



Short communication

Contralateral functional reorganization of the speech supplementary motor area following neurosurgical tumor resection

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ABSTRACT

We evaluated plasticity in speech supplemental motor area (SMA) tissue in two patients using functional magnetic resonance imaging (fMRI), following resection of tumors in or associated with the dominant hemisphere speech SMA. Patient A underwent resection of an anaplastic astrocytoma NOS associated with the left speech SMA, experienced SMA syndrome related mutism postoperatively, but experienced full recovery 14 months later. fMRI performed 32 months after surgery demonstrated a migration of speech SMA to homologous contralateral hemispheric regional tissue. Patient B underwent resection of an oligodendroglioma NOS in the left speech SMA, and postoperatively experienced speech hesitancy, latency and poor fluency, which gradually resolved over 18 months. fMRI performed at 64 months after surgery showed a reorganization of speech SMA to the contralateral hemisphere. These data support the hypothesis of dynamic, time based plasticity in speech SMA tissue, and may represent a noninvasive neural marker for SMA syndrome recovery.

1. Introduction

Resection of tumors involving the dominant hemisphere speech supplementary motor area (SMA) often results in immediate postoperative speech deficits which can range from complete mutism to a less severe but global reduction in spontaneous speech (Damasio & Van Hoesen, 1985; Masdeu, Schoene & Funkenstein, 1978; Vassal, Charroud, & Deverdun, 2017; Ziegler, Kilian, & Deger, 1997). This is a form of a variably intense SMA syndrome directly related to the somatotopic organization of the SMA (Thulborn, Carpenter, & Just, 1999; Tombari et al., 2004; Vassal et al., 2017). Speech SMA is represented by a cortical region anterior to the motor SMA, and contributes to the muscle groups supporting articulation and phonation (Bleasel, Comair, & Luders, 1996; Bogousslavsky & Regli, 1990; Pai, 1999; Riecker, Wildgruber, Grodd, & Ackermann, 2002; Rostomily et al., 1991; Rouiller et al., 1994; Zentner, Hufnagel, Pechstein, Wolf, & Schramm, 1996). Recovery occurs spontaneously over weeks to months and is characterized by gradual return to fluent speech with little to no paraphasic errors and normal grammar (Damasio & Van Hoesen, 1985; Masdeu et al., 1978; Ziegler et al., 1997). The mechanisms of the associated brain plasticity are incompletely understood, but likely involve cortical reorganization of the speech SMA (see Table 1).

Tumors grow, and induce modifications in local activity and connectivity, and therefore represent a model of brain plasticity (Thiel et al., 2001; Thulborn et al., 1999; Tombari et al., 2004; Vassal et al., 2017). While some infiltrated regions may retain their functionality, others migrate to the tumor periphery or there may be contralateral reorganization (Carey, Abbott, Egan, Bernhardt, & Donnan, 2005; Luft et al., 2004; Tombari et al., 2004; Vassal et al., 2017). Plasticity phenomena have indeed been observed before, during and after surgery, and a temporally trackable reorganization of sensorimotor networks following resection of tumors involving the motor SMA has been demonstrated (Fontaine, Capelle, & Duffau, 2002; Fox et al., 1996; Fried et al., 1991; Indefrey & Levelt, 2004; Kim et al., 2004; You et al., 2005). In contrast, only limited evidence exists to date regarding the functional reorganization in the speech SMA following dominant hemispheric lesions to this cortical region.

Imaging studies suggest that some eloquent dominant hemispheric cortical tissue (such as Wernicke's area or Broca's area) can functionally reorganize by recruiting homologous nondominant, contralateral tissue (Calvert et al., 2000; Carpentier et al., 2001; Karbe, Thiel, Weber-Luxenburger, Herholz, Kessler & Heiss, 1998). A functional magnetic resonance imaging (fMRI) study by Carpentier et al. found more bilateral activation in the speech SMA in patients with epileptogenic

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Table 1
Patient clinical characteristics.

	Patient A	Patient B
Age (in years)	39	35
Sex	Male	Male
Handedness	Right	Right
Tumor type	Anaplastic astrocytoma NOS	Oligodendroglioma, NOS
Tumor size/location	2.0 × 3.0 cm mass, left frontal lobe	2.5 × 3.5 cm mass, left parasagittal frontal lobe
Midline shift	None	None
Preoperative speech	Normal	Mild word finding difficulties
Postoperative speech	Mute	Hesitance, slowness in speech, poor fluency
Documented speech recovery	Full recovery at 14 months	Full recovery at 18 months
Repeat fMRI mapping	32 months after surgery	64 months after surgery

cm, centimeter; fMRI, functional magnetic resonance imaging.

tissue in the dominant speech SMA when compared to control subjects (Carpentier et al., 2001). In another fMRI study, Krainik et al. found increased language related activation in the nondominant speech SMA, contralateral to tumor locations, suggesting an atypical organization of the speech SMA in the presence of dominant hemispheric lesions (Krainik et al., 2003). However, to date, the extent to which contralateral speech SMA representation of language activity reflects brain plasticity in functional recovery following dominant hemispheric lesions remains unknown.

