Using Tractography & MEG to Infer Functional and Structural Motor Connectivity in Humans

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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), resting-state MEGI functional connectivity and structural connectivity of the white matter sensorimotor pathways (using dMRI) in 20 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 and functional connectivity of white matter tracts within the established sensorimotor network. ***MEG Data Acquisition and Analysis:*** 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. We used the resting state MEGI data to perform a functional connectivity analysis of the areas connected to the activation area for the hand motor. ***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:*** Anatomy based regions of interest 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. Task-based MEGI have been used as a refernce to locate the Hand motor region for each subject. Resting state MEGI has been used to perform a functional connectivity analysis of the areas activated and the results have been compared to the results from the structural connectivity analysis. The FT analysis has been performed using probabilistic resampled DW dataset; we seeded from the anatomical ROI based on the MEG activation site of the ipsilateral hand in the motor cortex (M1) in each voxel of M1 and targeted to the structural and functional ROIs of known hand motor the structural network as showed in Fig.1. The algorithm used for the fiber tracking is a probabilistic method developed in our laboratory using Python (Amirberkian 2011, Berman 2008). We also performed a non-parametric statistical analysis to assess the reliability of the fiber tracking results.

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 20 controls as showed in Figure 1. Transcallosal fiber tracts connecting Hand Primary Motor Cortex (Hand M1) to the contralateral Primary Motor Cortex and Supplementary Motor Area were not found in all the control subjects and interestingly the MEGI of the subjects without these connections showed a pattern of bilateral activation during both hands motor tasks.

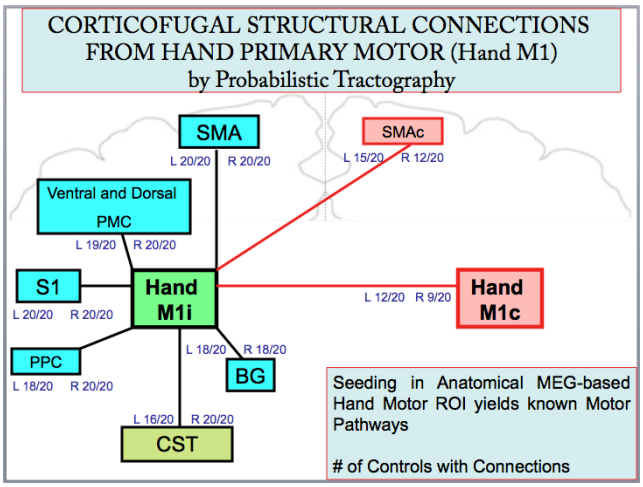

Figure 1. Structural hand motor network: Ipsilateral Regions connected to Hand Primary Motor Cortex (HandM1): (SMA) Supplementary Motor Area; Dorsal and Ventral (PMC) Premotor Cortex; (S1) Primary Sensory Cortex; (PPC) Posterior Parietal Cortex; (BG) Basal Ganglia; (CST) Ipsilateral Corticospinal Tract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

DISCUSSION: In this study we mapped the expected human structural hand motor network in 20 controls, using high-angular resolution diffusion MRI (HARDI) and probabilistic fiber tracking based on anatomical landmarks and functional MEG imaging. We also correlated the structural results with the results from the MEGI resting-state functional connectivity. Our results indicate that functional MEGI of motor cortex increases our ability to confidently locate the Hand Motor Region within the motor cortex.

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