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Change of the Corticospinal Tract in the Unaffected Hemisphere by Change of the Dominant Hand Following Stroke

A Cohort Study

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Abstract: We investigated the change of the corticospinal tract (CST) in the unaffected hemisphere by the change of the dominant hand in stroke patients, using diffusion tensor tractography (DTT).

Forty-eight stroke patients with right-hand dominance were recruited. The patients were assigned to 3 groups: group A (12 patients)—right-hand dominance was maintained after the right-hand weakness, group B (17 patients)—right-hand dominance changed to the left-hand dominance after the right-hand weakness, and group C (19 patients)—right-hand dominance was maintained after the left-hand weakness had developed. The function of the unaffected upper extremity was evaluated using the grip strength (GS), Manual Function Test (MFT), Purdue Pegboard Test (PPT), and modified Barthel Index (MBI). DTT was performed twice (1st DTT, 2nd DTT), and the fractional anisotropy (FA), apparent diffusion coefficient (ADC), and voxel number (VN) of the CST in the unaffected hemisphere were measured.

In group B, the VN on 2nd DTT was significantly increased compared with the 1st DTT, and all other clinical data (GS, MFT, PPT, and MBI) showed a significant increase between 1st and 2nd DTT ($P < 0.05$). The change of the VN showed moderate correlation with the change of the GS ($r = 0.499$, $P < 0.05$), PPT ($r = 0.531$, $P < 0.05$), and MBI ($r = 0.551$, $P < 0.05$).

We found that the fiber number of the CST in the unaffected hemisphere was increased by the change of the dominant hand in stroke patients. We believe that our results have important implications in terms of neurorehabilitation.

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Abbreviations: ADC = apparent diffusion coefficient, CST = corticospinal tract, DTI = diffusion tensor imaging, DTT = diffusion tensor tractography, FA = fractional anisotropy, GS = grip strength, MBI = modified Barthel Index, MFT = Manual Function Test, PPT = Purdue Pegboard Test, VN = voxel number.

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INTRODUCTION

Motor weakness is a major sequela in stroke patients; ~80% of stroke patients experience motor weakness and, among these, only 20% of patients show complete recovery.[1] In particular, the upper extremity, which is important to activities for daily living, remains in a nonfunctional state at 6 months after stroke onset in 30% to 60% of stroke patients.[2,3] On the other hand, ~80% of humans have right-hand dominance and 45% to 50% of strokes are known to occur in the left hemisphere.[4–6] As a result, a significant portion of stroke patients are obliged to change their dominant hand after stroke. Change of the dominant hand in the adult brain might be accompanied by change of neural tracts in the brain. Therefore, elucidation of change of neural tracts following change of the dominant hand might be useful in neurorehabilitation and neuroscience.

The corticospinal tract (CST), a major neural tract for motor function in the human brain, is mainly concerned with execution of movement of the hand, particularly fine motor activities.[7,8] Therefore, the change of the CST in the unaffected hemisphere might be prominent when the dominant hand is changed following stroke. The development of diffusion tensor tractography (DTT), which is derived from diffusion tensor imaging (DTI), has enabled 3-dimensional reconstruction and estimation of the CST.[9] Many studies using DTT have reported on the CST in stroke patients.[10–16] However, the majority of these studies have focused on the CST in the affected hemisphere and only a few studies have reported on change of the CST in the unaffected hemisphere.[10–16] No study on CST change in the unaffected hemisphere by change of the dominant hand in stroke patients has been reported so far.

In this study, we investigated the change of the CST in the unaffected hemisphere by the change of the dominant hand in stroke patients, using DTT.

SUBJECTS AND METHODS

Subjects

Forty-eight consecutive stroke outpatients (31 men, 17 women; mean, 52.94 ± 10.59 years, 25 patients: intracranial hemorrhage and 23 patients: cerebral infarct) were recruited according to the following criteria: (1) first-ever stroke; (2) age: 20 to 79 years; (3) show hemiparesis after stroke onset; (4) show right-hand dominance determined using the Edinburg Handedness inventory before stroke onset[17]; (5) no history of peripheral nerve injury or musculoskeletal disease (e.g., arthritis, musculotendinous injury, or bone fracture) in the unaffected upper extremity. Patients with severe cognitive problem (Mini-Mental State Examination score of <24) were excluded. The patients were assigned to 3 groups: group A—right-hand dominance was maintained due to mild weakness after development of dominant (right) hand weakness at stroke onset, group B—right-hand dominance changed to left-hand dominance due to severe weakness after development of dominant (right) hand weakness at stroke onset, and group C—right-hand dominance was maintained after development of nondominant (left) hand weakness at stroke onset; group A—12 patients (6 men, mean age; 51.50 ± 11.82 years, 5 patients: intracranial hemorrhage and 7 patients: cerebral infarct); group B—17 patients (12 men, mean age; 53.47 ± 9.28 years, 10 patients: intracranial hemorrhage and 7 patients: cerebral infarct); and group C—19 patients (13 men, mean age; 53.53 ± 11.59 years, 10 patients: intracranial hemorrhage and 9 patients: cerebral infarct). The patient provided signed, informed consent, and the study protocol was approved by Yeungnam University hospital Institutional Review Board.

