### Discordance between functional magnetic resonance imaging during silent speech tasks and intraoperative speech arrest

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*Object.* The goal of this study was to investigate discordance between the location of speech arrest during awake cortical mapping, a common intraoperative indicator of hemispheric dominance, and silent speech functional magnetic resonance (fMR) imaging maps of frontal language function.

*Methods.* Twenty-one cases were reviewed retrospectively. Images of silent speech fMR imaging activation were coregistered to anatomical MR images obtained for neuronavigation. These were compared with the intraoperative cortical photographs and the behavioral results of electrocorticography during awake craniotomy. An fMR imaging control study of three healthy volunteers was then conducted to characterize the differences between silent and vocalized speech fMR imaging protocols used for neurosurgical planning.

*Conclusions.* Results of fMR imaging showed consistent and predominant activation of the inferior frontal gyrus (IFG) during silent speech tasks. During intraoperative mapping, however, 16 patients arrested in the precentral gyrus (PRG), well posterior to the fMR imaging activity. Of those 16, 14 arrested only in the PRG and not in the IFG as silent speech fMR imaging predicted. The control fMR imaging study showed that vocalized speech fMR imaging shifts the location of the fMR imaging prediction to include the motor strip and may be more appropriate for neurosurgical planning.

## KEY WORDS • functional magnetic resonance imaging • awake craniotomy • language mapping • electrocorticography

UNCTIONAL MR imaging is increasingly relied on in presurgical planning for the identification of motor and sensory cortices.<sup>19,32,34</sup> In contrast, the effort to provide a map of language function that is consistent and reliable has proven to be more of a challenge. The reason is multifactorial: language maps may vary significantly with the choice of fMR imaging language paradigm, the type and extent of neurological disease, and the patient's ability to perform the task.<sup>8,28,30</sup> Other sources of variation include MR susceptibility artifacts in the orbitofrontal and temporal areas, statistical analysis method chosen, and patient head motion.<sup>6,10,13,18,23</sup> These sources of variability are compounded by the nature of the BOLD signal itself, making it, at present, impossible to distinguish between fMR imaging signals that are representative of essential as opposed to supportive function. Thus, from the surgeon's perspective, judgments about the risk of tumor resection cannot be solely based on fMR imaging results, particularly in language areas.

Of the sources of variability, head motion during lan-

guage mapping with fMR imaging is of particular significance when mapping neurological patients.<sup>6</sup> A small-tomoderate amount of motion during fMR image acquisition can pepper activation maps with Type I statistical errors (false positives). Head motion may be minimized using fMR imaging paradigms in which the patient responds silently (covertly) rather than aloud (overtly).<sup>37</sup> As a result, in presurgical planning the majority of researchers reported the use fMR imaging language paradigms that are covert rather than overt.<sup>2,9,12,17,29</sup>

The problem with silent speech fMR imaging paradigms for neurosurgical planning is that they may not adequately measure that which the surgeon aims most to preserve. They do not provide a map of the network of brain regions that drive the patient's ability to speak aloud. Silent speech maps might be sufficient if silent and vocalized speech maps varied only with the addition of the motor areas involved in speech production. It has been shown, however, that there are complicated differences between fMR imaging maps of silent and vocalized speech that vary more than the addition or subtraction of the motor areas.<sup>5,14</sup> This fact raises the question of how accurate silent speech fMR imaging maps may be for neurosurgical planning in which the aim is to preserve the patient's language function.

Abbreviations used in this paper: BOLD = blood oxygen leveldependent; fMR = functional magnetic resonance; IFG = inferior frontal gyrus; POG = postcentral gyrus; PRG = precentral gyrus.

