Evidence of Corticospinal Tract Injury at Midbrain in Patients With Subarachnoid Hemorrhage

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Background and Purpose—Clear elucidation of the exact pathophysiological mechanisms of motor weakness in patients with subarachnoid hemorrhage has not yet been achieved. We attempted to investigate injury to the corticospinal tract in patients with subarachnoid hemorrhage using diffusion tensor imaging.

Methods—Twenty-two patients with subarachnoid hemorrhage and 24 control subjects were recruited for this study. DTI-Studio software was used for reconstruction of the corticospinal tract. We measured fractional anisotropy and apparent diffusion coefficient values at 5 regions of interest along the corticospinal tract pathway including: the corona radiata, the posterior limb of the internal capsule, the upper midbrain, the midpons, and the upper medulla.

Results—Fractional anisotropy value for the midbrain region of interest was lower in the patient group compared with the control group without change of apparent diffusion coefficient value (P<0.05). By contrast, fractional anisotropy and apparent diffusion coefficient values of the other 4 regions of interest were not different between the patient and control groups.

Conclusions—Injury of the corticospinal tract at the midbrain was observed in patients with subarachnoid hemorrhage.

Injury of the corticospinal tract at the midbrain appears to be one of the various pathophysiological mechanisms for motor weakness after subarachnoid hemorrhage. (Stroke. 2012;43:2239-2241.)

Key Words: corticospinal tract • diffusion tensor imaging • subarachnoid hemorrhage

Subarachnoid hemorrhage (SAH) can be accompanied by various neurological complications including motor weakness, somatosensory deficit, and cranial nerve dysfunction.1,2 Previous studies have reported that incidence of motor weakness in patients with SAH was 14% to 29%.2 Various pathophysiological mechanisms of motor weakness in SAH have been suggested: vasospasm, primary brain damage by SAH, insufficient blood perfusion of paracentral areas, or compression of the corticospinal tract (CST) by aneurysm.2,3 However, the exact pathophysiological mechanisms are not clearly elucidated.

Recent advances in diffusion tensor imaging (DTI) have enabled investigators to estimate the state of the CST. Many studies have demonstrated the usefulness of DTI in estimating the state of the CST in patients with brain lesions who did not show specific lesions on conventional MRI. However, very little is known about injury of the CST in patients with SAH.

In the current study, we attempted to investigate injury of the CST in patients with SAH using DTI.

Subjects and Methods

Subjects

Twenty-two patients were recruited consecutively among 49 patients with SAH who had been admitted for rehabilitation, according to the following inclusion criteria: (1) first-ever stroke; (2) age 30 to 70 years; (3) motor weakness on extremities; and (4) DTI was scanned at a chronic stage (>4 weeks after onset). Severity of SAH was assessed according to Fisher CT grade.7 Patients who showed any lesion along the CST pathway or the CST origin areas including the primary somatosensory cortex, premotor cortex, supplementary motor area, and posterior parietal cortex were excluded. Delayed cerebral infarct in other areas was observed in 5 of the 22 patients. The Institutional Review Board of our hospital approved the study protocol.

Clinical Evaluation

Motricity Index (MI) was used for the measurement of motor function (maximum score 100) at time of DTI scanning.5 The reliability and validity of MI have been well established.5

Diffusion Tensor Imaging

DTI data were acquired at an average of 7.3 (±3.1) weeks after onset using a 1.5-T Philips Gyroscan Intera system equipped with a Synergy-L Sensitivity Encoding head coil. For each of the 32 noncollinear and noncoplanar diffusion sensitizing gradients, we acquired 60 contiguous slices. The imaging parameters were as follows: matrix=128×128 matrix, field of view=221×221 mm², TE=76 ms, TR=10 726 ms, and a slice thickness of 2.3 mm.

DTI-Studio software was used in reconstruction of the CST: the seed region of interest (ROI): the CST portion of the pontomedullary junction; and the target ROI: the CST portion of the anterior midpons. Fiber tracts passing through both ROIs were designated as the final tracts of interest. A fractional anisotropy (FA) threshold of >0.2 and direction threshold <60° were used in performance of

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fiber tracking. Voxel-based ROIs were drawn in the middle corona radiata, the posterior limb of the internal capsule, the midbrain at the level of superior colliculus, the midpons, and the medulla along the CST pathway (Figure). Mean FA value and mean apparent diffusion coefficient value were measured for each ROI.

**Statistical Analysis**

An independent *t* test was performed for determination of the statistically significant differences in particular variables between the patient and control groups. Correlation between DTI parameters for each ROI and MI score for the contralateral limbs were determined using the Spearman correlation test. Statistical analyses were performed using SPSS software (Version 15.0; SPSS, Chicago, IL), and statistical significance was set at *P*≤0.05.

**Results**

Twenty-two patients (8 males; mean age, 54.0 years; range, 40–70 years) and 24 age- and sex-matched control subjects (10 males; mean age, 52.8 years; range, 41–72 years) with no history of neurological or psychiatric disease were recruited for this study. Seven of 22 patients had undergone shunt surgery for treatment of hydrocephalus and 10 patients were accompanied with intracerebral hemorrhage or intraventricular hemorrhage. Average Fisher CT grade for the patient group was 3 (3–4) and average MI score for the patient group was 74.2 (59.5–100): quadripareisis in 19 patients and hemiparesis in 3 patients.

