

Original Article



Relationship Between Ipsilesional Upper Extremity Motor Function and Corpus Callosum Integrity in Patients With Unilateral Stroke: A Diffusion Tensor Imaging Study

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HIGHLIGHTS

- The corpus callosum correlated with upper limb motor function on the lesion side.
- There is a correlation between left callosal region I and left upper limb function.

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to this study.

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Relationship Between Ipsilesional Upper Extremity Motor Function and Corpus Callosum Integrity in Patients With Unilateral Stroke: A Diffusion Tensor Imaging Study

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ABSTRACT

This study aims to investigate the relationship between ipsilesional upper extremity (UE) motor function and the integrity of the subregions of the corpus callosum in hemiparetic stroke patients with motor deficits of the dominant or non-dominant ipsilesional side. Twenty participants with unilateral UE deficits after stroke were included. Each of the 10 participants had lesions on the left and right sides. The ipsilesional UE function was assessed with the Jebsen-Taylor hand function test (JHFT), the 9-hole peg test (9HPT), and grip and pinch strength tests. Fractional anisotropy (FA) was calculated for the integrity of the 5 subregions of the corpus callosum. Pearson's correlation analysis was conducted to investigate the relationship between UE function and the integrity of the callosal subregions. The results of JHFT and 9HPT showed a significant correlation with the FA value of the corpus callosum I projecting to the frontal lobe in the left lesion group ($p < 0.05$). There was no correlation between the ipsilesional UE motor function and the FA value of the ulnar subregion in the right lesion group ($p > 0.05$). These results showed that the motor deficits of the ipsilesional UE correlated with the integrity of callosal fiber projection to the prefrontal area when the ipsilesional side was non-dominant.

Keywords: Stroke; Corpus Callosum; Upper extremity; Motor skill; Diffusion Tensor Imaging

INTRODUCTION

Stroke is a leading cause of serious long-term upper extremity (UE) motor disabilities. Although contralesional influence is usually greater than ipsilesional influence, unilateral hemispheric damage from a stroke can result in ipsilesional UE motor deficits [1-4]. The results of a longitudinal study showed that ipsilesional UE motor deficits begin immediately after the stroke and extend through the subacute and chronic phases [3]. Since activities of

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Conflict of Interest

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daily living predominantly requires bilateral movements, motor deficits in ipsilesional UE can impede not only recovery of function but also performance on activities of daily living [5]. Therefore, a better understanding of the mechanisms underlying ipsilesional UE motor function after a stroke is crucial for the development of effective rehabilitation strategies.

One possible mechanism of ipsilesional UE motor deficits after a unilateral stroke is the involvement of the corpus callosum (CC) [2,6]. The CC is the major white matter fiber bundle in the human brain. The 200–800 million fibers in the CC interconnect the homotopic and heterotopic areas of the two hemispheres, and the CC plays an essential role in the interhemispheric transfer of different types of information, including sensory, cognitive, and motor functions [7-11]. Therefore, ipsilesional movement is continuously influenced by transcallosal connections [12]. Delvaux and the colleagues have suggested that abnormal motor responses that are evoked in the less-affected limb might result from transcallosal influence of the affected hemisphere on the less-affected one, which may be due to disruption of the transcallosal inhibitory pathway and vulnerable GABAergic neurons [13].

Previous studies have reported that the integrity of the corpus callosum is significantly correlated with motor function of the contralesional upper extremity of stroke patients [14-16]. These studies have demonstrated that better structural integrity of the CC is associated with less contralesional UE motor and neurological deficits in stroke patients. In particular, the integrity of the CC body is closely related to motor function. However, to the best of our knowledge, no studies have investigated the relationship between the CC and ipsilesional UE motor function in stroke patients.

Furthermore, although it is controversial, handedness could influence the CC. CC size and connectivity differs in left- and right-handed individuals [17-19]. A meta-analysis showed that left-handers have larger CCs than right-handers do [20]. Thus, because handedness might influence the CC, the side of ipsilesional UE, being dominant or not, might affect callosal interconnections after a stroke [14].

After a stroke, patients might need to change their hand preference if their dominant side is affected. For example, if right-handed individuals have right hemiplegia after a stroke, they are forced to use their left hand during daily activities. This compensatory behavior can alter brain connectivity [21]. Philip and Frey have reported that amputees who had their dominant hand amputated and, thus, who had to use their non-dominant hand might greatly rely on the cognitive control of goal-directed actions, while healthy people usually depend on feedback control [21]. This compensatory change in hand preference can cause an experience-dependent shift in brain activation from the dorsodorsal parietofrontal pathway, which is related to feedback control, to the prefrontal area, which is involved with cognitive control [21]. Therefore, we hypothesized that the extent to which callosal connectivity is affected after a stroke is related to whether the ipsilesional UE is dominant or not.

Therefore, the objective of this study was to investigate the relationship between ipsilesional motor function and the integrity of callosal subregions in patients who have suffered a stroke and have motor deficits on their ipsilesional side relative to the ipsilesional side being dominant or not.

