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Neural Network Related to Hand Movement: A Combined Study of Diffusion Tensor Tractography and Functional MRI

JI HEON HONG, PT, MS[1)], SUNG HO JANG, MD[1)]

[1)]*Department of Physical Medicine and Rehabilitation, College of Medicine, Yeungnam University: 317–1, Daemyungdong, Namku, Taegu, 705-717, Republic of Korea.*
TEL: 82-53-620-3269, FAX: 82-53-620-3269, E-mail: strokerehab@hanmail.net, belado@med.yu.ac.kr

Abstract. [Purpose] Little is known about the detailed anatomical connections of the neural network related to hand movement in the human brain. We investigated the neural network using diffusion tensor tractography (DTT) data analyzed in conjunction with functional MRI (fMRI) activation results. [Subjects and Method] We recruited 19 healthy volunteers for this study. Probabilistic tractography was used to analyze diffusion tensor imaging (DTI) data that were collected using fMRI activation induced by grasp-release movements of the hand at a rate of 1 Hz. [Results] The brain areas connected to the primary sensorimotor cortex (SM1), which is activated by hand movements, were the premotor cortex (100%), superior parietal lobule (100%), intraparietal sulcus (100%), supramarginal gyrus (97.37%), supplementary motor area (89.47%), thalamus (86.84%), putamen (81.58%), pars opercularis (81.58%), pars triangularis (68.42%), angular gyrus (65.79%), and cerebellum (60.53%) in the same hemisphere and the contralateral primary motor cortex (60.53%) in the opposite hemisphere. No significant difference was observed in the total incidence of connected tracts between hemispheres. [Conclusion] These results reveal that more brain areas are involved in hand movements than were previously thought necessary for motor planning and execution in the human brain.
Key words: Motor control, Neural network, Diffusion tensor tractography

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INTRODUCTION

It is necessary to investigate the neural network to understand the physiological mechanisms of normal movement in the human brain[1)]. Several brain evaluation techniques (e.g., functional neuroimaging, electroencephalography, magnetoencephalography) have been used to elucidate functional relationships between neural activity and movement control[2–7)]. Such studies have reported that various cortical and subcortical areas participate in movement control[2–7)]. However, these evaluation techniques are insufficient for resolving and visualizing the cortico-subcortical neural network for movement.

Diffusion tensor tractography (DTT), which is derived from diffusion tensor imaging (DTI), allows us to visualize and localize the architecture and integrity of subcortical neural tracts in three dimensions[8–10)]. Functional MRI (fMRI) is capable of precisely identifying cortical activation sites because of its high spatial resolution[11)]. Therefore, when DTT data are analyzed in conjunction with fMRI results (activation in response to movement) we can obtain a more accurate characterization of the cortico-subcortical neural network related to movement[12–14)].

In the current study we elucidated the neural network related to hand movements using DTT data analyzed in conjunction with fMRI activation results.

SUBJECTS AND METHOD

We recruited 19 right-handed normal subjects (17 male, 2 female; mean age: 28.9 years; range: 25–33 years) with no previous history of neurological, psychiatric, or physical illness. Handedness was evaluated using the Edinburgh Handedness Inventory[15)]. All subjects understood the purpose of this study, and they provided their written, informed consent prior to participation in this study. This study was approved by the institutional review board of our university hospital.

The blood oxygenation level dependent (BOLD) fMRI measurement, which employs the echo planar imaging (EPI) technique, was performed using a 1.5-T Philips Gyroscan Intera scanner (Hoffman-LaRoche, Ltd.; Best, the Netherlands) with a standard head coil. The EPI BOLD images were acquired over 20 identical axial sections, producing a total of 1,200 images for each subject. Imaging conditions were TR/TE = 2 sec/60 msec, FOV = 210 mm,