Clinical Evaluation

The grip strength (GS), Manual Function Test (MFT), Purdue Pegboard Test (PPT), and modified Barthel Index (MBI) were used for evaluation of function of the unaffected side. The GS was evaluated using a dynamometer (Jamar Hydraulic Hand Dynamometer, model-5030J1). Maximum grip strength in shoulder adduction and elbow flexion position was evaluated. The score was the average of measured values (unit: kg) by 3 trials.[18] The MFT is composed of 32 test (total score 32) items for evaluation of arm motions and manipulative activities. Arm motion activity consisted of elevation (forward and lateral) and touching (the occiput and dorsum with the palm). Manipulative activity consisted of grasping, pinching, carrying a cube, and pegboard. Each item was scored by either 0 (failure) or 1 (success).[19] The PPT consists of 5 separate tests: right hand; left hand; both hands; right plus left plus both hands; and assembly. We evaluated only the unaffected hand function that estimated the number of pins performed by the patient within 30 seconds.[20] We used the average peg counts by 3 trials. The MBI consisted of 10 items (range of score is 0–100). Higher score indicates more independence in ADL.[21] The reliability and validity of the GS, MFT, PPT, and MBI are well-established.[18,20–24] All evaluations were performed 2 times on the day of DTI scan, respectively (first evaluation: 1st DTT and follow-up evaluation: 2nd DTT).

Diffusion Tensor Tractography

A 1.5-T Philips Gyroscan Intera system equipped with a synergy-L Sensitivity Encoding head coil was used for DTI scanning twice (1st DTT: mean 23 ± 15.40 days after onset, 2nd DTT: mean 472 ± 449.17 days after onset). Sixty-seven slices were acquired parallel to the anterior commissure-posterior commissure line for each of the 32 noncollinear and noncoplanar diffusion-sensitizing gradients. DTI scanning parameters were as follows: matrix: 128×128 matrix, repetition time: 10,726 ms, echo time: 76 ms, parallel imaging reduction factor: 2, echo-planar imaging factor: 67, number of excitations: 1, and slice thickness: 2.3 mm.

Affine multiscale registration was used for removal of eddy current-induced image distortions and motion artifacts.[25] The Oxford Centre for Functional Magnetic Resonance Imaging of Brain (FMRIB) Software Library (FSL; www.fmrib.ox.ac.uk/fsl) was used for preprocessing of DTI datasets. The CST was reconstructed using DTI-Studio software (CMRM, Johns Hopkins Medical Institute). For 3-dimensional reconstruction of the CST, 2 regions of interest (ROIs) were placed as follows: the first ROI—the anterior blue portion (the CST area on the color map) of the upper pons, and the second ROI—the anterior blue portion (the CST area on the color map) of the lower pons.[26] Fiber tracking was performed using a fractional anisotropy (FA) threshold of >0.2 and direction threshold $<60°$.[27] The FA, apparent diffusion coefficient (ADC), and voxel number (VN) of the CST in the unaffected hemisphere were measured.

Data Analysis

SPSS software (v.17.0; SPSS, Chicago, IL) was used for data analysis. The Kruskal–Wallis test was used due to the small number of patients. Demographic data of patients and DTT parameters in terms of the FA, ADC, and VN at baseline (1st DTT) were compared between 3 groups to determine homogeneity of the group assignment of patients. The chi-square test was used for sex and stroke type. The Wilcoxon sighed-rank test was used to determine change in the CST between 1st DTT and 2nd DTT in each group and the change in clinical data (GS, MFT, PPT, and MBI) in group B. Spearman correlation analysis was used to determine correlation between the VN and clinical data in group B. The significant level of the P value was set at 0.05.

RESULTS

No significant differences in the demographic data and 1st DTT parameters (FA, ADC, and VN) were observed between 3 groups ($P > 0.05$) (Table 1). In group B, the VN on 2nd DTT was significantly increased compared with that of 1st DTT ($P < 0.05$). However, all other DTT parameters in 3 groups showed no significant difference between 1st and 2nd DTT ($P > 0.05$) (Table 2) (Figure 1).

In group B, all clinical data in terms of the GS, MFT, PPT, and MBI were significantly increased between 1st and 2nd DTT ($P < 0.05$). The change of the VN showed moderate correlation with the change of the VN: GS ($r = 0.499$, $P < 0.05$), PPT ($r = 0.531$, $P < 0.05$), and MBI ($r = 0.551$, $P < 0.05$).[28] However, no significant correlation was observed with the change of the MFT ($P > 0.05$) (Table 3).