MATERIALS AND METHODS

Participants

From a retrospective review of medical records from March 1, 2012 to February 29, 2017, 149 patients with DTI were identified. Among these patients, 20 participants who met the inclusion criteria were included: 10 participants in the left-lesioned group and 10 participants in the right-lesioned group. The following are the inclusion criteria that the participants were required to have: 1) a unilateral stroke with onset of less than three months, 2) ipsilesional UE deficits with a score of less than 91 on the Jebsen-Taylor hand function test (JHFT), and 3) scores over 18 on the Korean version of the Mini-Mental State Examination (MMSE-K). Participants with a history of additional strokes or other neurodegenerative diseases or who were unable to undergo the evaluations due to cognitive or physical limitations were excluded. Enrolled patients assessed ipsilesional UE function and took diffusion tensor imaging (DTI). The participants were asked which hand they preferred to use when they performed daily activities, such as writing and eating, to determine the dominant hand. All 20 participants were right hand-dominant, and no participants reported being left hand-dominant or ambidextrous. The Medical Research Council (MRC) muscle power scale was evaluated to confirm the severity of motor function on the affected side.

All patients or their legally authorized representatives provided written informed consent before inclusion in this study. The study protocol was approved by the Institutional Review Board of each participating hospital.

Behavioral measurements

JHFT

The JHFT, which is a standardized tool used to assess UE function, consists of seven subtests: 1) writing, 2) card turning, 3) picking up small objects, 4) simulated feeding, 5) stacking checkers, 6) lifting large and light objects, and 7) lifting large and heavy objects. According to the standardized instructions of the JHFT written in Korean, the participants were asked to perform each subtest as quickly as possible, and the time taken to complete each subtest was recorded using a digital stopwatch. The performance time in each subtest was converted into a score according to the scoring system developed by Han and colleagues [22]. The total of the scores of the seven subtests ranged from 0 to 105, with higher scores indicating better UE function. UE deficits were defined by scores less than 91, which is less than two standard deviations away from the mean [23].

Nine-hole peg test (9HPT)

The 9HPT, which is a standardized tool used to measure hand dexterity, required the participant to pick up one peg at a time and put it in a hole on the board. Once all nine holes were filled with pegs, the participants were asked to remove one at a time. The participants were instructed to perform all procedures as fast as possible. The total time taken to complete the task was recorded using a digital stopwatch [24], with longer durations indicating poorer performance.

Grip and pinch strength tests

Maximum grip and pinch strength were measured in kilograms using a JAMAR hand dynamometer and pinch gauge, respectively. In accordance with the standardized instructions, the participants were seated with their shoulder adducted and neutrally rotated, elbow flexed 90°, forearm in a neutral position, and hand slightly hyperextended. The

participants were instructed to grab and squeeze the handles of the dynamometer as hard as possible. Three trials with one-minute intervals in between were performed successively on each hand, and the results were recorded. The mean of the three trials was analyzed in this study [25].

Diffusion tensor imaging (DTI)

Data acquisition

The imaging data were acquired using a standard 8-channel phased-array head coil on a 3.0-Tesla magnetic resonance imaging system (Signa HDxt; GE Healthcare, Milwaukee, WI, USA). The DTI protocol involved echo planar imaging with the following parameters: matrix = 120×120 matrix; Repetition Time/Echo Time = 16,000/84 ms; field of view = 240×240 mm²; approximately 70 axial slices; and slice thickness = 2 mm. The diffusion-sensitizing gradients were applied at a b value of 800 mm²/s for each of the 15 non-collinear and non-coplanar directions.

Data analysis

An experienced investigator analyzed the DTI images using the DTI studio (<https://www.mristudio.org>). Before analyzing the DTI images, the raw image data were transferred in Digital Imaging and Communications in Medicine format, and all DTI images were corrected for eddy currents using FSL software (The Analysis Group, FMRIB, Oxford, UK; <http://www.fmrib.ox.ac.uk/fsl>). We calculated the fractional anisotropy (FA), which is the most commonly used parameter in DTI studies. FA is a measure of the structural integrity of white matter, and it has values ranging between 0 (isotropic) and 1 (anisotropic). Although higher FA values usually indicate greater white matter structural integrity along a primary direction, high FA values also reflect path geometry and the presence of fiber crossing pathways [26]. In this study, FA values were defined as the presence of fiber crossing pathways.

All DTI images processed by the FSL (version 5.0.10, <http://www.fmrib.ox.ac.uk/fsl>). We observed brain images by naked eye to detect any signal distortion or movement artifacts. After eddy current correction was also performed, the corrected data were processed by skull-stripping. For inter-subject image registration, we utilized the FMRIB's Linear Image Registration Tool (FLIRT) and the Montreal Neurological Institute (MNI) template. After spatial normalization, we drew region of interests (ROIs) manually on the mid-sagittal image of corpus callosum of each subject with the method which was used in the previous study and illustrated in **Fig. 1** [10]. Those method reflects the topology of transverse tract of corpus callosum. Region I is the most anterior one-sixth portion, of the CC, projecting to the prefrontal region. Region II, which is the remainder of the anterior half of the CC, projects to the premotor and supplementary motor cortices. Region III is the anterior two-thirds of the posterior half of the CC, and it projects to the primary motor cortex. Region IV, which is the posterior one-third excluding the posterior one-fourth, projecting to the primary sensory cortex. Finally, region V, which projects to the parietal, temporal, and occipital cortices, is the posterior one-fourth of the CC.