TABLE 1 Summary of characteristics in 21 patients undergoing awake craniotomy

Case No.	Handedness	Lesion Location
1	rt	lt frontal
2	rt	lt temporal
3	rt	lt frontal
4	rt	lt temporal
5	rt	lt temporoparietal
6	rt	lt temporoparietal
7	rt	lt temporal
8	rt	lt insular
9	ambidextrous	lt insular
10	rt	lt temporal
11	rt	lt frontal
12	rt	lt frontal
13	rt	lt temporal
14	rt	lt frontal
15	rt	lt frontal
16	rt	lt insular
17	rt	lt frontal
18	rt	lt temporal
19	rt	lt insular
20	rt	lt frontal
21	rt	lt parietal

The current gold standard for language mapping is awake craniotomy with electrocorticography.421 To better understand how accurately silent speech fMR imaging paradigms predict intraoperative findings, we retrospectively analyzed the results of intraoperative language mapping by direct cortical stimulation during awake craniotomies in which preoperative fMR imaging language studies had been performed. We compared sites of induced speech arrest with sites of BOLD signal activation during covert language tasks. We hypothesized that there would be a discordance between localization of the frontal speech areas determined on fMR imaging during a silent speech paradigm and that identified by speech arrest during direct cortical stimulation. To further characterize the discordance, we conducted a separate fMR imaging experiment with healthy controls comparing the distribution of activation in silent as opposed to overt speech paradigms.

#### **Clinical Material and Methods**

#### Case Data

Data were reviewed from 25 consecutive cases of awake craniotomy with frontal language mapping for tumor resection at Memorial Sloan-Kettering Cancer Center between 1999 and 2000. Three cases were excluded from analysis because of insufficient exposure of the inferior frontal region for adequate intraoperative mapping. One case was excluded because the right-sided craniotomy was in the nondominant hemisphere. Patient characteristics for the remaining 21 cases are listed in Table 1. Twenty patients were right-handed and one was ambidextrous as determined using the Edinburgh Handedness Inventory.<sup>22</sup> All patients had lesions in the left hemisphere. Tumor locations were as follows: eight frontal lesions, six temporal, two temporoparietal, one parietal, and four insular. Formal preoperative

neuropsychological testing scores were available in 17 of 21 cases, and preoperative neurological examinations were reviewed in the four remaining cases. Formal testing was repeated postoperatively in those patients who showed a new deficit on neurological examination.

#### Functional Imaging in Patients

Patient files were reviewed retrospectively. All patients underwent presurgical fMR imaging mapping. All patients were recruited and the study was conducted according to institutional review board-approved standards. Patient fMR imaging data were obtained using a standard battery of test paradigms and analysis methods.<sup>12,29,31</sup> Data were acquired on a 1.5-tesla General Electric MR imaging unit. The T<sub>2</sub><sup>\*</sup>weighted images were obtained using a gradient-echo EPI-BOLD pulse sequence that was sensitive to the BOLD response (TR 4000 msec, TE 60 msec, field of view 19 imes19, bandwidth 62.5 Hz, matrix  $128 \times 128$ , 4.5-mm slice thickness, no gap, 21 slices). Slices were aligned to the anterior and posterior commissures. Prior to imaging, a  $T_2^*$ scout image was always inspected for gross magnetic field inhomogeneities. High-resolution T<sub>1</sub>-weighted structural images were then acquired (TR 535 msec, TE minutes, field of view 24, bandwidth 15.63 Hz, matrix  $256 \times 256$ , 3-mm slice thickness, no skip, 60 slices).

Two trials were performed for each block-designed task. Thirty-six images were acquired during each trial. Thirteen images were obtained during an initial baseline epoch while the patient fixated on a cross-hair. Ten images were acquired during task performance and 13 images at the end served as a return to baseline. The first three images were discarded to allow for stabilization of the  $T_2$ -weighted signal. Visual stimuli were back-projected onto a screen at approximately 5 ft from the patient's feet. Patients viewed the visual stimuli through a mirror fixed to the head coil. Whenever necessary, patients were fitted with MR imaging–compatible lenses to correct vision.

A battery of fMR imaging tasks was used in each patient, always including both sensorimotor and language components as previously reported.12 During fMR imaging language mapping, two or three covert language tasks were performed, depending on each patient's enrollment criteria. The language tasks consisted of at least one nonvocalized expressive language paradigm and one passive-receptive language paradigm. The expressive tasks always included covert naming of visually presented objects. Patients were told to name the object to themselves by saying, "This is a. . ." Other tasks consisted of one of the following: silent generation of synonyms to visually presented nouns, cued covert counting (patients were cued to begin and cease counting to themselves), or silent picture naming in another language. During the receptive task, words were presented aurally and patients were instructed to imagine a use for the object.

