CASE REPORT

SIGNIFICANCE OF REHABILITATIVE MANAGEMENT DURING THE CRITICAL PERIOD FOR MOTOR RECOVERY IN INTRACEREBRAL HEMORRHAGE: A CASE REPORT

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Objective: The majority of motor recovery following stroke is known to occur within 3–6 months after onset; this period is therefore regarded as critical for motor recovery in stroke patients. We report here a case of a patient with intracerebral haemorrhage who showed changes in the affected motor function and in the damaged corticospinal tract (CST) at the primary motor cortex (M1) during rehabilitative management.

Case description: A 51-year-old woman underwent decompressive craniectomy and removal of haematoma due to a rupture of an arteriovenous malformation. Brain magnetic resonance imaging revealed a leukomalactic lesion at the fronto-parietal cortex centred on the precentral knob. Diffusion tensor imaging data were acquired 4 times (5, 8, 11 and 18 weeks after onset) and she started rehabilitation for right hemiplegia at 5 weeks after onset.

Results: We found close relationships between changes in the CST branch from M1 on diffusion tensor tractography, the state of motor weakness, and the rehabilitative management: the CST branch from M1 was observed concurrently with motor recovery and the process of rehabilitation.

Conclusion: This case report indicates the importance of active and comprehensive rehabilitative management during the critical period for motor recovery in stroke patients.

Key words: diffusion tensor imaging; brain plasticity; stroke; corticospinal tract; rehabilitation.

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INTRODUCTION

The brain is capable of neuronal reorganization after brain injury. This is known as brain plasticity, and can occur actively for a limited period following brain injury. In general, the majority of motor recovery following stroke is known to occur within 3–6 months after onset; therefore, this period is regarded as critical for motor recovery in stroke patients (1). On the other hand, the various therapeutic modalities used in rehabilitative management are known to facilitate motor recovery in stroke patients (2, 3). Therefore, for successful rehabilitation of motor recovery in stroke patients, active and comprehensive rehabilitative management during the critical period is important.

The corticospinal tract (CST) is the major neuronal pathway that mediates voluntary movements (4). Recovery of a damaged CST is one of the motor recovery mechanisms in stroke patients (5). Therefore, elucidation of the state of the CST is necessary in order to perform research on the motor recovery mechanism in stroke patients. Many animal studies have demonstrated neuronal changes in or around the injured primary motor cortex (M1) during motor recovery after brain injury (6, 7). However, there is little published evidence of this in the human brain.

Diffusion tensor tractography (DTT), which is derived from diffusion tensor imaging (DTI), can be used for visualization of the architecture of the CST in 3 dimensions (8). Therefore, DTT allows for follow-up of changes in the CST according to motor recovery during the critical period in stroke patients. Since the introduction of DTT, several studies have reported on changes in the damaged CST at the subcortical level during motor recovery in stroke patients (9–14). However, no DTT studies at the cortex level during motor recovery have been reported.

We report here a case of a patient with intracerebral haemorrhage (ICH) who showed changes in the affected motor function and in the damaged CST at M1 according to rehabilitative management, which was demonstrated by follow-up DTT studies.

CASE REPORT

A 51-year-old, right-handed woman underwent decompressive craniectomy and removal of haematoma, which resulted from rupture of an arteriovenous malformation, at the Department of Neurosurgery of Yeungnam University Hospital. Five weeks after ICH onset, she was transferred to the rehabilitation department of the same university hospital for rehabilitation of right hemiplegia. Brain computed tomography (CT), which was taken at onset of ICH, showed a haematoma in the left fronto-parietal cortex, and brain magnetic resonance imaging (MRI), which was scanned at 5 weeks after onset, revealed a leukomalactic lesion at the fronto-parietal cortex centred on the pre-central knob and underlying white matter (Fig. 1). The

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Fig. 1. (A) Brain computed tomography (CT) at onset of intracerebral haemorrhage showed a haematoma in the left fronto-parietal cortex, and brain magnetic resonance imaging (MRI) 5 weeks after onset revealed a leukomalactic lesion at the primary sensori-motor cortex centred on the precentral knob and underlying white matter. (B) Results of diffusion tensor tractography (DTT) of the unaffected hemisphere showed that fibre tracts originated from the cerebral cortex, including the primary motor cortex (M1), and passed along the known corticospinal tract (CST) pathway. The 5-week DTT of the affected (*left*) hemisphere showed that the affected CST originated from the premotor area (Broadmann area: 6). A branch that originated from M1 appeared on the 8-week DTT. However, this new branch had disappeared by the 11-week DTT. By the 18-week DTT, a branch from M1 had appeared again.

patient provided signed, informed consent and our institutional review board approved the study protocol.