This procedure was done by the designated experienced researchers who had shown high intra-rater reliability in various studies using DTI as main method of study. To standardize the ROIs, 2 investigators devised the training sessions. The ROIs were drawn after obtaining consensus about the boundaries of ROIs using a few selected images. A second investigator confirmed the accuracy of all ROI masks that were drawn by the first investigator (**Fig. 1**).

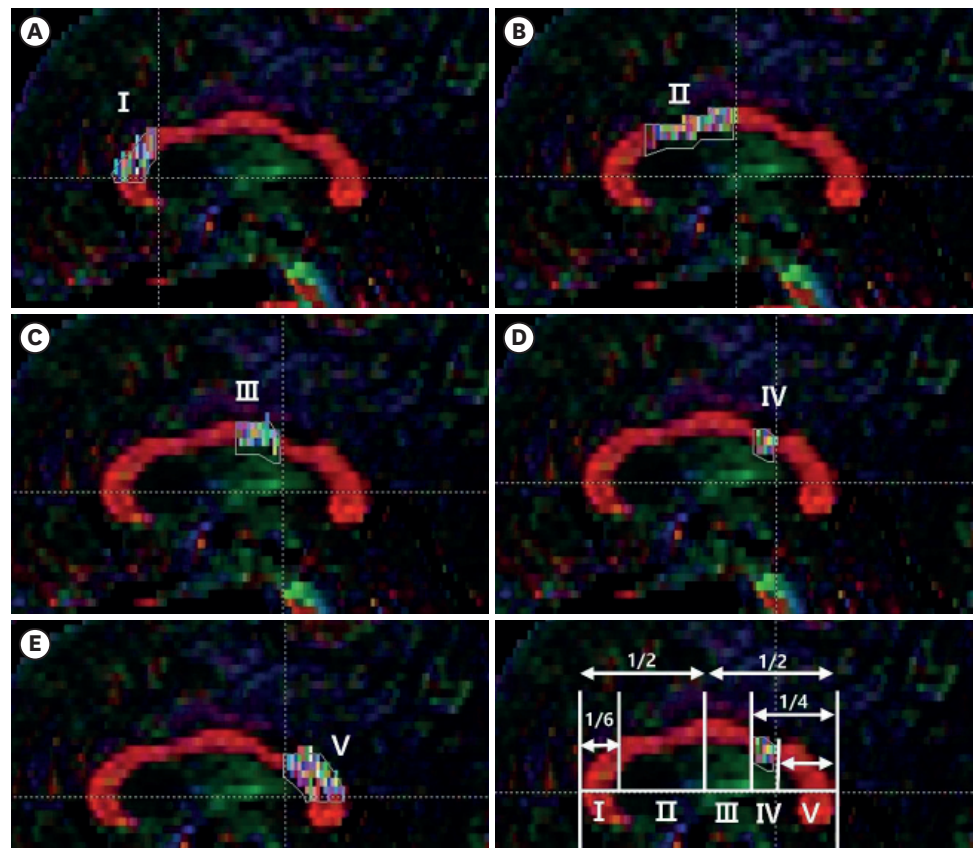


Fig. 1. Diffusion Tensor Imaging analysis of the corpus callosum in patient 10 from the left-lesioned group. (A) Region I, (B) Region II, (C) Region III, (D) Region IV, and (E) Region V.

Statistical analysis

Clinical characteristics, including age, length of time between the stroke onset to the date of DTI taken, JHFT score, and MMSE-K score were compared between the right- and left-lesioned groups using independent t-tests. As a result of Kolmogorov-Smirnov normality test, FA values of callosal subregions showed a normal distribution ($p > 0.05$). Thus, Pearson correlation analyses were applied to investigate the correlations between the FA values of the callosal subregions and ipsilesional UE function in the stroke patients. We used SPSS for Windows 17.0 (IBM Corporation, Armonk, NY, USA) for the statistical analyses, and the statistical significance level was set at 0.05.

RESULTS

Participant characteristics

A total of 20 participants were divided into two groups: the right-lesioned group, which consisted of 10 participants whose ipsilesional side was dominant, and the left-lesioned group, which consisted of 10 participants whose ipsilesional side was non-dominant. The right-lesioned group included seven men and three women, and the left-lesioned group contained six men and four women. Both groups included two infarctions and eight hemorrhages each. All participants were right hand-dominant (**Table 1**). There were no significant differences in age, MMSE-K scores, MRC muscle power scale (affected side), JHFT scores (non-affected side),