The rolandic cortex was identified through separate sensory and motor tasks in all cases. During the sensory task, the patient's contralateral hand was stimulated passively. During the motor task, patients were cued to produce sequenced contralateral finger movements. All baseline periods for all of the aforementioned tasks were "resting baselines" and consisted of a cross-hair projected onto the center of the screen.

#### Silent speech fMR imaging and intraoperative speech arrest

#### Functional MR Imaging Data Analysis in Patients

Images were reconstructed using a standard script (Epirecon; General Electric Medical Systems, Milwaukee, WI) and were aligned using the AIR algorithm.<sup>36</sup> All images were aligned to allow for direct comparison between tasks. A spatial gaussian filter of 1.5 mm full width half-maximum was applied; no temporal filtering was used. Statistically significant signal changes were identified by a custom analysis program developed by the personnel at the fMR imaging lab, as previously described.<sup>12,29,31</sup> The voxel-wise average signal intensities were compared between the sets of images in the baseline and activity epochs within a trial by using an unpaired t-statistic. Each task was presented in two separate runs and these were aligned and analyzed separately. Only voxels that had a significant t-score in both runs were included into the functional map. The per-run significance thresholds were set at probability levels less than 0.01, 0.05, and 0.1. No erosion processes or cluster thresholding was used.

#### Navigational Imaging and Coregistration

Functional MR imaging results were coregistered to T<sub>1</sub>weighted high-resolution images by rigid translation/rotation, performed using an automated algorithm (BrainLAB, GmbH, Heimstetten, Germany), and confirmed on visual inspection. The volume of fMR imaging activity in distinct anatomical regions was measured with the navigational workstation. The regions of interest consisted of the postcentral, precentral, and inferior frontal gyri. These regions were delimited on the high-resolution T<sub>1</sub>-weighted images by using the navigational system. The anatomical region within the precentral sulcus dividing the IFG and the PRG was split as evenly as possible to the capacity of the high-resolution matrix ( $128 \times 128$ ). Measurements of fMR imaging activity during silent speech paradigms were then classified as inferior frontal, precentral, and postcentral gyri. Volume of fMR imaging activity was measured in relation to this anatomical segmentation. In 18 cases, a photograph of the craniotomy site was also available so that surface features (veins and sulci) could be segmented on MR images and visually aligned to the intraoperative photograph. To measure the relationship of fMR imaging activation to resection borders, the postoperative  $T_2$ -weighted images were coregistered with preoperative navigational images and fMR imaging results in 17 of 21 cases, as described previously. Postoperative brain shift or contraction of the cavity was accounted for, when possible, by manual adjustment of the alignment.

#### Intraoperative Mapping

All patients underwent intraoperative monitoring during awake cortical stimulation as previously described.<sup>4,21</sup> Epicortical recordings of somatosensory evoked potentials and direct cortical bipolar stimulation were performed at 60 Hz, 1-msec pulse width, 1- to 3-second trains, from 2 to 12 mA, adjusted to stimulation threshold based on motor response. Electroencephalography recordings were monitored through cortical surface electrodes throughout mapping in all cases. In the event afterdischarges were evoked, stimulation was temporarily suspended and the current was typically reduced. Behavioral phenomenon associated with afterdischarges were not counted as focal findings. During surgery patients performed tasks that were the same or similar to those used in the fMR imaging environment except that they were vocalized, whereas the fMR imaging tasks were performed silently. While the patient counted and/or named pictures, the cortex was stimulated with the bipolar stimulator. Speech arrest and speech errors were elicited in all cases. Dysarthria and tongue movement were distinguished from speech arrest. Motor speech disturbances like dysarthria and speech arrest were distinguished from word finding difficulty, paraphasic errors, hesitations, or neologisms. Sterile paper tickets were placed on the cortical surface in areas eliciting a response. In 18 cases, a photograph of the mapped cortex was obtained.

The cortical photographs were used to relate the results of the corticography to the coregistered high-resolution  $T_1$ -weighted image/fMR image. Cortical surface features and sulcal topography were used as landmarks. In 18 cases three-dimensional models were made using the neuronavigational system to aid alignment with surface features visible on the intraoperative photograph. Alignment was validated by comparing the central sulcus identified on intraoperative motor mapping with that predicted by the sensorimotor component of the fMR imaging battery.