The objective of this study was to directly identify the functional reorganization of the speech SMA, using fMRI, in patients with medial frontal lobe tumors who exhibited a postoperative SMA syndrome following surgical resection. We investigated this plasticity by assessing the language related speech SMA activity preoperatively and postoperatively, when full recovery of language abilities had been achieved. We also aimed to evaluate with fMRI whether the functional reorganization in speech SMA represented a dynamic shift over time following lesions of this region, by temporally tracking language related speech SMA activity.

2. Methods

2.1. Patients

Following Institutional Review Board (IRB) approval, we performed a retrospective chart and imaging review of two patients with lesions of the language dominant hemispheric frontal lobe. Patient A was a 39-year-old, right handed, Caucasian male with a 2.0 × 3.0 cm anaplastic astrocytoma NOS in the left frontal lobe. Patient B was a 35-year-old, right handed, Japanese-American male with a 3.5 × 2.5 cm oligodendroglioma NOS in the left parasagittal frontal lobe. English was the primary language for both subjects. Tumor resection was carried out without complication in both patients. All preoperative and postoperative neurological assessments were performed both by neurologists and neurosurgeons. Speech functions were assessed clinically with verbal comprehension, spontaneous speech, narrative tasks, verbal fluency, and repetition (Fig. 1).

2.2. Imaging

Preoperative imaging was performed during the week prior to surgery. Postoperative imaging was acquired 32 months following neurosurgical tumor resection for Patient A and 64 months following surgery for Patient B. Magnetic resonance (MR) imaging was performed using a 3-Tesla magnet (General Electric Medical Systems [Milwaukee, WI] equipped with EPI from Advanced NMR [Wilmington, MA]). Prior to

acquisition of functional images, a fast spin-echo sequence was used to obtain high-resolution structural maps (TR 5000 msec, TE 18 msec, flip angle 90°, matrix size 256 × 256, field of view 24 × 18 cm, 36 3-mm-thick axial slices with no gap). For functional images, an EPI gradient-echo sequence (TR 2500 msec, TE 45 msec, matrix size 64 × 64; field of view 20 cm) was used to collect 84 functional images over 17 axial slices (4-mm-thick slices with a 1-mm gap). Each language task included three 30-second blocks with 30 s of rest between each activation block, starting and ending with a rest period. Language tasks employed were visual object naming and word list generation (tasks described below). Visual stimuli were presented through MR-compatible goggles, which were fitted over the patients' eyes before the patients were placed in the imaging unit. Binaural auditory stimuli were delivered via MR-compatible headphones. Auditory and visual stimuli were controlled and presented using a Macintosh computer running Mac-Stim software (Apple Computers, Inc., Cupertino, CA).

2.3. fMRI preprocessing and analysis

Data preprocessing and analyses were performed with a single subject approach, as is necessary for precise functional localization for neurosurgical and clinical guidance. Task paradigm models used a categorical approach with boxcar functions consisting of fMRI activation during the speech tasks versus the respective rest periods. The boxcar functions were convolved with a model of the hemodynamic response by using software developed at our center (<http://www.brainmapping.org>) (Cohen, 1997). Following global normalization and smoothing, statistical analyses were performed for each task and each subject individually, using analytic technique previously described (Pouratian, Bookheimer, Rex, Martin, & Toga, 2002). Cortical extractions of each patient's brain were used as a common space for comparing different mapping modalities. Fast spin-echo images of each patient's brain were used to extract cortical surfaces for each patient. Images were corrected for radiofrequency nonuniformity (Pouratian, Bookheimer, & O'Farrell, 2000; Pouratian et al., 2002; Sled, Zijdenbos, & Evans, 1998). A three-dimensional active surface algorithm was used to generate an external cortical surface mesh for each patient. Functional MR imaging activations were aligned with the cortical extractions by aligning the coplanar high-resolution EPI images by rigid body transformations with the fast spin-echo images used to create the cortical extraction. This transformation was done based on the principal of maximizing mutual information. Electrocortical stimulation maps (ESM) were projected onto the cortical extraction by matching sulcal landmarks on the cortical extraction with the photograph of the exposed cortex covered by ESM tags and subsequently warping the image onto the surface. Most important in this process was that ESM sites directly overlapped with fMRI activations to be considered colocalized. Thus, statistical maps of activated regions were overlaid onto coplanar high-resolution anatomical images for each subject (Pouratian et al., 2000, 2002). This utility of this technique to identify critical speech areas has previously been validated and its applicability demonstrated (Pouratian et al., 2002). Due to distortions introduced by mass effect related to tumor and the need to perform analyses in single subject space, standardized coordinates were not assessed as they are not likely to be generalizable.

2.4. Language tasks

Patients performed visual object naming and word generation language tasks while lying inside the MR magnet. Language tasks were performed covertly to minimize motion artifact.

2.5. Visual object naming

The patients were asked to silently name objects presented from the Boston Naming Test, which is a standardized test of object naming of line drawings (Kaplan, Goodglass, & Weintraub, 1983). Visual object

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