Table 1. Demographic characteristics

| Number | Sex | Stroke subtype | Lesion side | Dominant hand | MRC of affected side | Lesion |
|--|--------|----------------|-------------|---------------|----------------------|----------------------------|
| The right lesioned group (Ipsilateral hand is dominant) | | | | | | |
| 1 | Female | Infarction | Right | Right | 3 | F |
| 2 | Male | Hemorrhage | Right | Right | 4 | BG |
| 3 | Male | Hemorrhage | Right | Right | 4 | BG |
| 4 | Male | Infarction | Right | Right | 3 | Subcortex |
| 5 | Male | Infarction | Right | Right | 2 | F, T |
| 6 | Male | Infarction | Right | Right | 2 | Thalamus |
| 7 | Male | Infarction | Right | Right | 2 | Insula, Posterior thalamus |
| 8 | Female | Infarction | Right | Right | 1 | F, T |
| 9 | Female | Infarction | Right | Right | 4 | Brainstem |
| 10 | Male | Infarction | Right | Right | 2 | BG, F, T, O |
| The left lesioned group (Ipsilateral hand is non-dominant) | | | | | | |
| 1 | Female | Hemorrhage | Left | Right | 3 | Thalamus |
| 2 | Male | Infarction | Left | Right | 4 | O |
| 3 | Male | Infarction | Left | Right | 3 | CR |
| 4 | Male | Infarction | Left | Right | 5 | BG, CR |
| 5 | Female | Infarction | Left | Right | 5 | IC, CR |
| 6 | Female | Infarction | Left | Right | 3 | CR, F-T |
| 7 | Female | Infarction | Left | Right | 5 | Pontine |
| 8 | Male | Infarction | Left | Right | 3 | Brainstem |
| 9 | Male | Infarction | Left | Right | 3 | BG, CR |
| 10 | Male | Hemorrhage | Left | Right | 2 | T-P |

MRC, Medical Research Council; F, frontal; BG, basal ganglia; T, temporal; O, occipital; CR, corona radiata; IC, internal capsule; P, parietal.

and DTI dates from onset between the groups ($p > 0.05$). In the comparison between the two groups, there was a significant difference in the FA value of region V ($p < 0.05$), and there was no significant difference in subregions I-IV ($p < 0.05$, **Table 2**).

Correlations between ipsilesional UE function and callosal subregion FA values

In the right-lesioned group, no significant correlations were found between the results of the UE function evaluations (JHFT, 9HPT, and grip and pinch strength tests) and the FA values of the callosal subregions ($p > 0.05$, **Table 3**). However, in the left-lesioned group, the JHFT and 9HPT results were significantly correlated with the FA of callosal region I ($r = 0.69$ and $r = -0.71$, respectively; $p < 0.05$; **Table 4**). Of the JHFT subtests, the picking up of small objects and simulated feeding were correlated with the FA of callosal region I ($r = 0.73$ and $r = 0.74$, respectively; $p < 0.05$). In addition, the lifting of large and light objects and the lifting of large and heavy objects subtests were correlated with the FA value of callosal region II ($r = 0.73$ and

Table 2. Comparisons of the right- and left-lesioned groups

| Variables | Right-lesioned group (n = 10) | Left-lesioned group (n = 10) | p value |
|---|-------------------------------|------------------------------|---------|
| Age (yr) | 64.7 ± 12.13 | 64.4 ± 10.43 | 0.95 |
| MMSE-K (score) | 23.9 ± 4.43 | 24.4 ± 3.69 | 0.09 |
| MRC muscle power scale (affected side) | 2.7 ± 1.059 | 3.6 ± 1.07 | 0.08 |
| JHFT-ipsilesional hand (score) (non-affected side) | 71.9 ± 9.87 | 67.5 ± 24.76 | 0.79 |
| 9 Hole peg board test (sec) (non-affected side) | 32.16 ± 5.92 | 34.89 ± 14.56 | 0.59 |
| The length of time between the onset of stroke and the date of DTI taken (days) | 41.0 ± 13.58 | 30.7 ± 11.75 | 0.61 |
| FA values of callosal subregions | | | |
| CC1 | 0.61 ± 0.12 | 0.61 ± 0.04 | 0.92 |
| CC2 | 0.56 ± 0.10 | 0.59 ± 0.05 | 0.40 |
| CC3 | 0.56 ± 0.10 | 0.58 ± 0.07 | 0.76 |
| CC4 | 0.56 ± 0.14 | 0.56 ± 0.11 | 0.97 |
| CC5 | 0.70 ± 0.04 | 0.66 ± 0.03 | 0.03* |

MMSE-K, The Korean version of the Mini-Mental Status Examination; MRC, Medical Research Council; JHFT, Jebsen-Taylor hand function test; DTI, diffusion tensor image; FA, fractional anisotropy; CC, corpus callosum.

* $p < 0.05$.

Table 3. Correlations between the FA values of the callosal subregions and ipsilateral upper extremity function in the right-lesioned group (n = 10)

| Variables | CC1 Prefrontal | CC2 Premotor | CC3 Motor | CC4 Sensory | CC5 Others |
|--------------------|----------------|--------------|-----------|-------------|------------|
| JHFT (total score) | -0.014 | -0.227 | 0.110 | 0.355 | 0.521 |
| Writing | -0.205 | -0.166 | -0.284 | 0.033 | 0.237 |
| Card | 0.331 | 0.141 | 0.463 | 0.352 | 0.461 |
| Small object | -0.155 | -0.257 | -0.014 | 0.218 | 0.142 |
| Feeding | 0.366 | 0.198 | 0.357 | 0.429 | 0.332 |
| Checker | -0.325 | -0.255 | -0.160 | -0.087 | 0.223 |
| Large light | -0.082 | -0.489 | 0.271 | 0.364 | 0.409 |
| Large heavy | 0.345 | -0.100 | 0.212 | 0.466 | 0.352 |
| Grip strength | 0.166 | -0.045 | 0.103 | 0.384 | 0.352 |
| Pinch strength | 0.302 | -0.034 | 0.320 | 0.427 | 0.539 |
| 9HPT | -0.011 | -0.016 | 0.013 | -0.249 | -0.265 |

CC, corpus callosum; JHFT, Jebsen-Taylor hand function test; 9HPT, 9-hole pegboard test.