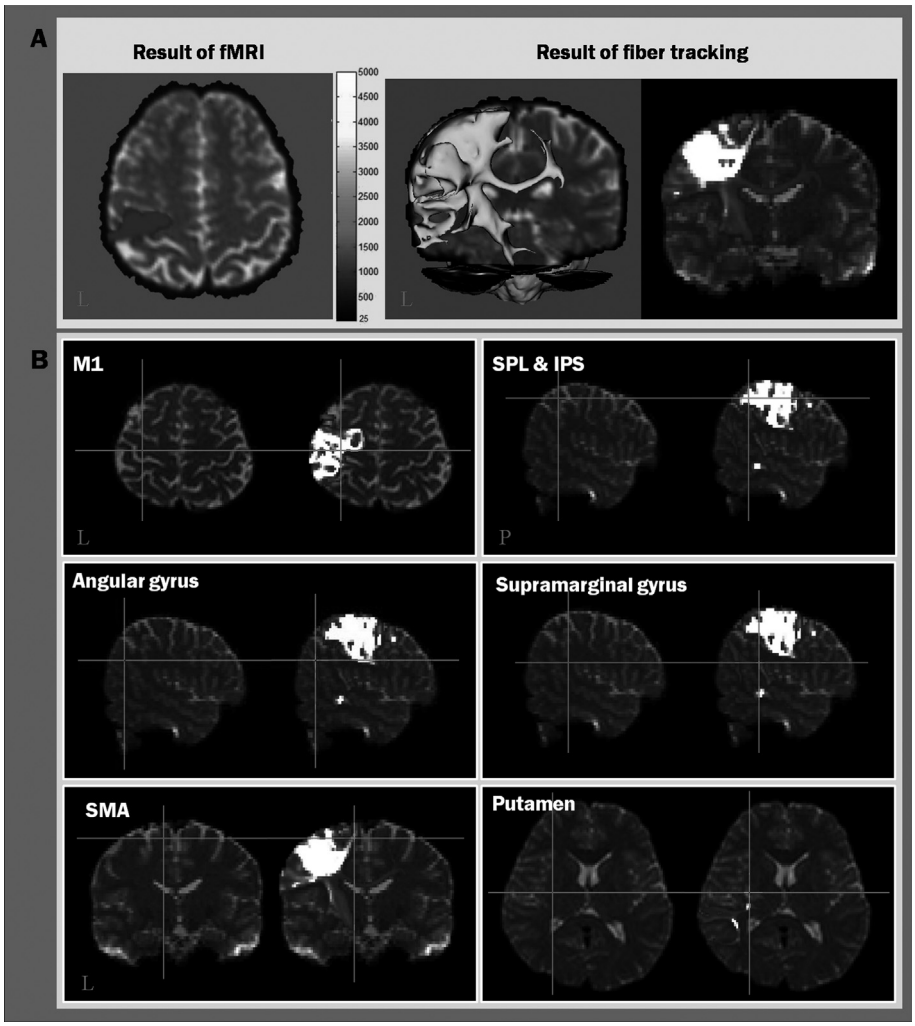

Fig. 1. (A) The contralateral primary sensorimotor cortex, which was activated by hand movements, was chosen as the seed region of interest (left). The probabilistic map of the neural network-related hand movements (right). (B) The quantitative network is color coded for 25 (dark red) to 5,000 (white) samples passing through the voxel. M1: primary motor cortex; SPL: superior parietal lobule; IPS: inferior parietal sulcus; SMA: supplementary motor area.

matrix size = 64 × 64, and slice thickness = 5 mm. Subjects were examined supine with their eyes closed, and they were secured firmly with the forearm in supination. A repetitive alternating cycle of control (rest for 20 seconds) and stimulation (activity for 20 seconds) with grasp-release hand movements at a metronome-guided frequency of 1 Hz was performed for the motor task. Each "control and stimulation" task (40 seconds) was repeated three times.

The DTIs were acquired using a synergy-L Sensitivity-encoding (SENSE) head coil on a 1.5-T Philips Gyroscan Intera scanner (Hoffman-LaRoche, Ltd.; Best, the Netherlands) with a navigator echo. The DTI data were collected using a single-shot spin-echo planar imaging sequence of 1.73×1.73×2.3 mm^3. Sixty-seven contiguous slices (matrix=128×128, field of view=221×221 mm^2, repetition time/echo time=10,726/76 ms, SENSE factor=2, EPI factor=67, b=1000 s/mm^2, NEX=1, and thickness=2.3 mm) were acquired for each of the 32 non-collinear diffusion-sensitizing gradients.

The fMRI data were analyzed using SPM2 software (Wellcome Department of Cognitive Neurology, UK) run in MATLAB (Mathworks, USA). The functional images were realigned by slice timing and motion corrected. The data were coregistered and resliced using the diffusion-weighted EPI volume with the highest signal-to-noise ratio (no diffusion weighting, b=0) for each subject as a template[16]. The final data were smoothed with an 8 mm isotropic Gaussian kernel. Statistical parametric maps were obtained, and voxels were considered significant at a p-value of 0.05, corrected for Familywise Error (FWE).