#### Healthy Volunteers

A separate experiment was designed to characterize the differences between silent and vocalized speech paradigms and nonspeech-related tongue movement. Three healthy volunteers, two men and one woman, participated. All were determined to be strongly right-handed according to the Edinburgh Handedness Inventory.<sup>22</sup> All patients were recruited and the study was conducted according to institutional review board–approved standards.

#### Functional Imaging in Healthy Volunteers

Data were acquired using the same General Electric MR unit. In control volunteers, the trials were expanded to 136 acquisitions to gain additional statistical power. This longer acquisition period was not used in patients, because it requires sustained attention and head motion control over a much longer period of time.

Two trials were performed for each block-designed run. Each run consisted of six stimulation epochs both preceded and followed by a baseline of equal length during which volunteers fixated on a cross-hair. The stimulation epoch consisted of 10 images, with the initial and final baselines lasting 13 images each. Control volunteer data acquisition procedures were the same as those described in *Functional Magnetic Resonance Imaging Data Analysis in Patients*.

Volunteers performed four different productive speech tasks within a single run. Each run was repeated twice. The tasks consisted of object naming, syllable counting, homonym judgment, and a synonym generation task. This paradigm was performed both silently and aloud on separate runs.

To localize the central sulcus and distinguish its activity from silent and vocalized speech paradigms, volunteers performed cued tongue movement. All task runs for both patients and volunteers were acquired using the same interstimulus interval of 10 images (40 seconds).

Volume of fMR imaging activity during silent speech paradigms in 21 patients					
	Vol of Active Voxels (cm <sup>3</sup> )				
Case No.	IFG	PRG	POG		
1	2.88	0.97	0.62		
2	3.66	0.34	0.58		
3	3.43	0	0		
4	2.56	0.1	0		
5	2.21	0	0		
6	8.36	0.25	5.43		
7	0.083	0.15	1.07		
8	2.86	0	0		
9	1.6	0	0		
10	1.07	0.11	0		
11	3.35	0.47	0.17		
12	4.39	0	0		
13	3.79	0.36	0		
14	3.2	0	0		
15	4.09	0.19	0		
16	6.52	1.89	0		
17	4.84	0	0		
18	5.82	0	0.1		
19	3.65	0	0		
20	3.67	0.4	0		
21	4.08	0.35	0.18		
sum	76.86	5.58	8.15		
mean	3.66	0.26	0.39		
sum w/o outlier			2.72		
mean w/o outlier			0.136		
standard deviation w/o outlier	1.81	0.44	0.29		

TABLE 2

#### Data Analysis in Healthy Volunteers

Data were analyzed using MEDx (http://medx.sensor. com). Data analysis for the healthy volunteers was performed in a uniform fashion as previously described.<sup>12</sup> In addition, MEDx was used for the normal study to perform contrasts between the different tasks. Before being imported into MEDx, images were reconstructed and aligned using the same protocol as that used during fMR imaging in patients. An average anatomical  $T_2^*$ -weighted image was created for registration with both the activation maps and the  $T_1$ -weighted images. Spatial filtering was applied and fMR imaging maps were generated using correlation with a boxcar base function (p < 0.05).

The volume of fMR imaging activity was measured and compared two ways within MEDx. Regions of interest (postcentral, precentral, and inferior frontal gyri) were defined on high-resolution T<sub>1</sub>-weighted images. Volumes of fMR imaging activity were then measured in each region during silent speech, vocalized speech, and tongue movements.

#### Results

#### Patient fMR Imaging

Preoperative silent speech fMR imaging paradigms yielded BOLD activity in frontal speech areas in all 21 patients. The mean volume of fMR imaging activity in the IFG during silent speech paradigms was 3.66 cm<sup>3</sup>, compared with 0.26 cm<sup>3</sup> in the PRG and 0.39 cm<sup>3</sup> in the POG (Table 2). In all cases, the patient's fMR imaging results predicted speech localization predominantly in the IFG

#### speech arrest



SSEP reversal

tongue movement

FIG. 1. *Left:* Representative fMR imaging data were coregistered and displayed on a surface rendering. Pink represents fMR imaging activity; green, the central sulcus (determined by somatosensory fMR imaging); and purple, the cortical veins segmented for alignment landmarks. Compare the surface rendering with the intraoperative photograph. *Right:* Numbers on the cortex correspond to the yellow markers on the rendering. Numbers 3 and 4 are represented by a single point on the rendering. The most prominent locations of speech arrest and speech errors (in this case) are located posterior to the fMR imaging–predicted location of the Broca area. In this particular case, somatosensory evoked potential (SSEP) reversal was found on the posterior border of the POG.