*p < 0.05.

Table 4. Correlations between the FA values of the callosal subregions and ipsilateral upper extremity function in the left-lesioned group (n = 10)

| Variables | CC1 Prefrontal | CC2 Premotor | CC3 Motor | CC4 Sensory | CC5 Others |
|--------------------|----------------|--------------|-----------|-------------|------------|
| JHFT (total score) | 0.694* | 0.595 | -0.136 | -0.314 | -0.433 |
| Writing | 0.538 | 0.199 | -0.012 | 0.176 | -0.351 |
| Card | 0.495 | -0.143 | -0.292 | -0.312 | 0.139 |
| Small object | 0.728* | 0.482 | -0.165 | -0.375 | -0.293 |
| Feeding | 0.736* | 0.617 | 0.007 | -0.405 | -0.339 |
| Checker | 0.539 | 0.340 | -0.181 | -0.276 | -0.245 |
| Large light | 0.451 | 0.733* | -0.185 | -0.558 | -0.363 |
| Large heavy | 0.351 | 0.756* | -0.180 | -0.382 | -0.488 |
| Grip strength | 0.315 | 0.610 | 0.032 | -0.323 | -0.229 |
| Pinch strength | 0.249 | 0.577 | -0.108 | -0.498 | -0.095 |
| 9HPT | -0.711* | -0.613 | 0.165 | 0.452 | 0.322 |

CC, corpus callosum; JHFT, Jebsen-Taylor hand function test; 9HPT, 9-hole pegboard test.

*p < 0.05.

r = 0.76, respectively; p < 0.05). **Fig. 2** illustrates the significant relationships between the callosal subregions and motor performance of upper extremity.

DISCUSSION

In this study, we investigated the relationship between ipsilesional UE function and the FA values of the callosal subregions, depending on whether the ipsilesional side was dominant or not. In order to create groups according to the dominance of the ipsilesional side, the patients were classified into the right-lesioned group with the ipsilesional side being dominant (right) and the left-lesioned group with the ipsilesional side being non-dominant (left). The upper extremity severity on the affected side was evaluated by the MRC muscle power scale, and there was no significant difference between the two groups. There was no significant difference in FA values in callosal subregions I to IV, but there was a significant difference in region V (splenium) between the left and the right lesion groups. This difference is considered to be influenced by the size and location of the left-right lesion.

Meanwhile, in the comparison of lesion-side callosal subregions and ipsilesional upper extremity function, there was a correlation between the FA value of left callosal region I and left UE function in left-lesioned group. We confirmed that the JHFT and 9HPT results of left-lesioned group significantly correlated with the FA values of region I, which consisted of the callosal projections to the prefrontal area.