Diffusion-weighted imaging data were analyzed using the Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB) Software Library (FSL; www.fmrib.ox.ac.uk/fsl). DTI data were edited for eddy current-induced image distortions using affine, multi-scale, two-dimensional registration. Fiber tracking was performed using a probabilistic tractography method based on a multifiber model. In the present study we used tractography

routines implemented in the FMRIB Diffusion Toolbox (FDT) (5,000 streamline samples from voxel seeds, 0.5 mm step length, 0.2 curvature threshold)[17–19]. The seed areas were determined from the fMRI results of each subject (the activated cluster including the precentral knob) (Fig. 1). Of the 5,000 samples generated from each seed voxel, the results for each contact were visualized at a minimum threshold of 25 streamlines[17] and a maximum of 5,000 streamlines per voxel for analysis. Finally, we defined several regions of interest (ROIs) in the brain. The neural network developed from the fMRI results was investigated to determine its incidence in the ROIs. Percentage of incidence (N%) was calculated using the following equation:

$$N\% = \frac{\text{The term of total incidence in each ROI}}{\text{Total case (38 hemispheres)}} \times 100$$

Several ROIs were defined using the diffusion-weighted EPI volume with the highest signal-to-noise ratio (no diffusion weighting, b=0) in each subject`s brain. We subdivided the frontal cortex into the primary motor cortex (M1); Bordmann area (BA) 4, the premotor cortex (PMC); posterior part of BA 6[20], the supplementary motor area (SMA); anterior and medial part of BA 6, the pars opercularis; BA 44; and the pars triangularis, BA 45[21]. The temporal cortex was classified into three gyri, according to morphology: the superior temporal gyrus, middle temporal gyrus, and inferior temporal gyrus. The parietal cortex was subdivided into the primary somatosensory cortex (S1); BA 3, 1, and 2; superior parietal lobule (SPL); intraparietal sulcus (IPS); the supramarginal gyrus[22,23]; and the angular gyrus[10]. The thalamus was subdivided into the lateral group (including the ventral posterior lateral nucleus (VPL)), medial group, posterior group, and anterior group[24]. The putamen was defined as having anterior, middle, and posterior areas[25]. The cerebellum was divided into contralateral and ipsilateral hemispheres.

The terms of total incidence in each ROI were used to perform a chi-square test for the determination of variances between the right and left hemispheres. Statistical significance was chosen as $P < 0.05$.

RESULTS

The contralateral SM1s are activated during movements of either hand in all subjects. Therefore, we used the activation of SM1 as a seed for analysis of the neural network for hand movement. We defined a successful result as a connection with SM1 that was observed in more than half of the total number of hemispheres (all subjects) in each ROI. In the frontal lobe activations of the contralateral SM1 were connected with the contralateral PMC (100%), contralateral SMA (89.47%), contralateral pars opercularis (81.58%), contralateral pars triangularis (68.42%), and ipsilateral M1 (60.53%). These were also connected with the contralateral SPL (100%), contralateral IPS (100%), contralateral supramarginal gyrus (97.37%), and contralateral angular gyrus (65.79%) in the parietal lobe, and the contralateral superior temporal gyrus (71.05%) and contralateral middle temporal gyrus (89.47%) in the temporal lobe. The contralateral VPL nucleus of the thalamus (86.84%), contralateral posterior one-third of the putamen (81.58%), and contralateral hemisphere of the cerebellum (60.53%) were connected with the ipsilateral SM1 activation region (Table 1) (Fig 1). There was no significant difference in the total ROI incidence between the right and left hemispheres ($p>0.05$).

Table 1. Percentage of tracks that reached the region of interest

Regions of interest	Total (%)
Contralateral premotor cortex (PMC) (BA 6)	100
Contralateral superior parietal lobule (SPL) (BA 5,7)	100
Contralateral intraparietal sulcus (IPS)	100
Contralateral supramarginal gyrus (BA40)	97.37
Contralateral supplementary motor area (SMA) (BA 6)	89.47
Contralateral middle temporal gyrus (BA 21)	89.47
Contralateral VPL nucleus of thalamus	86.84
Contralateral posterior one-third of putamen	81.58
Contralateral pars opercularis (BA 44)	81.58
Contralateral superior temporal gyrus (BA 41,42,22)	71.05
Contralateral pars triangularis (BA 45)	68.42
Contralateral angular gyrus (BA 39)	65.79
Ipsilateral M1 (BA 4)	60.53
Contralateral cerebellum hemisphere	60.53

Total (%) indicates percentage of the tracks that reached anatomical areas in both hemispheres.