FA value of the midbrain ROI was lower in the patient group compared with the control group (*P*≤0.05); in contrast, no differences in FA values of the other 4 ROIs for the CST were observed between the patient and control groups (*P*>0.05; Table). We could not observe any difference in apparent diffusion coefficient value between the patient and control groups (*P*>0.05). On the other hand, in the patient group, no correlation was observed between MI scores and DTI parameters for each ROI for the CST (*P*>0.05).

**Discussion**

In the current study, we investigated injury of the CST in patients with SAH using DTI and found FA value of the midbrain ROI for the CST was lower in the patient group compared with the control group (*P*<0.05); in contrast, no differences in FA values of the other 4 ROIs for the CST were observed between the patient and control groups (*P*>0.05; Table). We could not observe any difference in apparent diffusion coefficient value between the patient and control groups (*P*>0.05). On the other hand, in the patient group, no correlation was observed between MI scores and DTI parameters for each ROI for the CST (*P*>0.05).
No study of the pathophysiological mechanism of CST injury at the midbrain as a result of SAH has been conducted. However, based on the pathophysiological mechanism of periventricular white matter injury by intraventricular hemorrhage, we can make the assumption that the CST at the midbrain in patients with SAH can be exposed to hemorrhage such as injury to periventricular white matter by intraventricular hemorrhage.7 Findings from previous studies have suggested that injury to periventricular white matter could occur through mechanical (increased intracranial pressure or direct mass) or chemical mechanisms (a blood clot itself can cause extensive damage).8 In this study, considering the location of the CST from the cerebral cortex to the medulla, due to its close proximity to the cistern, the CST at the midbrain can easily be affected by hemorrhage.7 In addition, frequent occurrence of SAH into perimesencephalic cisterns could be ascribed to injury of the CST at the midbrain.1 These mechanisms of injury might be associated with mild weakness (mean MI, 74.2) of subjects in the patient group, which was similar to 4/5 on the Medical Research Council. This mild weakness might have contributed to the result showing no correlation between FA value at the midbrain and motor function in the patient group. In addition, weakness of the patient group might be ascribed in part to injury observed in other nonpyramidal motor tracts such as the corticoreticulospinal tract.

In conclusion, we observed injury of the CST at the midbrain in patients with SAH. Injury of the CST at the midbrain appears to be one of the various pathophysiological mechanisms for motor weakness after SAH. To the best of our knowledge, this is the first study to demonstrate injury of the CST at the subcortical area in patients with SAH. The major limitation of this study was the small number of subjects. In addition, we recruited the patients among the patients with SAH who had been admitted for rehabilitation. Therefore, it is possible that we recruited patients with severe clinical manifestations among all patients with SAH.

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Disclosures
None.

References

| Table. Comparison of Diffusion Tensor Image Parameters of Regions of Interest |
|---------------------------------|---------------------------------|----------------|----------------|
| CR FA 0.62 (0.09) 0.61 (0.06) | Control CR FA 0.60 (0.06) 0.60 (0.06) | t 0.837 0.405 | P Value 0.80 (0.06) 0.78 (0.04) |
| CR ADC 0.80 (0.06) 0.78 (0.04) | Control CR ADC 0.78 (0.06) 0.76 (0.04) | t 1.773 0.080 | P Value 1.790 0.078 |
| PL FA 0.64 (0.09) 0.66 (0.06) | Control PL FA 0.76 (0.06) 0.76 (0.04) | t 0.332 0.187 | P Value 0.135 0.080 |
| PL ADC 0.78 (0.06) 0.76 (0.04) | Control PL ADC 0.76 (0.06) 0.76 (0.04) | t 0.132 0.080 | P Value 0.135 0.080 |
| Midbrain FA 0.65 (0.08) 0.71 (0.06) | Control Midbrain FA 0.61 (0.06) 0.61 (0.06) | t 0.332 0.187 | P Value 0.135 0.080 |
| Midbrain ADC 0.86 (0.14) 0.83 (0.07) | Control Midbrain ADC 0.83 (0.07) 0.83 (0.07) | t 0.135 0.080 | P Value 0.135 0.080 |
| Pons FA 0.49 (0.07) 0.51 (0.06) | Control Pons FA 0.51 (0.06) 0.51 (0.06) | t 0.332 0.187 | P Value 0.135 0.080 |
| Pons ADC 0.74 (0.05) 0.75 (0.08) | Control Pons ADC 0.76 (0.06) 0.76 (0.04) | t 0.135 0.080 | P Value 0.135 0.080 |
| Medulla FA 0.42 (0.08) 0.44 (0.08) | Control Medulla FA 0.44 (0.08) 0.44 (0.08) | t 0.332 0.187 | P Value 0.135 0.080 |
| Medulla ADC 1.03 (0.25) 1.04 (0.28) | Control Medulla ADC 1.04 (0.28) 1.04 (0.28) | t 0.332 0.187 | P Value 0.135 0.080 |

Values represent means (SD).
CR indicates corona radiata; FA, fractional anisotropy; PL, posterior limb; ADC, apparent diffusion coefficient.
*P < 0.05.
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