Probabilistic fiber tracking from the pre-SMA and SMA Proper: Implications for language and motor white matter networks

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Introduction

The supplementary motor area (SMA) can be divided into a rostral pre-SMA, involved in higher-level processing and a caudal SMA-proper, involved with motor execution. Recently, Peck et al. reported that using a motor and language combined functional paradigm, a common central area of fMRI activation ("central SMA") can be defined. This central SMA was located on the border of the pre-SMA and the SMA proper, and was shown to be maximally activated compared to the motor-only or language-only tasks [1]. The results of these studies suggest that by judiciously exploiting the application of fMRI paradigms, more detailed topographic maps of the anatomic structure of the SMA can be derived. In this study, we seek to expand on this study by using diffusion tensor imaging to compare the pattern of white matter fibers originating from two different fMRI guided seed regions; the pre-SMA and the SMA-proper defined by fMRI language and motor paradigm respectively. We hypothesized that pre-SMA seed derived from the language paradigm will connect more readily to the frontal areas known to be associated with language function including Broca's Area.

Subjects and Functional Tasks

12 right-handed patients with brain tumors were recruited for this study. Two different functional paradigms were used, including a motor task (finger tapping) and a language task (phonemic fluency). These tasks were performed as block paradigms (6 cycles; 20sec active and 30sec rest). Self-paced sequential tapping of the thumb against the forefinger were used to localize the SMA-proper and the primary motor cortex (PMC) activation. During the language task to localize the pre-SMA, patients were presented with a letter and asked to silently generate words which begin with the letter. The subject's task performance and head motion were monitored using software (Brainwave, Medical Numerics) that observe the brain activity in real time.

Methods and Data Analysis

Functional images were acquired with a single shot gradient echo EPI sequence (TR/TE=4000/35ms; 128×128 matrix; 4.5 mm thickness). DTI data was acquired using a single shot spin echo EPI sequence (25 directions, TR/TE=11000/64ms, 128×128 matrix; 3 mm thickness, 1000 s/mm^2 b value). 2D and 3D T1 weighted anatomical images were acquired with a spin echo and a spoiled GRASS sequence. fMRI and probabilistic DTI analysis was performed using AFNI [2] and DTI&FiberTools (Department of Diagnostic Radiology, University Hospital, Freiburg, Germany) [3], respectively. For fMRI, the reconstructed data was aligned using a 3D registration method. Spatial smoothing, using a gaussian filter of 4mm was performed. Functional maps were generated using cross-correlation analysis. Functional images showing the pre-SMA and SMA-proper activation were generated at a threshold of $p<0.0001$. Then, peak voxels of activation in these regions were used to define seed regions for fiber tracking. Tracking area was defined as a region with Tr(D)<0.002 and FA>0.1 and the probability map of connectivity was generated individually through these tracking area using the software. The probability map was extracted based on a probabilistic model in an Monte Carlo simulation of Random Walks using the Probabilistic Index of Connectivity (PICo) approach [4] but with DTI data as basis.
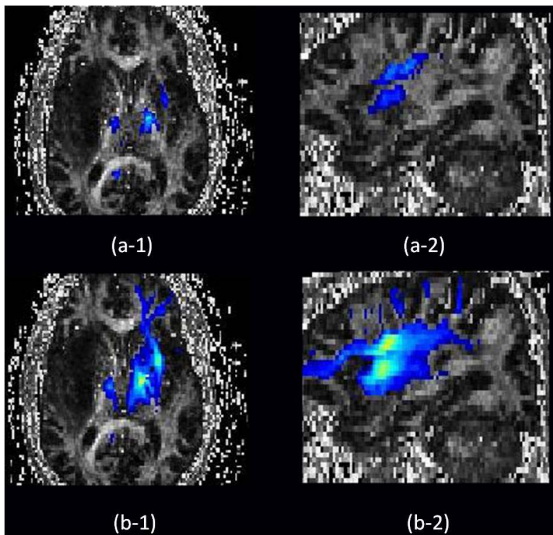
Results and Discussion

(a-1) (a-2) (b-1) (b-2)

fMRI SMA Activation: Individual subject analysis indicated that significant pre-SMA and SMA proper activation were observed during the motor and language tasks respectively in all 12 subjects. *Probabilistic fiber tracking*: Seeding of the pre-SMA (associated with language) demonstrated a much more extensive white matter tracts network when compared to the SMA-proper (associated with motor function). The white matter network obtained from the pre-SMA seed extended to involve multiple structures in the frontal lobes known to be involved in language formation including the inferior lateral frontal gyrus (Broca's area), the insula and the middle frontal gyrus (dorsal lateral prefrontal cortex – DLPFC). In contrast, the white matter network extending form the SMA-proper seed was much less extensive and was essentially limited to the cortico-spinal tract (which is the main white matter tract involved in motoric function) seen in its known location in the posterior aspect of the posterior limb of the internal capsule. The figure shows connectivity maps obtained using the probabilistic tracking algorithm in the axial and sagittal planes. Results obtained from SMA-proper seed (a-1and a-2) and pre-SMA seed regions (b-1 and b-2) are shown. The maps show that using probabilistic tracking, white matter connectivity was established between the SMA and frontal lobe areas known to be involved in language production (including Broca's area). No connectivity was demonstrated between the SMA-proper seed region and the essential cortical language areas. Our results give further support to the functional subdivision of the SAM as well as the ability of probabilistic tractography to identify important white matter connections between even small cortical areas.

References: 1) Peck et al., Neuroreport 20, 487-491, 2009. 2) Cox , *Comput Biomed Res* 29, 162-173, 1996, 3) Kreher B et al., Neuroimage, 43, 81-89, 2008, 4) Parker et al., J MRI, 18, 242-254, 2003.