DISCUSSION

In the current study we elucidated the neural network for hand movement using a combined fMRI/DTT method. Our results show that SM1 connected to the PMC (100%), SPL (100%), IPS (100%), supramarginal gyrus (97.37%), SMA (89.47%), VPL nucleus of the thalamus (86.84%), posterior one-third of the putamen (81.58%), pars opercularis (81.58%), pars triangularis (68.42%), angular gyrus (65.79%), and cerebellum (60.53%) in the same hemisphere and the contralateral primary motor cortex (60.53%) in the opposite hemisphere. The classical conception of motor control holds that the corticospinal tract (CST) is the most important motor pathway for voluntary movements in humans. The majority of CSTs originate from pyramidal neurons, which are situated in SM1[26,27]. In this study the contralateral SM1 was activated during hand movements of either hand in all subjects. Previous neurophysiology studies have reported that neurons of the PMC, SMA, and cerebellum are involved in the control of movement velocity, amplitude, and directional tuning with SM1[28–31]. It is widely accepted that motor areas receive afferents from a specific set of parietal areas[32,33]. Several researchers have demonstrated that the SPL- and IPS-integrated somatosensory and visual information participate in goal-direction actions[32–34]. Other neuroimaging studies have provided evidence that these areas are involved in the praxis along with the SMA, PMC, and cerebellum[35–39]. In addition to these areas, linearly increasing activations corresponding to movement amplitude and velocity were observed in the putamen and thalamus[3,35,39]. The supramarginal gyrus and

angular gyrus areas are concerned with motor planning and cognitive judgments, such as mechanical problem solving[22,40,41]. For example, increase of neural activation in the supramarginal gyrus and angular gyrus is based on preparation of pointing movements. This cortical recruitment is related to the more complex coordinate transformations needed to plan a pointing movement[22]. Rao et al. verified that the pars opercularis and pars triangularis connections were activated more substantially during the performance of the complex task than during the simple task[42]. According to other studies the pars opercularis and pars triangularis were activated by imitation and observation of finger movements[43,44]. Therefore, these areas seem to constitute a high-level sensorimotor interface integrating sensory stimuli and cognitive tasks with the related motor representations of hand movements[45]. We also found connections to the ipsilateral M1 in the opposite hemisphere. Many previous studies have demonstrated the contribution of the ipsilateral M1 to motor control in normal portions of the injured brain[36,46,47]. We observed unexpected connections to the middle and superior temporal gyri. These areas are involved in the recognition of an object[23]; therefore, there may be potential partial volume contamination in the centrum semiovale[48].

There have been many neuroimaging and neurophysiologic studies of neural control of hand movement, and our results generally coincide with those of previous studies[3,28–31,34–39]. To the best of our knowledge, only one DTT study has addressed this topic. Guye et al. investigated the connectivity of M1 using combined fMRI and DTI[12]. They implemented fast-marching tractography to define connectivity maps within the whole brain, and the connectivity maps were normalized. The results showed strong connections from M1 to the CST, premotor areas, parietal cortices, thalamus, and cerebellum. In contrast, we used probabilistic tractography to analyze DTI data. Probabilistic tractography, which is a multi-tensor model, estimates multiple dominant diffusion orientations within an imaging voxel[10,18,48]. Behrens et al. reported that probabilistic tractography was more sensitive than traditional tensor methods or single-fiber approaches[17]. We found that SM1 is connected with brain areas, such as the supramarginal gyrus, angular gyrus, pars opercularis, pars triangularis, and contralateral M1, in addition to the areas previously identified in the study of Guye et al.[12].

In conclusion, we visualized the neural network related to hand movements and found this neural network consisted of many brain areas in addition to those previously identified for motor planning and execution. We believe the results and methodology of this study will be helpful in the investigation of motor control in the human brain. Limitations of the present study included the false positives generated by the multi-fiber approach due to the inability of DTI to fully reflect the underlying fiber architecture because of regions of fiber complexity and crossing[17,25]. A clear understanding of the relationship between fiber bundle structure and DTI will allow us to elucidate a more accurate neural network for movements.

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