Summary of patients with fMR imaging activation or speech arrest*				
		No. of Patients†		
	PRG	PRS	IFG	
fMR imaging speech arrest	6 (0) 16 (14)	12 (0) NA	15 (3) 4 (2)	

TADLES

\* NA = not applicable; PRS = precentral sulcus.

<sup>†</sup> Parenthetical numbers represent those patients demonstrating activation or arrest exclusively in that area.

and did not assign a role for language to the PRG. Note that the mean volume of activity in the POG for the patient in Case 6 during silent speech was an outlier and affected the mean. Excluding this value, the relative comparison of means changes to 3.66, 0.26, and 0.18 cm<sup>3</sup> in the inferior, precentral, and postcentral gyri, respectively.

#### Direct Cortical Stimulation in Patients

The PRG was identified intraoperatively by eliciting motor hand flexion/extension and or facial muscle fasiculations with bipolar cortical stimulation. The central sulcus defined in this manner matched the fMR imaging-predicted location of the central sulcus in all surgical cases. At least one frontal site of reproducible speech arrest and/or error was identified in all 21 left-hemisphere craniotomies. Speech arrest during direct cortical stimulation, distinct from dysarthria, occurred most often in the motor strip just posterior to the site in the IFG of maximal activation during silent speech fMR imaging. Figure 1 demonstrates a representative case. Most patients exhibited speech arrest in the PRG (16 patients). Fewer patients did so in the IFG (four patients) or both gyri (two patients). Of the 16 who arrested in the PRG, 14 did so only in the PRG and not in the IFG as silent speech fMR imaging results would have predicted (Table 3). Additionally, during stimulation of the PRG, two patients experienced speech errors including word-finding difficulty and phonemic or semantic paraphasic errors. The facts that silent speech fMR imaging generally did not predict speech localization in the motor strip and that direct cortical stimulation did in all cases can be regarded as a systematic false-negative result in the silent speech fMR imaging measurement.

### Correlation of Resection Volume, fMR Imaging Activation, and Language Deficit

We compared the postoperative MR images with preoperative fMR images in 17 of 21 patients. In only three cases was a region of fMR imaging activation included in the resection volume; all three involved temporal resections and the sites were found to be silent during cortical mapping. In two cases there was no change in language function, and in the third there was mild dysfunction consisting of word finding difficulty, which persisted 5 months after surgery. In 12 other cases, resection volume did not include areas of positive fMR imaging activation. In these cases, we measured the distance from the resection volume to the nearest fMR imaging activation spot; the median distance was 12 mm, and in only two patients was the distance less than 10



FIG. 2. Functional MR images demonstrating the pattern of activity in three control volunteers performing a speech task silently and aloud, compared with nonspeech tongue movement. Results are displayed at a probability level of 0.05. *Blue arrow* denotes the central sulcus. Silent speech predominantly activates the IFG, vocalized paradigms activate a mixture of inferior frontal and precentral gyri, and tongue movement mainly activates pre- and postcentral gyri.

mm. In both of these latter cases there was a postoperative decrement in language function, whereas a decrement did not occur in the 10 cases in which the distance was greater than 10 mm. Both patients were evaluated pre- and postoperatively through formal neuropsychological testing whose results verified the new deficits.

The patient in Case 9 (Table 1) underwent partial resection of a large insular low-grade glioma, which included the temporal tip (< 4 cm) and frontal operculum. Functional MR imaging activation was seen within 9 mm of the resection boundary. Results of formal postoperative neuropsychological testing revealed a significant decline on the Boston Naming performance, from 59/60 to 50/60, and a mild nonspecific decline in most other cognitive domains including fluency and attention. In the patient in Case 17, anaplastic oligodendroglioma was resected from the middle frontal gyrus to within 3 mm of an fMR imaging activation site in the supplementary motor area. Postoperatively, the patient showed a dense transcortical motor aphasia, which improved gradually over 6 months.