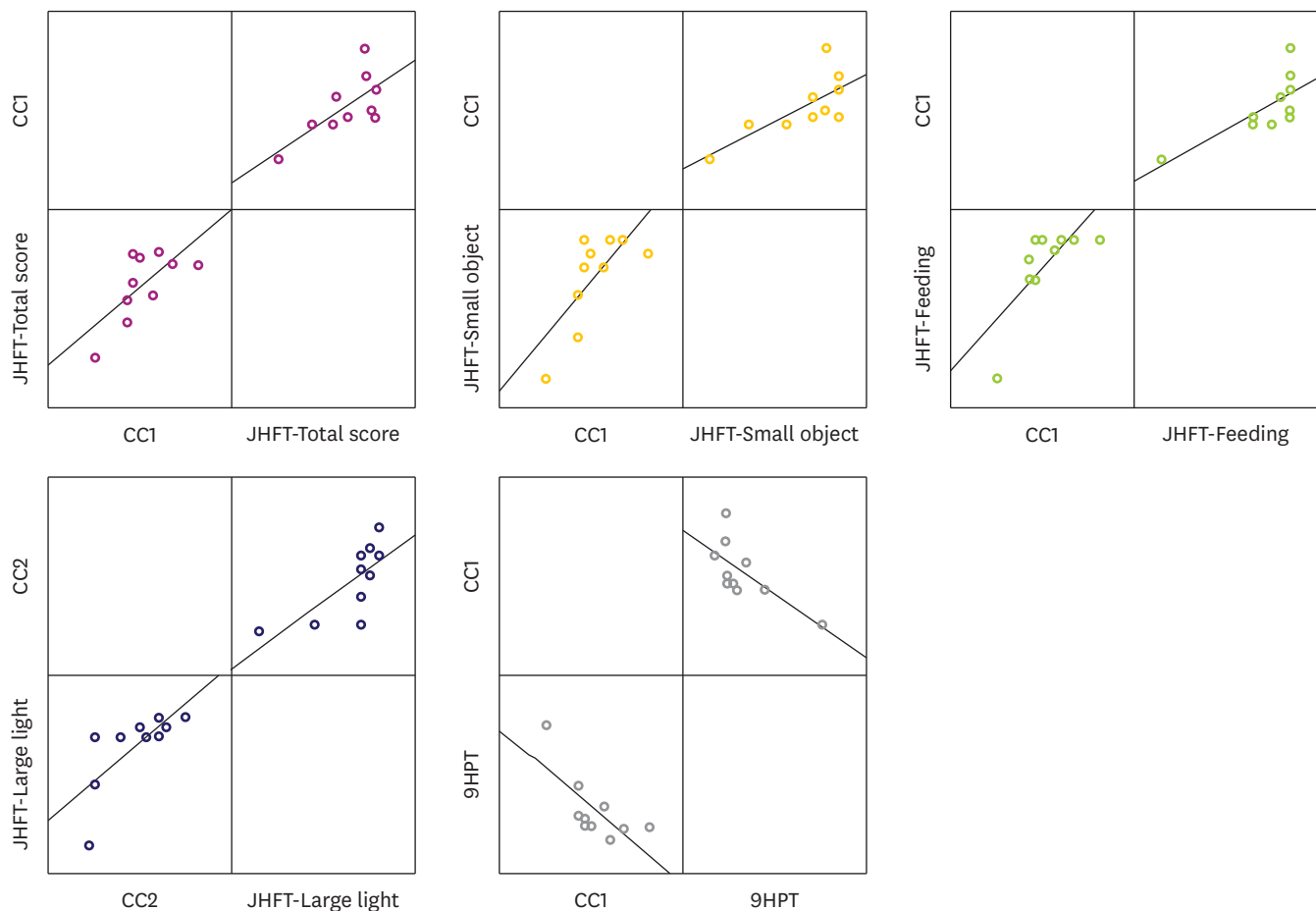


Fig. 2. Scatter plots showing correlation. The relationships between the callosal subregions and motor performance of upper extremity.

After an injury, a significant portion (up to 35%) of individuals needs to change their handedness [27]. Specifically, because the dominant hand of all participants in this study was the right hand, the participants with right hemiplegia after the unilateral stroke (left-lesioned group) were forced to heavily rely on their left UE, which is the less-affected side and which was non-dominant before the stroke. This compensatory change could increase the interhemispheric connectivity between the non-dominant and dominant hand representations because the activity of the non-dominant hand was newly associated with the territory of the formerly dominant hand [21]. Thus, the strengthening of the interhemispheric connectivity during non-dominant hand motor learning might eventually result in plastic changes in the human brain.

Moreover, although higher FA values usually indicate greater integrity, including increased axonal density and/or myelination, high FA values also reflect path geometry and the presence of fiber crossing pathways [26], some of which might be influenced by experience-dependent changes. For example, alterations in experiences, such as undergoing intensive skill training, result in changes in white matter structures, including the CC. Therefore, the correlations between the FA values of the left callosal region I of that projects to the prefrontal area and ipsilesional UE function might be owing to the motor learning of the non-dominant hand after the stroke. Furthermore, all of the participants have suffered from the stroke at least two weeks before DTI scans were taken in this study, an average length of

time between the stroke onset to the DTI taken were 30.7 days on the left lesioned group and 41 days on the right lesioned group. Two weeks are a sufficient amount of time for substantial and persistent improvements in non-dominant hand function supported by changes in functional connectivity to occur [28]. Thus, since persons with stroke are forced we propose that the correlations between ipsilesional UE function and the FA values of callosal region I in the left-lesioned group might have resulted from the effects of the motor learning of the non-dominant hand.

The majority of previous studies have revealed that contralesional UE motor functions are related to callosal projections in the motor and supplementary motor areas [14,15]. On the other hand, our findings showed that ipsilesional UE motor functions after stroke were significantly correlated with the FA values of region I of the callosal projections in the prefrontal area in the left-lesioned group. Since FA values reflect the presence of fiber crossing pathways, these results suggest that the callosal connections in the left-lesioned group might reflect the motor learning of the non-dominant hand after the stroke. The compensatory changes in hand dominance after an injury could result in an experience-dependent transition from feedback control to the cognitive control of action [21]. Since prefrontal regions are related with the cognitive control of goal-directed actions [21,29], our results could have been affected by the motor learning of the non-dominant hand after the stroke. In this regard, we suggest that although other research showed contralesional UE motor functions are related to callosal projections in the motor and supplementary motor areas, correlation between ipsilesional UE motor functions and the callosal projections in the prefrontal area might result from the motor learning of the non-dominant hand after the stroke which requires cognitive control of action.

Furthermore, in this study, no correlations were found between ipsilesional UE motor function and the FA of callosal subregions in the right-lesioned group. Because their dominant hands were not on the affected side, these participants did not need to change their handedness. In other words, individuals who had strokes could still use their originally preferred hand, which was usually the one on the right side. This might have not facilitated motor learning in the brain. Thus, our results suggested that the FA values of the callosal subregions did not correlate with ipsilesional UE function in the right-lesioned group, and these findings support our results that the correlations seen in the left-lesioned group might have been affected by the motor learning of the non-dominant hand after the stroke.

Our study also showed that, in the left-lesioned group, more complex and fine motor tasks such as writing subtest and picking up small object subtest of the JHFT and the 9HPT were associated with the callosal projections in the prefrontal area whereas relatively simple motor tasks such as lifting large and heavy objects subtests of the JHFT revealed correlation with the callosal projections in the premotor area. These results might be supported by a previous study that the prefrontal cortex showed greater involvement in performances of more complex fine motor tasks compared to the relatively simple ones [30]. In addition, our results indicated that grip and pinch strength showed no correlations. Remple and colleagues suggested that stronger muscles are not correlated to a larger representation of the muscles in the primary motor cortex in rats [31]. Another previous study also supports our results that strengthening can result from different neural adaptation with motor skills [32].

