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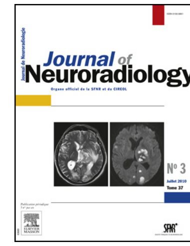


ORIGINAL ARTICLE

# Probabilistic fiber tracking of the language and motor white matter pathways of the supplementary motor area (SMA) in patients with brain tumors

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**KEYWORDS**
DTI;
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Probabilistic fiber tracking;
SMA;
Brain tumor

**Summary**
*Background and purpose:* Accurate localization of anatomically and functionally separate SMA tracts is important to improve planning prior to neurosurgery. Using fMRI and probabilistic DTI techniques, we assessed the connectivity between the frontal language area (Broca's area) and the rostral pre-SMA (language SMA) and caudal SMA proper (motor SMA).
*Materials and methods:* Twenty brain tumor patients completed motor and language fMRI paradigms and DTI. Peaks of functional activity in the language SMA, motor SMA and Broca's area were used to define seed regions for probabilistic tractography.
*Results:* fMRI and probabilistic tractography identified separate and unique pathways connecting the SMA to Broca's area — the language SMA pathway and the motor SMA pathway. For all subjects, the language SMA pathway had a larger number of voxels ($P < 0.0001$) and higher connectivity ($P < 0.0001$) to Broca's area than did the motor SMA pathway. In each patient, the number of voxels was greater in the language and motor SMA pathways than in background pathways ($P < 0.0001$). No differences were found between patients with ipsilateral and those with contralateral tumors for either the language SMA pathway (degree of connectivity: $P < 0.36$; number of voxels: 0.35) or the motor SMA pathway (degree of connectivity, $P < 0.28$; number of voxels, $P < 0.74$).

*Abbreviations:* BOLD, blood oxygen level-dependent; FA, fractional anisotropy; fMRI, functional MRI; MD, mean diffusivity; ROI, region of interest; SMA, supplementary motor area.

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*Conclusion:* Probabilistic tractography can identify unique white matter tracts that connect language SMA and motor SMA to Broca's area. The language SMA is more significantly connected to Broca's area than is the motor subdivision of the SMA proper.
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## Introduction

The supplementary motor area (SMA) comprises of rostral pre-SMA involved in language (language SMA) and a caudal SMA proper involved in motor planning (motor SMA) [1—3]. The locations of these subdivisions of the SMA, however, vary in individual cases. The SMA is relevant to neurosurgical planning, since resection of the SMA can lead to postoperative deficits including mutism in extreme cases [4]. Iatrogenic speech dysfunction may occur in up to half of brain tumor resections near the SMA [5,6], implying that the SMA plays an integral part in the motor execution of speech. Studies in normal subjects have qualitatively described structural connectivity between these subdivisions of the SMA and Broca's area, using anatomically defined seed regions and probabilistic tractography [7,8]. These prior studies, however, did not quantify nor compare the connectivity of the generated pathways [9,10].

Diffusion tensor imaging (DTI) can non-invasively identify white matter tracts in the human brain [11,12]. In addition, DTI can define the relationships of essential white matter tracts to a brain tumor to optimize the planning and resection of the tumor in patients with brain tumors [4,13—15]. Functional magnetic resonance imaging (fMRI) has confirmed the importance of classical language-related areas, including Broca's area and Wernicke's area, as well as secondary language area such as the SMA that contribute to language expression and reception [3,16—18]. Combination of fMRI and DTI tractography by identifying region of interest (ROI) as activation peaks in task-based fMRI data can increase the accuracy of fiber tracking. Identifying the correct ROI for tractography is critical to extract true structural connectivity, especially in brain tumor patients with distortion of normal anatomy.

The purpose of our study was to apply probabilistic tractography to identify and quantify the fiber connectivity between the 2 SMA subdivisions and Broca's area. Based on the voxels activated by the fMRI language and motor paradigms, seed ROIs for tracking were placed in Broca's area (BA seed), language SMA, motor SMA and 2 background areas. We quantitatively assessed the degrees of connectivity and the numbers of voxels in the pathways from the SMA ROIs to Broca's area. We hypothesize that there is higher connectivity between Broca's area and the language SMA than between Broca's area and the motor SMA, as well as between either subdivision of the SMA and Broca's area than between the background areas and Broca's area.

## Methods

### Subjects

The Institutional Review Board and Privacy Board approved this retrospective study performed according to Health Insurance Portability and Accountability Act regulations. Twenty patients (10 males and 10 females, mean age = 43.8 years [range, 28—65]) with unilateral brain tumors in the right or left brain who underwent both fMRI and DTI over an 18-month period were studied. fMRI and DTI were performed in each case because the patient had signs or symptoms of speech difficulty and/or the tumor was located near ($\leq$ 2 cm) the expected language centers and/or tracts. The tumors consisted of astrocytomas ($n$ = 8), oligodendrogliomas ($n$ = 6), glioblastomas ($n$ = 2) and metastases ($n$ = 4). All patients were 100% right-handed as determined by the Edinburgh Handedness Inventory [19] and were native English speakers.

### MRI

The fMRI and DTI data were acquired as part of the routine clinical workup for each patient. Scanning was performed on a 3T magnet (3T GE, Milwaukee, Wisconsin) using a standard quadrature head coil. BOLD fMRI was acquired with a single-shot gradient-echo echo-planar imaging sequence (TR/TE = 4000/35 ms; 128 $\times$ 128 matrix; 4.5-mm thickness with no gap, 240-mm FOV). DTI data were acquired using a single-shot spin-echo echo-planar imaging sequence (25 directions, TR/TE = 11,000/64 ms, 128 $\times$ 128 matrix; 3-mm thickness, 1000 s/mm$^2$ b value). T1-weighted spin-echo images (TR/TE = 600/8 ms, 256 $\times$ 256 matrix, 4.5-mm thickness with no gap, 240-mm FOV) and 3D T1-weighted anatomic images with a spoiled gradient-recalled-echo sequence (TR 22 ms, TE 4 ms, 256 $\times$ 256 matrix, 30$^\circ$ flip angle, 1.5-mm thickness, 240-mm FOV) were also acquired.

### Functional tasks

All patients underwent 2 paradigms: a motor task (finger tapping) and a language task (phonemic fluency). Each paradigm was presented as a block paradigm consisting of 90 images, alternating between 20 seconds of activation and 40 seconds for both hands in response to an auditory cue. Self-paced finger tapping task was used at approximately 2 Hz by sequential finger tapping of fingers 2-5 against finger 1 to localize the motor SMA and the primary motor cortex. The language task was used to localize the language SMA and Broca's area. During the task, letters appeared on the screen and patients were asked to silently generate words that began with that letter. Each subject's real-time brain activity and head motion were monitored using software (Brainwave, GE Healthcare, Milwaukee, Wisconsin).

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