#### Results of fMR Imaging in Healthy Volunteers

Covert language mapping in healthy volunteers showed a distribution of fMR imaging activity similar to that in patients (Fig. 2). When the controls performed the language tasks silently, a preponderance of the fMR imaging activity at a probability level of 0.05 occurred in the IFG. In contrast, two of three contols showed an increase in the volume of the BOLD activation in the IFG during vocalized speech. There was also a substantial increase in the motor strip during vocalized speech in all controls.

TABLE 4 Volume of fMR imaging activity during speech tasks and tongue movement in three control volunteers

	Vol of Active Voxels (cm <sup>3</sup> )		
Task	IFG	PRG	POG
silent speech			
Control 1	4.88	0.68	0.039
Control 2	4.08	0.719	0
Control 3	5.04	2.05	2
mean	4.67	1.15	0.68
vocalized speech			
Control 1	5.81	7.45	2.78
Control 2	3.72	9.68	2.25
Control 3	6.3	9.33	6.85
mean	5.28	8.82	3.96
tongue movement			
Control 1	2.85	6.33	4.27
Control 2	3.25	8.42	6.35
Control 3	1.14	7.45	6.54
mean	2.41	7.4	5.72

The volume of fMR imaging activation in the IFG during silent speech tasks at a probability level of 0.05 in controls was 4.88, 4.08, and 5.04 cm<sup>3</sup>, respectively (Table 4). During vocalized speech, the activity was 5.81, 3.72, and 6.3 cm<sup>3</sup>. This increased volume of fMR imaging activation for vocalized over silent speech is consistent with other studies.14 Functional MR imaging activity in the motor strip during silent speech paradigms in Controls 1, 2, and 3 was 0.68, 0.719, and 2.05 cm<sup>3</sup>, respectively, at a probability level of 0.05. Nevertheless, the fMR imaging signal in the motor strip increased to 7.45, 9.68, and 9.33 cm<sup>3</sup>, respectively, during vocalized speech.

#### Discussion

Our results are consistent with the hypothesis that silent speech paradigms does not activate the PRG as robustly as vocalized fMR imaging speech paradigms and might not be the most accurate measure of a patient's entire speech network. We chose to focus on the intraoperative finding of speech arrest because it is the most salient form of language disruption during awake language mapping. In the case of frontal speech mapping, intraoperative speech arrest routinely occurred posterior and across the precentral sulcus to the silent speech fMR imaging prediction. We found that silent speech paradigms preferentially activated the dominant IFG. In contrast, the distribution of fMR imaging activity in the frontal lobe during a vocalized speech paradigm shifts posteriorly to include the PRG. Our results support the idea that silent speech fMR imaging, while reliably activating the frontal speech areas, does not activate the entire speech production system. It is important that this caveat of silent speech paradigms be kept in mind by the operating neurosurgeon while attempting a resection adjacent to the expected location of the frontal language area.

The role of the motor strip in speech production and linguistic processing is yet unresolved.<sup>15,25,26</sup> In our study, most patients who arrested in the PRG did so only in the PRG and not in the IFG as predicted by the silent speech fMR imaging results. Two patients also experienced linguistic errors

in the PRG, further supporting the role of the PRG in lan-

guage processing. Wilson, et al.,<sup>35</sup> used fMR imaging to map the response in the motor strip during listening to nonspeech sounds, speech sounds, and the vocalization of phonemes. Results from this study indicate that the motor strip is involved in the articulatory representation of acoustic input. This finding is in accord with data on mirror neurons in the motor strip that may aid in motor learning and imitation.<sup>27</sup> Although our silent speech maps did yield some minimal motor strip activity as well, it is clear that vocalized speech fMR imaging and symmetry of testing modalities in the operating room may aid the effort to study the linguistic role of the motor strip.