Even though our findings are important, this study had several limitations. First, the initial stroke volume or initial FA values of the callosal subregions were not determined. However,

the majority of FA values of the callosal subregions (regions I to IV), especially those that were correlated with ipsilesional UE function, did not differ significantly between the right- and left-lesioned groups, which suggested that the initial values might not have significantly influenced the correlation results. For future studies, we suggest that interhemispheric inhibition also needs to be evaluated in order to understand the precise roles of the CC in the ipsilesional hand function of stroke patients because handedness might be related to inhibitory interhemispheric interactions [33]. In addition, the small sample size is one of limitation of this study. It was inevitable because our retrospective study had the strict exclusion criteria to minimize the effect of confounders. The lack of subgroup comparison analysis according to the respective lesion is also a limitation of this study. However, we do not say that the small asymmetry of lesion distribution compromise the integrity of comparison analysis because the left-lesion group had 6 subcortical strokes and the right-lesion group had 5 subcortical strokes as shown in **Table 1**. Finally, we split the handedness of enrolled patients into three distinct group rather than continuous numerical scale such as Edinburgh Handedness Inventory to confirm the degree of handedness which was also one of limitation in this study.

In conclusion, it is evident that individuals who had unilateral strokes can have ipsilesional UE motor deficits. Thus, a better understanding of the mechanisms underlying ipsilesional UE motor function in stroke is critical in order to provide optimal rehabilitation services. Our results suggested that ipsilesional UE motor function was correlated with the callosal fibers that project to the prefrontal area of the ipsilesional UE is non-dominant, and these correlations might arise from the motor learning of the non-dominant hand in individuals who have been forced to use their non-dominant UE after the stroke because their affected side was dominant. The present study is clinically meaningful because, to our knowledge, it is the first study to investigate the relationship between ipsilesional motor function and the corpus callosum after stroke, and the results of the study provide useful information for understanding functional and anatomical mechanisms of ipsilesional UE motor function in stroke patients.

REFERENCES

1. Jones RD, Donaldson IM, Parkin PJ. Impairment and recovery of ipsilateral sensory-motor function following unilateral cerebral infarction. *Brain* 1989;112:113-132.
[PUBMED](#) | [CROSSREF](#)
2. Marque P, Felez A, Puel M, Demonet JF, Guiraud-Chaumeil B, Roques CF, Chollet F. Impairment and recovery of left motor function in patients with right hemiplegia. *J Neurol Neurosurg Psychiatry* 1997;62:77-81.
[PUBMED](#) | [CROSSREF](#)
3. Noskin O, Krakauer JW, Lazar RM, Festa JR, Handy C, O'Brien KA, Marshall RS. Ipsilateral motor dysfunction from unilateral stroke: implications for the functional neuroanatomy of hemiparesis. *J Neurol Neurosurg Psychiatry* 2008;79:401-406.
[PUBMED](#) | [CROSSREF](#)
4. Laufer Y, Gattenio L, Parnas E, Sinai D, Sorek Y, Dickstein R. Time-related changes in motor performance of the upper extremity ipsilateral to the side of the lesion in stroke survivors. *Neurorehabil Neural Repair* 2001;15:167-172.
[PUBMED](#) | [CROSSREF](#)
5. Sainburg R, Good D, Przybyla A. Bilateral synergy: a framework for post-stroke rehabilitation. *J Neurol Transl Neurosci* 2013;1:1025.
[PUBMED](#)

