to brain structure misalignment and thus, incorrect template normalization. In this study, the skull effect on spatial normalization was minimized not only by adapting the skull stripped CT template but also by the procession of skull stripping of pre-contrast pCT images. This improved spatial normalization process

enabled one location in one group' brain scan to be correlated to the same location in another group' brain scan.

Our results demonstrated that statistically significant perfusion deficits mainly on the left AG along with the left SMG are detected in mTBI patients, as compared to control (p = 0.002 ~ 0.032, FWE corrected). The AG, which is located in the posterior part of the inferior parietal lobule corresponding to Brodmann area 39, has been shown to be involved in semantic processing, word reading and comprehension, number processing, memory retrieval, attention and spatial cognition, reasoning, and social cognition. With its location at the junction between the occipital, temporal, and parietal lobes, the AG is considered an important interface that conveys and integrates information between different modalities and processing subsystems (22, 23). Joseph R. defined the AG as a processing center "where cross-modal associations such as visual, somesthetic and other sensory-motor concomitants are aroused, integrated, organized, assimilated, and finally comprehended (24). Converging multisensory inputs are integrated in the AG in a context-dependent fashion. This integration ultimately contributes in external events comprehension and reasoning or internal mental representations and results in a set of core processes (semantic access, fact retrieval, categorization of events, and shift attention to relevant events)(22). Along with the SMG, the AG functions as a multisensory association area, which combines last-stage recognized visual, auditory, and somatosensory stimuli via the respective sensory association and primary sensory areas (22). Severely disturbed sensory integration processes after mTBI could

result in impaired neurocognitive function including memory, attention and execution. This could be a reason why mTBI patients complain of subjective and subtle symptoms.

Besides this, the AG is thought to get activated together with other brain regions when the mind is not engaged in an explicit task and does not have an obvious goal—default mode network (DMN) (25–27). The AG forms one of the most consistent resting state networks engaging in the manipulation of conceptual knowledge and mental representation when people are not engaged in external interactions (28). These task—independent deactivations include specifically the bilateral inferior parietal, medial frontal, and posterior cingulate cortices. The deactivation in the inferior parietal cortex that includes the bilateral AG is remarkably reliable (29). Perfusion deficits in one of the resting state network areas might be the reason behind these subtle symptoms observed in mTBI patients. However, most of the previous studies on mTBI patients suggested that disturbed perfusion or disrupted balance in abnormal connectivity is observed mainly in the pre—rolandic area, which is presumed to result in impaired neurocognitive performance (8, 9, 30–32). These results were supported by the disruption of several important brain networks following mTBI (33, 34). Contrary to previous studies, our investigation demonstrates that the immediate perfusion changes following mTBI occur around the AG. Our data further suggest that the primary perfusion deficits occur in the posterior component of the DMN rather than in the anterior component. In support of this, Zhou et al. also observed significantly decreased functional connectivity in the posterior DMN

components and increased functional connectivity in the medial prefrontal cortex (mPFC) within 2 months after mTBI (30). No frontal clusters demonstrating significantly changed perfusion were detected in our study. However, increased mPFC activation might reflect a compensatory mechanism of increased frontal baseline activity or indicate the increased usage of mPFC neural resources to compensate for impaired neurocognitive function. This is worthy of future longitudinal studies focusing on the subacute and chronic phases of mTBI to determine if the above-mentioned changes are related to symptom evolution.

The results of the present study support the presence of early cerebral hemodynamic changes following even mTBI by voxel-wise mapping. Our data further suggest that the location of the perfusion deficits is a multisensory association area including the AG, one of the most consistent resting state networks. To our knowledge, perfusion reduction in the AG during the early phase of mTBI has not been reported previously in these patients. A possible reason for that is the fact that most studies have been conducted on the post-acute mTBI phase by ROI analysis rather than voxel-wise whole-brain analysis (8, 35-41).

We noticed an interesting phenomenon where perfusion maps showed a reduced MTT in areas surrounding decreased CBF region. There are actually few studies comparing time parameters (MTT or TTP) of perfusion with that of normal controls in acute mTBI (8, 37). Although our finding is consistent with those previously reported, no studies have addressed the reason why the MTT decreased during the acute phase of mTBI. The precise mechanism

behind the decreased MTT in the low CBF areas is uncertain. It is that the MTT corresponds to the average time that red blood cells spend within a determinate volume of capillary circulation. When the perfusion pressure drops beyond the threshold of the brain's autoregulation, the compensatory cerebral vasodilatation becomes overwhelmed, and then the CBF starts to decrease. As a result, MTT would be expected to increase for red blood cells, so that they can have a longer contact with capillaries to allow for increased oxygen extraction. In other words, one would always expect the MTT to increase in a region where blood flow is reduced. However, Junger et al. reported that approximately one third of the patients with minor head injury demonstrate poorly functioning or absent cerebral autoregulation as compared to controls (42). Their study indicates that a significant number of patients with mTBI may be at increased risk for secondary ischemic neuronal damage during an as yet undefined period following their head injury. Meanwhile, even though CBF and MTT are the typical parameters of choice for stroke, there is no clear consensus among neuroradiologist (12).