DISCUSSION

In this study, change of the CST in the unaffected hemisphere by the change of the dominant hand following stroke was investigated using DTT. Our results were as follows: first, in group B patients, whose dominant hand changed to the left hand after stroke, the VN of the CST in the unaffected hemisphere was increased on 2nd DTT compared with 1st DTT without significant change in the FA and ADC values, whereas patients in the other groups (groups A and C) showed no significant change in terms of all DTT parameters (FA, ADC, and VN); second, all clinical data (GS, MFT, PPT, and MBI) showed significant improvement on 2nd DTT compared with 1st DTT in group B patients; and third, the change of the VN of the unaffected CST in group B patients showed significant correlation with the change of the GS, PPT, and MBI.

The FA value represents the degree of directionality of water diffusion, whereas the ADC value indicates the

TABLE 1. Demographic and First Diffusion Tensor Tractography Data of the Patients

	Group A (n = 12)	Group B (n = 17)	Group C (n = 19)	P
Age (y)	51.50 (11.82)	53.47 (9.28)	53.53 (11.59)	0.831
Sex (M:F)	6:6	12:5	13:6	0.406
Type (hemorrhage: infarct)	5:7	10:7	10:9	0.695
Duration to 1st DTT (days)	20.00 (10.16)	29.47 (19.58)	18.95 (10.92)	0.219
Duration to 2nd DTT (days)	593.17 (359.72)	499.88 (466.91)	377.10 (481.39)	0.090
FA on 1st DTT	0.54 (0.02)	0.56 (0.02)	0.55 (0.03)	0.055
ADC on 1st DTT	0.85 (0.06)	0.78 (0.21)	0.82 (0.14)	0.242
VN on 1st DTT	1334.92 (756.85)	1124.00 (388.44)	1506.00 (623.39)	0.120

Kruskal–Wallis test (sex, type was used the chi-square test). Values indicate mean (standard deviation).
ADC = apparent diffusion coefficient, DTT = diffusion tensor tractography, FA = fractional anisotropy, VN = voxel number.

magnitude of water diffusion.[29,30] The VN is determined by the included number of voxels in a neural tract.[31] Therefore, the increased VN without change in the FA and ADC values in the unaffected CST in group B suggests increment of total number of neural fibers of the CST in the unaffected hemisphere following change of the dominant hand to the left hand. In other words, the CST in the unaffected hemisphere in group B patients showed a compensatory and proliferative phenomenon in terms of the number of neural fibers by the increment of usage of the originally nondominant hand following change of handedness. As a result, the total fiber number of the CST in the unaffected hemisphere was increased.

In the left hand of group B patients, the functional improvement in terms of the GS, MFT, PPT, and MBI with the change of the dominant hand, and the clinical correlation of the functional improvement of the unaffected side in terms of the GS, PPT, and MBI with the VN of the unaffected CST appears to be consistent with the above-mentioned results. The result showing correlation of the increment of the VN in the unaffected CST in group B patients with the increment of the GS and PPT, indicating grip strength and fine motor ability, respectively, appears to coincide with previous studies reporting association of the main function of the CST with the grip power and fine motor ability of the hand.[7,8,32–35] However, no correlation of the MFT with the increment of the VN in the unaffected CST in group B patients appears to be ascribed to the characteristics of the MFT, which is the test for proximal part as

TABLE 2. First and Second Diffusion Tensor Tractography Data in the 3 Groups

	1st DTT	2nd DTT
FA	0.52 (0.04)	0.54 (0.02)
Group A (n = 12)		
ADC	0.85 (0.57)	0.84 (0.47)
VN	1334.92 (756.85)	1166 (609.58)
FA	0.56 (0.02)	0.58 (0.08)
Group B (n = 17)		
ADC	0.78 (0.21)	0.84 (0.06)
VN*	1124 (3.8844)	1391 (568.39)
FA	0.55 (0.03)	0.55 (0.03)
Group C (n = 19)		
ADC	0.84 (0.06)	0.84 (0.10)
VN	1506 (623.39)	1341.94 (588.77)

Wilcoxon sighed-rank test, Values indicate mean (standard deviation).
* $P < 0.05$.