From the surgeon's perspective, fMR imaging maps should either resolve an anatomical ambiguity, such as the location of the central sulcus, or they should make a predictive claim about the results of lesioning in an area. Functional magnetic resonance imaging is well suited to make claims about how well a region is connected to a network that is driven during task performance.7,24 The BOLD signal is more representative of synaptic input than neuronal output and as such has been used for characterization of language networks.<sup>3,11,16</sup> Nevertheless, it may be less wellsuited to answer the question of whether an area is safe to resect. To this end, it is necessary to correlate the results of cortical stimulation and postoperative deficits with the fMR imaging prediction. Although fMR imaging activation during nonvocalized speech tasks has been reported to be predictive of regions of language disruption during awake cortical mapping,<sup>21,28,29</sup> there remains discordance and variability that may in part be explained by the mismatch in behavioral testing. In the present study we attempted to characterize a portion of that variability by showing that silent speech paradigms predict speech localization at a more anterior location than intraoperative speech arrest reveals.

The overwhelming proportion of the fMR imaging neurosurgical planning literature is based on silent speech paradigms.<sup>9,12,17,29,33</sup> Therefore, it might be tempting to assume that the difference between silent and vocalized speech is both predictable and inconsequential in practice, as the fMR imaging maps should vary only with the addition of the motor areas. The assumption that vocalized speech activates the combined domains of silent speech and vocalization may be an oversimplification. Using positron emission tomography, Bookheimer, et al.,<sup>5</sup> found differences between silent and overt speech that did not adhere to this simple hierarchical relationship. Huang, et al.,14 in developing a method of extracting motion-induced artifacts, found that significantly greater tissue volume within the Broca area is activated through overt compared with silent speech paradigms in a letter-naming task. Significantly, these authors also found differences in the magnitude and spatial extent of the BOLD signal in different overt language tasks. Thus, not only have silent speech maps been shown to differ significantly from vocalized speech maps, there exists further complexity under the umbrella of vocalized speech that may be subdivided into task-related differences.

Silent speech paradigms have dominated the field in an attempt to circumvent the artifact inherent in overt speech fMR imaging. This limitation is increasingly disappearing. Recent data acquisition protocols have made it possible to decrease these artifacts and make overt language paradigms

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competitive with silent paradigms. One such protocol takes advantage of the temporal separation between the motion induced by speaking and the delayed hemodynamic response.<sup>14</sup> Others have developed compressed image acquisition protocols in which components of the pulse sequence itself pause to allow for overt responses during a silent scanning period.1 Nelles, et al.,20 developed a spectral subtraction method that removes MR gradient acoustic noise, thus allowing for better intelligibility of overt responses. This technique allows the investigator to record behavioral responses without having to alter the acquisition parameters. Together, these techniques appear to be poised to allow for the use of vocalized speech paradigms and will close the behavioral gap between brain mapping techniques and may reveal more concordant results in cognitive analysis across testing modalities.

#### Conclusions

Data in the present study demonstrate a systematic difference between the pattern of fMR imaging activation for silent speech paradigms and the results obtained in testing for speech arrest during intraoperative cortical mapping. This discordance may in part be explained by the inherent difference in testing modalities: fMR imaging reveals areas associated with the generation of silent speech, whereas intraoperative cortical stimulation detects areas of the brain in which vocalized speech is interrupted by cortical stimulation. Using vocalized speech during the fMR imaging session may aid in closing part of this gap by having symmetry of testing modalities. It is imperative for the operating neurosurgeon to recognize this discrepancy when interpreting silent speech fMR imaging activation in the vicinity of the frontal language center.

#### References

- Abrahams S, Goldstein LH, Simmons A, Brammer MJ, Williams SC, Giampietro VP, et al: Functional magnetic resonance imaging of verbal fluency and confrontation naming using compressed image acquisition to permit overt responses. Hum Brain Mapp 20: 29–40, 2003
- Baciu MV, Rubin C, Decorps MA, Segebarth CM: fMRI assessment of hemispheric language dominance using a simple inner speech paradigm. NMR Biomed 12:293–298, 1999
- Baciu MV, Watson JM, McDermott KB, Wetzel RD, Attarian H, Moran CJ, et al: Functional MRI reveals an interhemispheric dissociation of frontal and temporal language regions in a patient with focal epilepsy Epilepsy Behav 4:776–780, 2003
- Berger MS, Ojemann GA: Intraoperative brain mapping techniques in neuro-oncology. Stereotact Funct Neurosurg 58: 153–161, 1992
- Bookheimer SY, Zeffiro TA, Blaxton T, Gaillard W, Theodore W: Regional cerebral blood flow during object naming and word reading. Hum Brain Mapp 3:93–106, 1995
- Bullmore ET, Brammer MJ, Rabe-Hesketh S, Curtis VA, Morris RG, Williams SC, et al: Methods for diagnosis and treatment of stimulus-correlated motion in generic brain activation studies using fMRI. Hum Brain Mapp 7:38–48, 1999
- 7. Cohen L, Dehaene S: Specialization within the ventral stream: the case for the visual word form area. **Neuroimage 22:**466–476, 2004

