

# Modification of Cerebellar Afferent Pathway in the Subacute Phase of Stroke

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**Background:** This study aims to identify the relationship between corticopontocerebellar tract (CPCT) and corticospinal tract (CST) integrity as well as motor function after stroke. **Materials and Methods:** A total of 33 patients with stroke (18 left, 15 right hemispheric lesions) who underwent diffusion tensor imaging within 2 months of stroke onset and 17 age- and sex-matched healthy controls were retrospectively enrolled. Tract volume and the asymmetry index based on tract volume ( $AI_{TV}$ ) of the CST and CPCT were used to identify structural changes in individual tracts and the correlation between those tracts. Motor function was assessed using the Medical Research Council (MRC) muscle scale, manual function test (MFT), functional ambulation category, and modified Barthel index. **Results:** The volume of the affected CPCT was lower, and that of the unaffected CPCT was higher than the volumes in the control group ( $P < .001$ ,  $P = .001$ , respectively). The CPCT  $AI_{TV}$  showed a strong positive correlation with the CST  $AI_{TV}$  in patients with either left or right hemispheric lesions ( $r_s = .779$ ,  $P < .001$ ;  $r_s = .732$ ,  $P = .003$ , respectively). The CPCT  $AI_{TV}$  negatively correlated with the MRC muscle scale of the shoulder, wrist, and ankle muscles ( $r = -.490$ ,  $-.490$ ,  $-.416$ ;  $P = .004$ ,  $.004$ ,  $.016$ , respectively). A higher unaffected CPCT volume was indicative of less affected upper extremity function, as assessed by MFT ( $r_s = -.546$ ,  $P = .029$ ). **Conclusions:** Modification of the CPCT depended on CST integrity and was associated with the severity of hemiplegia and hemiplegic upper extremity function. The CPCT may complement the role of the CST and help to predict the motor function. **Key Words:** Stroke—cerebellum—middle cerebellar peduncle—recovery of function—diffusion tensor imaging.

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## Introduction

The cerebellum is structurally connected to the sensorimotor cortex via the corticopontocerebellar tract (CPCT) and integrates sensory and motor function. Crossed cerebellar diaschisis can arise from damage to the frontal parietal cortex and the territory of the deep middle cerebral artery, including the internal capsule and lentiform nucleus.<sup>1-3</sup> It accounts for hypoperfusion or hypometabolism via deafferentation of the contralateral cerebellum from lesioned cerebral structures<sup>4,5</sup> and has been attributed to the CPCT.<sup>1,6,7</sup> The functional consequences of crossed cerebellar diaschisis include severe motor impairment, ataxic hemiplegia, poor hand function, and poor functional independence.<sup>1,8-11</sup>

Poststroke changes in cerebrocerebellar connectivity have been identified using functional neuroimaging tools. Their pattern suggests a regulatory role of the cerebellum in motor recovery.<sup>12-15</sup> However, there is little evidence of structural changes in the cerebellar afferent pathway. Only 1 tractography study, in pediatric patients with congenital unilateral brain injury, demonstrated an asymmetric CPCT.<sup>16</sup>

The aim of this diffusion tensor tractography study was to determine whether the CPCT is structurally modified after supratentorial stroke, and whether the modifications are linked to corticospinal tract (CST) integrity and motor function in the subacute phase of stroke. We hypothesized that (1) supratentorial stroke leads to degeneration of the CPCT, with interactive changes in this tract bilaterally; (2) the degree of corticospinal degeneration influences CPCT integrity; and (3) the loss of CPCT integrity is associated with poor motor function.