6. Metrot J, Froger J, Hauret I, Mottet D, van Dokkum L, Laffont I. Motor recovery of the ipsilesional upper limb in subacute stroke. *Arch Phys Med Rehabil* 2013;94:2283-2290.
[PUBMED](#) | [CROSSREF](#)
7. Aboitiz F, Montiel J. One hundred million years of interhemispheric communication: the history of the corpus callosum. *Braz J Med Biol Res* 2003;36:409-420.
[PUBMED](#) | [CROSSREF](#)
8. de Lacoste MC, Kirkpatrick JB, Ross ED. Topography of the human corpus callosum. *J Neuropathol Exp Neurol* 1985;44:578-591.
[PUBMED](#) | [CROSSREF](#)
9. Gazzaniga MS. Cerebral specialization and interhemispheric communication: does the corpus callosum enable the human condition? *Brain* 2000;123:1293-1326.
[PUBMED](#) | [CROSSREF](#)
10. Hofer S, Frahm J. Topography of the human corpus callosum revisited--comprehensive fiber tractography using diffusion tensor magnetic resonance imaging. *Neuroimage* 2006;32:989-994.
[PUBMED](#) | [CROSSREF](#)
11. Innocenti GM. General organization of callosal connections in the cerebral cortex. In: Jones EG, Peters A, eds. *Sensory-motor areas and aspects of cortical connectivity*. New York, NY: Plenum Press; 1986:291-353.
12. Ween JE. Functional imaging of stroke recovery: an ecological review from a neural network perspective with an emphasis on motor systems. *J Neuroimaging* 2008;18:227-236.
[PUBMED](#) | [CROSSREF](#)
13. Delvaux V, Alagona G, Gérard P, De Pasqua V, Pennisi G, de Noordhout AM. Post-stroke reorganization of hand motor area: a 1-year prospective follow-up with focal transcranial magnetic stimulation. *Clin Neurophysiol* 2003;114:1217-1225.
[PUBMED](#) | [CROSSREF](#)
14. Li Y, Wu P, Liang F, Huang W. The microstructural status of the corpus callosum is associated with the degree of motor function and neurological deficit in stroke patients. *PLoS One* 2015;10:e0122615.
[PUBMED](#) | [CROSSREF](#)
15. Stewart JC, O'Donnell M, Handlery K, Winstein CJ. Skilled reach performance correlates with corpus callosum structural integrity in individuals with mild motor impairment after stroke: a preliminary investigation. *Neurorehabil Neural Repair* 2017;31:657-665.
[PUBMED](#) | [CROSSREF](#)
16. Wang LE, Tittgemeyer M, Imperati D, Diekhoff S, Ameli M, Fink GR, Grefkes C. Degeneration of corpus callosum and recovery of motor function after stroke: a multimodal magnetic resonance imaging study. *Hum Brain Mapp* 2012;33:2941-2956.
[PUBMED](#) | [CROSSREF](#)
17. Bernard JA, Taylor SF, Seidler RD. Handedness, dexterity, and motor cortical representations. *J Neurophysiol* 2011;105:88-99.
[PUBMED](#) | [CROSSREF](#)
18. Westerhausen R, Kreuder F, Dos Santos Sequeira S, Walter C, Woerner W, Wittling RA, Schweiger E, Wittling W. Effects of handedness and gender on macro- and microstructure of the corpus callosum and its subregions: a combined high-resolution and diffusion-tensor MRI study. *Brain Res Cogn Brain Res* 2004;21:418-426.
[PUBMED](#) | [CROSSREF](#)
19. Witelson SF. The brain connection: the corpus callosum is larger in left-handers. *Science* 1985;229:665-668.
[PUBMED](#) | [CROSSREF](#)
20. Driesen NR, Raz N. The influence of sex, age, and handedness on corpus callosum morphology: a meta-analysis. *Psychobiology (Austin Tex)* 1995;23:240-247.
[CROSSREF](#)
21. Philip BA, Frey SH. Compensatory changes accompanying chronic forced use of the nondominant hand by unilateral amputees. *J Neurosci* 2014;34:3622-3631.
[PUBMED](#) | [CROSSREF](#)
22. Han TR, Kim JH, Lee SJ, Kim SB. The significance of the hand function test in the hemiplegic patients. *J Korean Acad Rehabil Med* 1992;16:423-430.
23. Kim YH, Choi MS, Kim BO. Assessment of hand function in normal Korean adults by Jebsen Hand function test. *J Korean Acad Rehabil Med* 1984;8:109-114.
24. Oxford Grice K, Vogel KA, Le V, Mitchell A, Muniz S, Vollmer MA. Adult norms for a commercially available Nine Hole Peg Test for finger dexterity. *Am J Occup Ther* 2003;57:570-573.
[PUBMED](#) | [CROSSREF](#)

25. Mathiowetz V, Kashman N, Volland G, Weber K, Dowe M, Rogers S. Grip and pinch strength: normative data for adults. *Arch Phys Med Rehabil* 1985;66:69-74.
[PUBMED](#)
26. Johansen-Berg H, Della-Maggiore V, Behrens TE, Smith SM, Paus T. Integrity of white matter in the corpus callosum correlates with bimanual co-ordination skills. *Neuroimage* 2007;36 Suppl 2:T16-T21.
[PUBMED](#) | [CROSSREF](#)
27. Walsh WW, Belding NN, Taylor E, Nunley JA. The effect of upper extremity trauma on handedness. *Am J Occup Ther* 1993;47:787-795.
[PUBMED](#) | [CROSSREF](#)
28. Philip BA, Frey SH. Increased functional connectivity between cortical hand areas and praxis network associated with training-related improvements in non-dominant hand precision drawing. *Neuropsychologia* 2016;87:157-168.
[PUBMED](#) | [CROSSREF](#)
29. Rushworth MF, Walton ME, Kennerley SW, Bannerman DM. Action sets and decisions in the medial frontal cortex. *Trends Cogn Sci* 2004;8:410-417.
[PUBMED](#) | [CROSSREF](#)
30. Rao H, Di X, Chan RC, Ding Y, Ye B, Gao D. A regulation role of the prefrontal cortex in the fist-edge-palm task: evidence from functional connectivity analysis. *Neuroimage* 2008;41:1345-1351.
[PUBMED](#) | [CROSSREF](#)
31. Remple MS, Bruneau RM, VandenBerg PM, Goertzen C, Kleim JA. Sensitivity of cortical movement representations to motor experience: evidence that skill learning but not strength training induces cortical reorganization. *Behav Brain Res* 2001;123:133-141.
[PUBMED](#) | [CROSSREF](#)
32. Jensen JL, Marstrand PC, Nielsen JB. Motor skill training and strength training are associated with different plastic changes in the central nervous system. *J Appl Physiol (1985)* 2005;99:1558-1568.
[PUBMED](#) | [CROSSREF](#)
33. Takeuchi N, Oouchida Y, Izumi S. Motor control and neural plasticity through interhemispheric interactions. *Neural Plast* 2012;2012:823285.
[PUBMED](#) | [CROSSREF](#)