The standardized Motricity Index (MI) and Medical Research Council (MRC) were used for determination of motor function of the affected extremities. The MI, with a maximum score of 100, is a measure of the integrity of the motor function of an extremity. The reliability and validity of the MI are well-established (15). She presented with complete weakness of the right upper and lower extremities at onset of ICH (MI: 0) (Table I). For 3 weeks, from 5 to 8 weeks after onset, she received comprehensive rehabilitative management, including administration of neurotrophic drugs (methylphenidate: 10 mg/day (maximum dose: 60 mg/day), ropinirole: 2 mg/day (maximum dose: 24 mg/day), bromocriptine: 10 mg/day (maximum dose: 15 mg/day), levodopa: 375 mg/day (maximum dose: 750 mg/day), amantadine: 200 mg/day (maximum dose: 400 mg/day)) (2, 3, 16), movement therapy, procedures for spasticity control of the left finger flexors, and neuromuscular electrical stimulation of affected finger extensors and ankle dorsiflexors (20 min × 2 times/day, 6 days/week). Movement therapy focused on improvement of the motor function of the right upper and lower extremities and was performed at the sections of physical therapy and occupational therapy, respectively, 5 times per week (70 min/day). The training for the activities of daily activity was performed

Table I. Patient's clinical data

	Duration from onset							
	5 weeks (1 st DTT)	8 weeks (2 nd DTT)	11 weeks (3 rd DTT)	18 weeks (4 th DTT)				
MRC								
Shoulder abductor	1	2	2	3				
Elbow flexor	1	3	2	3				
Finger flexor	1	2	1	2				
Finger extensor	0	1	1	2				
Hip flexor	1	3	2	3				
Knee extensor	0	4	4	4				
Ankle dorsiflexor	0	2	2	3				
MI								
Upper extremity	30	51	39	56				
Lower extremity	28	57	53	62				
Total	29	54	46	59				

DTT: diffusion tensor tractography; MRC: Medical Research Council, 0: no contraction, 1: palpable contraction, but no visible movement, 2: movement without gravity, 3: movement against gravity, 4: movement against a resistance lower than the resistance overcome by the healthy side, 5: movement against a resistance equal to the maximum resistance overcome by the healthy side. MI: motricity index, score 0–100.

35 min/day, 5 times/week. Weakness of her right extremities recovered from an MI score of 29 points (5 weeks) to 54 points (8 weeks) during a 3-week period of rehabilitation. As a result, she was able to flex her fingers without gravity at 8 weeks after onset. She was transferred to a local rehabilitation hospital to receive continuous rehabilitative management; however, some neurotrophic drugs (ropinirole, bromocriptine, and levodopa) were stopped at that hospital. After 3 week's admission at the local rehabilitation hospital, her motor weakness was found to be aggravated to an MI score of 46 points and she was unable to flex her affected fingers without gravity. Her aggravated motor function did not show improvement despite an additional 3-week period of rehabilitation at the same local rehabilitation hospital. Therefore, she was obliged to be readmitted to the rehabilitation department of Yeungnam University Hospital to receive further intensive rehabilitative management. We re-administrated the stopped neurotrophic drugs (ropinirole, bromocriptine, and levodopa) in order to facilitate motor recovery and performed rehabilitation again. After a 4-week period of rehabilitation, her motor weakness showed improvement, to an MI score of 59 points, and she was able to flex and extend her affected fingers without gravity at 18 weeks after onset.

Diffusion tensor imaging

DTI data were acquired 4 times (5, 8, 11 and 18 weeks after onset) using a 6-channel head coil on a 1.5 T Philips Gyroscan Intera (Philips Ltd, Best, The Netherlands) with single-shot echo-planar imaging. For each of the 32 non-collinear diffusion sensitizing gradients, we acquired 67 contiguous slices parallel to the anterior commissure-posterior commissure line. Imaging parameters were as follows: acquisition matrix = 96×96 , reconstructed to matrix = 128×128 matrix, field of view = 221×221 mm², TR = 10,726 ms, TE = 76 ms, parallel imaging reduction factor (SENSE factor)=2, EPI factor=49 and b = 1,000 s/mm², NEX = 1, and a slice thickness of 2.3 mm (acquired isotropic voxel size $2.3 \times 2.3 \times 2.3$ mm³).

Affine multi-scale two-dimensional registration at the Oxford Centre for Functional Magnetic Resonance Imaging of Brain (FMRIB) Software Library (FSL; www.fmrib.ox.ac. uk/fsl) was used for removal of eddy current-induced image distortions (17). DTI-Studio software (CMRM, Johns Hopkins Medical Institute, Baltimore, MD, USA) (18) was used for evaluation of the CST. Fibre tracking was based on the fibre assignment continuous tracking algorithm and a multiple regions of interest (ROIs) approach. CSTs were determined by selection of fibres passing through two ROIs, which were placed on the ponto-medullary junction (anterior blue colour) and pons (anterior blue colour) (19, 20). Fibre tracking was started at the centre of a seed voxel with a fractional anisotropy (FA) > 0.15 and ended at a voxel with a fibre assignment of < 0.15 and a tract turning-angle of < 60 degrees. We measured the fibre number and FA value of each DTT for CST.