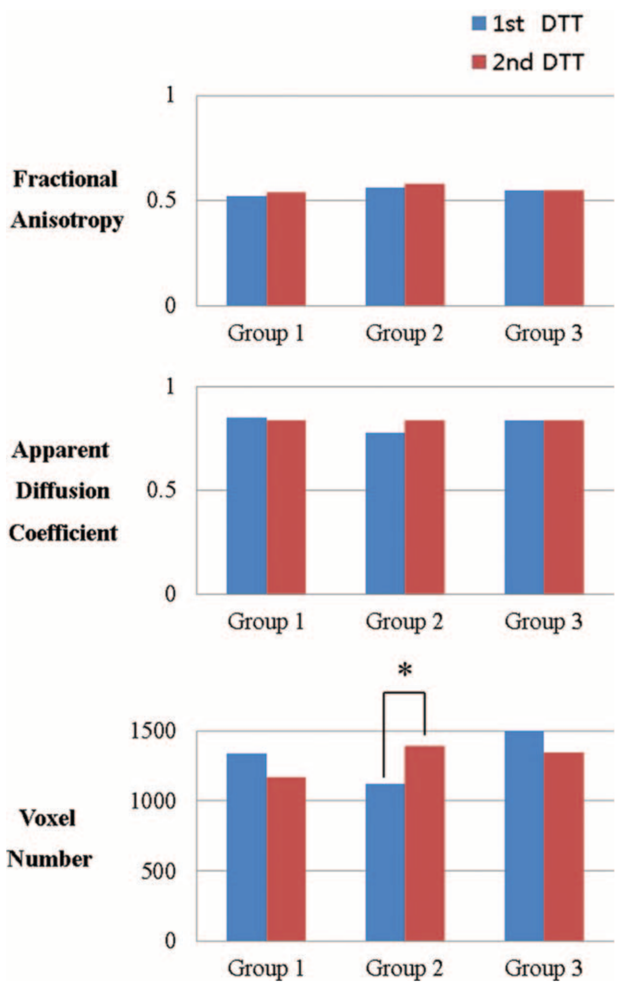

FIGURE 1. Comparison of the fractional anisotropy, apparent diffusion coefficient, and voxel number of the corticospinal tract in the unaffected hemisphere in each group. The voxel number increased significantly in group B.

TABLE 3. Comparison of Clinical Data Between First and Second Diffusion Tensor Tractography in Group B

Group B	GS*	MFT*	PPT*	MBI*
1st	21.86 (12.88)	25.41 (5.94)	9.59 (4.70)	26.82 (24.72)
2nd	30.50 (8.94)	30.53 (1.55)	12.94 (3.17)	65.88 (20.67)
			Correlation coefficient	
VN	0.499*	0.255	0.531*	0.552*

Wilcoxon sighed-rank test and Spearman correlation analysis. Values indicate mean (standard deviation).
GS = grip strength, MBI = Modified Barthel Index, MFT = Manual Function Test, PPT = Purdue pegboard test.
* $P < 0.05$.

well as distal part in upper extremity.[19] On the other hand, the result showing that the change of the MBI, which indicates the degree of activities of daily living including leg function suggests that patients should participate more actively in their own activity of daily living with residual function to change the dominant hand.[21,24] This result might suggest that change of the dominant hand is necessary to patient's volition as well as CST compensation in the unaffected hemisphere.

Since the introduction of DTI, many studies have reported on an injured CST in stroke patients.[10–16] However, the majority of these studies have focused on recovery of the CST and association of the injured CST in the affected hemisphere with motor function.[10–14] Only a few studies have reported on change of the CST in the unaffected hemisphere.[15,16] In 2010, Kwak et al investigated change of the CST in the unaffected hemisphere at the early stage of stroke in 53 patients with intracerebral hemorrhage using DTT and found that the VN of the unaffected CST was increased significantly compared with normal subjects.[15] In 2012, Jang et al investigated change of the anterior CST in the unaffected hemisphere of 32 chronic stroke patients using DTT and reported that the VN of the anterior CST in the unaffected hemisphere showed negative correlation with motor function of the affected extremities.[16] Thus, to the best of our knowledge, this is the first study on change of the CST in the unaffected hemisphere by change of the dominant hand following stroke. However, limitations of this study should be considered; first, the relatively small number of patients; second, the high standard deviation of duration to 2nd DTT from onset; third, the unequal proportions of hemorrhage and infarct in 3 groups; and fourth, limitations of DTT analysis; DTT technique might be operator dependent and regions of fiber complexity and crossing may cause underestimation of reconstruction of a neural tract.[36,37] Therefore, further studies to overcome the above-mentioned limitations should be encouraged.

In conclusion, we found that the fiber number of the CST in the unaffected hemisphere was increased by change of the dominant hand in stroke patients. We believe that our results have important implications in terms of neurorehabilitation. In detail, when stroke patients are obliged to change their dominant hand due to severe injury of the CST in the affected hemisphere or when showing a low functional state in the unaffected hand after change of the dominant hand, clinicians and therapists can induce rapid change of the dominant hand or functional improvement of the changed dominant hand by application of modalities to increase the fiber number of the CST in the unaffected hemisphere. Therefore, further research on modalities to increase the fiber number of the CST should be encouraged.

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