## Methods

### *Subjects*

This was a retrospective study from the cohort of a university hospital. The study population consisted of 33 patients who underwent diffusion tensor imaging (DTI) within 2 months of stroke onset who were selected between March 2015 and June 2016. The inclusion criteria were first-ever hemorrhagic or ischemic stroke, age >30 years, right-hand dominance, modified Rankin scale  $\geq 3$ , stroke confined to the frontal lobe (hemorrhage), basal ganglia (hemorrhage or infarction), and middle cerebral artery territory (infarction). The exclusion criteria were additional neurological disorders other than stroke, bi-hemispheric stroke, and an acute serious medical complication interfering with rehabilitation beyond the bed. All of the patients received comprehensive rehabilitation therapy including physical, occupational, and speech-language therapy if indicated. The 1-hour sessions were provided twice a day, 5 days a week, at the specialized rehabilitation center during hospitalization after acute stroke management. The 17 age- and sex-matched healthy controls were retrospectively enrolled from the cohort of the Health Promotion Center of our institution. All of the controls were right-handed and had no history of neurological disorder. The institutional review board of our institution approved the protocols of this study, which were in accordance with the Belmont Report and Declaration of Helsinki. The requirement for informed consent was waived.

### *Functional Assessment*

Each patient underwent a Medical Research Council (MRC) muscle scale test of muscle strength of the upper and lower limbs,<sup>17</sup> a manual function test (MFT) for upper

extremity function,<sup>18</sup> a functional ambulation category (FAC) evaluation of mobility,<sup>19</sup> and a modified Barthel index (MBI) evaluation of the level of independence in activities of daily living<sup>20</sup> at the time of DTI. The MRC muscle scale was used to determine muscle strength in key muscles including shoulder flexor, wrist extensor, hip flexor, and ankle dorsiflexor on the hemiplegic side. Scoring ranges from 0 (no contraction) to 5 (normal power). The MFT is a 32-point scale that is used in hemiplegic patients to evaluate the unilateral manual performance of the proximal arm as well as fine-motor function of the hand. The MFT is composed of 8 subscales in the evaluation of the upper proximal arm: forward elevation of the arm, lateral elevation of the arm, touching the occiput with the palm, touching the back with the palm, grasping, pinching, carrying cubes, and pegboard manipulation. The total score ranges from 0 (severely impaired) to 32 (full function). The FAC is a 6-point scale used to visually categorize patients according to their basic motor skills with respect to ambulation. A score of 1 indicates nonfunctional ambulation and a score of 6 indicates independent ambulation on level and nonlevel surfaces. The MBI is a 100-point scale that reflects the poststroke functional and disability status. Its 10 domains address personal hygiene, bathing, eating, toileting, stair climbing, dressing, bowel control, bladder control, ambulation, and chair/bed transfer. The total MBI score ranges from 0 (total dependent daily living) to 100 (independent daily living).

### *DTI Acquisition*

DTI was performed using a 3.0 T magnetic resonance imaging (MAGNETOM Verio, Siemens, Erlangen, Germany) equipped with a 6-channel head coil. The data were acquired in the form of single-shot spin-echo echo-planar images, with axial slices covering the whole brain across 70 interleaved slices of 2.0 mm thickness (no gap); repetition time/echo time = 14,300/84 ms; field of view =  $256 \times 256$  mm<sup>2</sup>; matrix  $128 \times 128$ ; voxel size  $2 \times 2 \times 2$  mm<sup>3</sup> (isotropic), and number of excitation = 1. Diffusion sensitizing gradients were applied in 30 noncollinear directions with a b-value of 1,000 ms/mm<sup>2</sup>. The b = 0 images were scanned before acquisition of the diffusion-weighted images, with 31 volumes in total.

### *Image Processing*

The images were processed using the programs in the FMRIB Software Library (FSL) version 5.0.9 (the Analysis Group, FMRIB, Oxford, UK) (<http://www.fmrib.ox.ac.uk/fsl>). Source data were corrected for eddy currents and head motion by registering all of the data to the first b = 0 image, with affine transformation. For probabilistic tractography, probability distributions in 2 fiber directions were modeled at each voxel using the BEDPOSTX program, based on a multifiber diffusion model.

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