Results of DTT of the unaffected hemisphere showed that fibre tracts originated from the cerebral cortex, including the M1, and passed along the known CST pathway (Fig. 1). Five-week DTT of the affected (left) hemisphere showed that the affected CST originated from the premotor area (Broadmann area: 6). A branch originating from the M1 centred on the precentral knob appeared on the 8-week DTT. However, this new branch had disappeared by the 11-week DTT. By the 18-week DTT, a branch from the M1 appeared again. The fibre number of left CST was increased to 215 on the 8-week DTT from 197 on the 5-week DTT; however, it was decreased to 80 on the 11-week DTT, and then increased to 263 on 18-week DTT (Table II). By contrast, the FA value of the left CST was decreased to 0.42 on the 11week DTT and increased to 0.45 on the 18-week DTT.

DISCUSSION

In the current study, we attempted to follow up changes in the affected CST in M1 centred on the precentral knob, which is the main centre of the hand somatotopy of the CST, along with changes in motor weakness during the critical period for motor recovery in a hemiparetic patient with ICH. We found close relationships between changes in the CST branch from M1 on DTTs, the changes in DTT parameters (fibre number and FA value: the degree of directionality of microstructures

Table II. Changes in diffusion tensor tractography (DTT) parameters of the patient

	Duration from onset										
	5 weeks (1 st DTT)		8 weeks (2 nd DTT)		11 weeks (3 rd DTT)		18 weeks (4 th DTT)				
	R	L	R	L	R	L	R	L			
Fibre number Fractional	621	197	746	215	768	80	808	263			
anisotropy	0.54	0.46	0.50	0.46	0.50	0.42	0.51	0.45			

R: right; L: left.

in the CST), the state of motor weakness, and the rehabilitative management as follows: on 5-week DTT, which was scanned at the start of rehabilitation, no CST branch from M1 was observed. After a 3-week period of comprehensive rehabilitation, motor weakness of the affected side had recovered to some extent, as much as 25 points on MI score (from 29 points: 5 weeks after onset, to 54 points: 8 weeks after onset). We observed the CST branch from M1 on 8-week DTT. After a 3-week rehabilitation period at a local rehabilitation hospital, motor function of the affected side was aggravated as much as 9 points on MI score (from 54 points: 8 weeks after onset, to 46 points: 11 weeks after onset) concurrent with disappearance of the CST branch from M1 on the 11-week DTT. Therefore, she underwent rehabilitation for 4 weeks at the rehabilitation department of Yeungnam University Hospital; motor weakness of the affected side then showed recovery of as much as 13 points (from 46 points: 14 weeks after onset, to 59 points: 18 weeks after onset) with reappearance of the CST branch from M1 on 18-week DTT. On the other hand, changes in the affected CST appeared to be well-correlated with changes in the motor function of the affected hand, which indispensably requires the CST (4, 5): the patient was able to flex the affected fingers with the appearance of the CST branch from M1 at 8 weeks after onset, and the patient could not flex her affected fingers with the disappearance of the CST branch from M1 at 11 weeks after onset. At 18 weeks after onset, the patient was able to flex and extend her affected fingers with the reappearance of the CST branch from M1.

The results of this study indicate the importance of active and comprehensive rehabilitative management during the critical period for motor recovery in stroke patients. This is because the CST branch from M1 concurrent with motor recovery appeared to have been induced by the first rehabilitative management; however, after changing the rehabilitation team and stopping some neurotrophic drugs, the CST branch from M1 disappeared in concurrence with aggravation of motor weakness of the affected side (2, 3, 16, 21, 22). However, the aggravated motor weakness showed improvement with reappearance of the CST branch from M1 after a 4-week period of rehabilitation by the initial rehabilitation team and re-administration of the stopped neurotrophic drugs. Various modalities employed in rehabilitative management for stroke patients are known to facilitate motor recovery (2, 3). These modalities include neurotrophic drugs, physical therapy, constraint-induced movement therapy, neuromuscular electrical stimulation, and repetitive transcranial magnetic stimulation (2, 3). Many rehabilitative modalities were employed for rehabilitation of this patient; therefore, we were not able to estimate how much each modality contributed to motor recovery. However, the motor function of the affected side and the CST branch from M1 on DTT seemed to be changed by the change of rehabilitation team and by administration of some neurotrophic drugs; however, we were not able to discern which factor contributed to motor recovery or by how much.

In conclusion, we describe here a patient with ICH who showed changes in the damaged CST and motor function of the affected side according to the changes in rehabilitation team and neurotrophic drugs. To the best of our knowledge, this is the first DTT study to demonstrate changes in the affected CST at M1 concurrent with changes in motor function in stroke patients. This result indicates the importance of rehabilitative management during the critical period for motor recovery in stroke patients. However, because it is a case report, this study is limited. In addition, we could not rule out other possible factors that may have contributed to motor recovery in this patient. Further complementary studies involving larger case numbers are warranted.

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