Human Structural Hand Motor Network Inferred by Probabilistic q-ball Tractography & MEG

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INTRODUCTION: Neuroscientists face the challenge of explaining how functional brain states emerge from the interactions of dozens, perhaps hundreds, of brain regions, each containing millions of neurons. Much evidence supports the view that highly evolved nervous systems are capable of real-time integration of information across brain regions. This integration is the functional outcome of dynamic interactions within and between the complex structural networks of the brain. Human motor function is one example of a result of dynamical processes unfolding within the networks of the human brain. In the healthy brain, neural activity in the motor areas of both hemispheres are functionally coupled and equally balanced in terms of mutual inhibitory control. Thus, the lateralization of neural activity during unimanual movements is likely to be related —at least in part— to interhemispheric inhibition between motor areas exerted via transcallosal connections, which results in an inhibition of motor areas ipsilateral to the moving hand. The relevant structural network for hand motor has been largely determined in non-human primates by tracer injection techniques. In humans, less is known about these pathways, and diffusion MRI is the first method that can estimate axonal bundles in vivo. Our aim is to achieve a closer understanding of how motor function is dependent on the structure of the human brain, as an integrated network. This study, within the concept of interhemispheric competition, is designed to further investigate and map the structural inter-regional connectivity of the hand motor network, by combining functional Magnetoencephalography Imaging (MEGI) with diffusion MRI (dMRI).

METHODS: We performed a neuroimaging assessment with active task-based spatiotemporal data (using MEGI) and structural connectivity of the white matter sensorimotor pathways (using dMRI) in 10 normal controls. High angular resolution diffusion imaging (HARDI) have been used in conjunction with probabilistic tractography methods and MEGI to estimate the number, integrity and structural connectivity of white matter tracts within the established sensorimotor network. ***MEG Data Acquisition:*** We collected functional imaging data using task-based MEGI assessed by localizing the associated time frequency dynamics of bihemispheric motor cortices during a self-paced index finger button press task of index finger flexion/extension. ***MRI Image Acquisition:*** Magnetic resonance images have been acquired using a 3T system. We acquired diffusion tensor images using high angular resolution diffusion imaging (HARDI) with a single-shot, twice refocused spin echo sequence (55 directions, b=2000 s/mm^2, sense factor = 2, 2.2 mm per side isotropic voxels). ***Data Analysis:*** Task-based MEGI at each evaluation have been used to define seed and target regions of bilateral primary and/or secondary sensorimotor areas contributing to corticospinal, inter-hemisperic and Inter-regional cortico-cortical tracts. The FT analysis has been performed using *q*-ball probabilistic resampled DW dataset, seeded from the MEG activation site of the affected hand in the motor cortex (M1) in each voxel of M1 and targeted to the structural and functional ROIs found in the new structural network as showed in Fig.1. The algorithm used for the fiber tracking is a probabilistic QBall method developed in our laboratory (Berman 2008) and based on the non-parametric estimates of the uncertainties in fiber tracking directions with the residual bootstrap which we have previously validated for use with diffusion MRI data (Chung 2006). The advantages of this diffusion fiber tracking method is the ability to perform accurate delineation in the presence of voxels with complex diffusion distributions due to intravoxel crossing of distinct fiber bundles.

RESULTS: Using high-angular resolution diffusion MRI (HARDI) and probabilistic fiber tracking based on functional MEG imaging we were able to map consistently the normal structural hand motor network in 10 controls as showed in Figure 1. Transcallosal fiber tracts connecting Hand Primary Motor Cortex (Hand M1) to the contralateral Primary Motor Cortex, Supplementary Motor Area and Dorsal Premotor Cortex were not found in all the control subjects and interestingly the MEGI of these subjects showed a pattern of bilateral activation during both hands motor tasks. In addition, the Ventral Premotor Cortex connected inconstantly to the ipsilateral Hand Primary Motor Cortex and as previously demonstrated in animal tracing studies and functional studies using TMS, this connection could produce a robust modulation of motor outputs from M1 and is functionally lateralized. We have found lateralization in 3 of 10 controls.

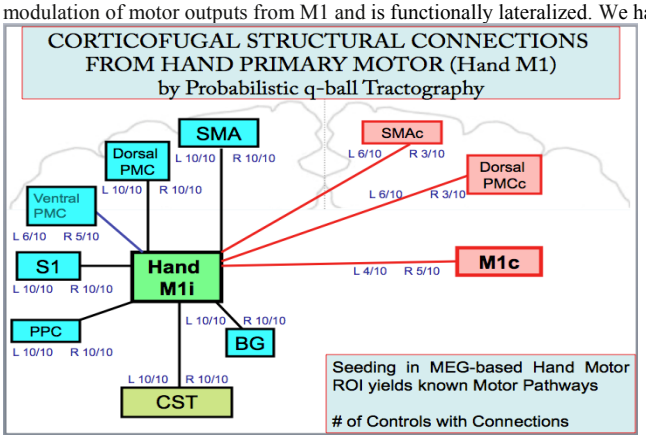

Figure 1. Structural hand motor network: Ipsilateral Regions connected to Hand Primary Motor Cortex (HandM1): (SMA) Supplementary Motor Area; (Dorsal PMC) Dorsal Premotor Cortex; (Ventral PM) Ventral Premotor Cortex; (S1) Primary Sensory Cortex; (PPC) Posterior Parietal Cortex; (BG) Basal Ganglia; (CST) Ipsilateral Corticospinal Tract from/to Cerebral Peduncle. **Contralateral Regions connected to Hand Primary Motor Cortex (HandM1) via Transcallosal Fiber Tracts:** (SMA) Supplementary Motor Area; (M1c) contralateral primary motor cortex; (Dorsal PMC) Contralateral Dorsal Premotor Cortex.

DISCUSSION: In this study we mapped the expected human structural hand motor network in 10 controls, including connections previously not characterized in vivo, using high-angular resolution diffusion MRI (HARDI) and probabilistic fiber tracking based on functional MEG imaging. Our preliminary data indicate that functional MEGI of motor cortex increases our ability to confidently delineate the structural connectivity involved in the motor network through HARDI fiber tracking. Further investigations of the normal human motor network are necessary in order to understand underlying structural changes that may be clinically relevant in conditions, such as neuroplasticity in stroke during rehabilitation and regeneration.

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