We presumed that the MTT decrease in the nearby low CBF locations might be related to flow diversion with increased tissue pressure. This idea has already been proposed by Pranevicius et al. following pertinent literature review (43). The authors hypothesized that increased tissue pressure reduces blood flow not only by decreasing the focal perfusion pressure but also by diverting flow in a steal-like manner. An effective outflow pressure gradient leads to blood flow diversion from the center to the periphery of the injury. The average time for blood to pass through tissue might be shortened via flow

diversion to perifocal areas, something that is clinically undetectable. It is well known that the autoregulation response becomes less effective at lower CPP levels (44). If autoregulation is impaired or exhausted, even small focal tissue pressure increases could significantly reduce capillary perfusion in the presence of the diversion pathway, with a lower effective outflow pressure (43). It seems that the focal impairment of autoregulation with unexpected perfusion profile occurred in our patients.

Our study has several limitations that need to be mentioned. Firstly, we did not include detailed neuropsychological data for either the patient or control group for a more relevant comparison according to the observed patient symptoms. Moreover, we initially planned to extend our study with follow-up pCT scanning several months later to evaluate temporal changes in perfusion parameters. The main reason for not performing follow-up pCT scans was the unwillingness of most patients to undergo additional radiation exposure. One could also argue that pCT scanning is outdated and obsolete in the context of mTBI in the era of MRI and other advanced protocols. Notwithstanding the above limitation, our observations are convincing as the same imaging modality and the same protocol was applied in both the patient and control groups. In addition, this study uniquely demonstrated that AG perfusion is decreased during the early phase of mTBI, as detected by VBM and pCT. However, it should be noted that our imaging findings were derived from between-group comparisons. Hence, clinical application of pCT imaging in mTBI needs further examination and neuropsychological assessment. We

further hope that future studies with more patients and appropriate modalities will further aid in uncovering the mechanisms behind mTBI pathophysiology.

Conclusion

The results of the present study demonstrate the presence of early cerebral hemodynamic changes following even mTBI as detected by voxel-wise mapping. Our data further suggest that the location of these perfusion deficits involves a multisensory association area including the AG, one of the most consistent resting state networks.

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국문 초록

목적 : 중등도 이상의 외상성 뇌손상 환자에 비하여 경도 외상성 뇌손상 환자에 있어 이들의 대뇌 관류 변화를 관찰한 연구는 현재까지는 충분히 논의되지 못하였다. 더욱이 기존의 몇몇 연구들은 대뇌의 대표적인 엽 단위(전두엽, 측두엽, 후두엽)에 대해 흥미영역 (Region of Interest, ROI)을 정해 연구한 것이 대부분이어서 뇌 전체에 대해 살펴보지 못하였으며, 이 연구자체가 재현성, 객관성에 한계가 있어 경도 외상성 뇌손상 환자의 수상 이후 관류 변화에 대한 보다 적절한 방법의 연구가 필요하다고 판단하였다. 이에 본 연구는 경도 외상성 뇌손상 환자에서 촬영한 뇌관류 전산화 촬영(perfusion CT) 결과를 복셀 기반의 형태 계측(voxel based morphometry, VBM) 방법을 적용하여 대뇌 혈류 변화를 살펴보고자 하는데 그 목적이 있다.

방법 : 2017년 1월부터 2017년 7월까지 국립중앙의료원 응급실을 통해 신경외과로 입원치료한 연속된 21명의 경도 외상성 뇌손상 환자와 15명의 정상인에 대해 각각 뇌관류 전산화 단층촬영 (perfusion CT) 검사를 하였다. 환자군에 대해 촬영한 pCT 는 입원 당일에 촬영하였으며 응급실 도착 후 pCT 촬영까지 걸린 시간은 평균 6.9 시간이었다. 검사한 영상 데이터를 통계적 매개변수 사상 (statistical parametric mapping, SPM) 방법으로 적용이 가능한 파일로 변환을 한 후, Matlab 프로그램을 이용하여 Montreal Neurological Institute 틀에 공간적 정규화를 시킨 이후, 각각의 관류변수에 대해 환자군과 정상군사이의 평균비교를 하였다.

결과 : 경도 뇌손상 환자군의 초기 뇌관류 전산화 단층촬영 결과를 복셀 기반의 형태 계측 방법을 이용하여 정상군과 비교 결과, 관류가 감소하는 해부학적 부위가 관찰되었으며 이 부위는 주로 왼쪽 모서리이랑(left angular gyrus), 모서리위이랑 (supramarginal gyrus) 를 포함하는 부위로 나타났다. (p=0.002, FWE

corrected). 그 외 다른 관류변수에 대해서도 왼쪽 모서리이랑과 모서리위이랑이 주로 포함된 부위에서 통계적으로 의미있는 관류감소가 관찰되었다. (CBV, p=0.032, MTT, p=0.002~0.021, and TTP, p=0.002~0.006, all FWE corrected).

결론 : 본 연구는 복셀 기반의 형태 계측 방법을 이용하여 경도 외상성 뇌손상 환자의 초기에서도 대뇌혈류변화가 나타남을 증명하였다. 또한 이러한 혈류변화가 왼쪽 모서리이랑과 모서리위이랑을 포함하는 부위에서 관류결손으로 나타난 바, 모서리이랑과 모서리위이랑이 대표적인 휴식기 네트워크 (resting state network) 를 이루는 영역임을 고려할 때, 경도 외상성 뇌손상 환자들이 사고 이후 주로 호소하는 증상을 설명하는 하나의 단서가 될 수 있을 것이다.

주요어: 경도 외상성 뇌손상, 대뇌혈류변화, 관류 전산화단층촬영, 복셀기반의 형태계측방법, 모서리이랑, 휴식기 네트워크

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