- Fernandez G, Specht K, Weis S, Tendolkar I, Reuber M, Fell J, et al: Intrasubject reproducibility of presurgical language lateralization and mapping using fMRI. Neurology 60:969–975, 2003
- FitzGerald DB, Cosgrove GR, Ronner S, Jiang H, Buchbinder BR, Belliveau JW, et al: Location of language in the cortex: a comparison between functional MR imaging and electrocortical stimulation. AJNR 18:1529–1539, 1997
- Hajnal JV, Myers R, Oatridge A, Schwieso JE, Young IR, Bydder GM: Artifacts due to stimulus correlated motion in functional imaging of the brain Magn Reson Med 31:283–291, 1994
- Heim S, Opitz B, Friederici AD: Distributed cortical networks for syntax processing: Broca's area as the common denominator. Brain Lang 85:402–408, 2003
- Hirsch J, Ruge MI, Kim KH, Correa DD, Victor JD, Relkin NR, et al: An integrated functional magnetic resonance imaging procedure for preoperative mapping of cortical areas associated with tactile, motor, language, and visual functions. Neurosurgery 47: 711–722, 2000
- Holodny AI, Schulder M, Liu WC, Wolko J, Maldjian JA, Kalnin AJ: The effect of brain tumors on BOLD functional MR imaging activation in the adjacent motor cortex: implications for imageguided neurosurgery. AJNR 21:1415–1422, 2000
- Huang J, Carr TH, Cao Y: Comparing cortical activations for silent and overt speech using event-related fMRI. Hum Brain Mapp 15:39–53, 2002
- Larner AJ, Robinson G, Kartsounis LD, Rakshi JS, Muqit MM, Wise RJ, et al: Clinical-anatomical correlation in a selective speech production impairment. J Neurol Sci 219:23–29, 2004
- Li P, Jin Z, Tan LH: Neural representations of nouns and verbs in Chinese: an fMRI study. Neuroimage 21:1533–1541, 2004
- Liegeois F, Connelly A, Cross JH, Boyd SG, Gadian DG, Vargha-Khadem F, et al: Language reorganization in children with earlyonset lesions of the left hemisphere: an fMRI study. Brain 127: 1229–1236, 2004
- McGonigle DJ, Howseman AM, Athwal BS, Friston KJ, Frackowiak RS, Holmes AP: Variability in fMRI: an examination of intersession differences. Neuroimage 11:708–734, 2000
- Moritz C, Haughton V: Functional MR imaging: paradigms for clinical preoperative mapping. Magn Reson Imaging Clin N Am 11:529–542, 2003
- Nelles JL, Lugar HM, Coalson RS, Miezin FM, Petersen SE, Schlaggar BL: Automated method for extracting response latencies of subject vocalizations in event-related fMRI experiments. Neuroimage 20:1865–1871, 2003
- Ojemann GA: Functional mapping of cortical language areas in adults. Intraoperative approaches. Adv Neurol 63:155–163, 1993
- Oldfield RC: The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 9:97–113, 1971
- Price CJ, Friston KJ: Scanning patients with tasks they can perform. Hum Brain Mapp 8:102–108, 1999
- Price CJ, Winterburn D, Giraud AL, Moore CJ, Noppeney U: Cortical localisation of the visual and auditory word form areas: a reconsideration of the evidence. Brain Lang 86:272–286, 2003
- Quinones-Hinojosa A, Ojemann SG, Sanai N, Dillon WP, Berger MS: Preoperative correlation of intraoperative cortical mapping with magnetic resonance imaging landmarks to predict localization of the Broca area. J Neurosurg 99:311–318, 2003
- 26. Riecker A, Ackermann H, Wildgruber D, Meyer J, Dogil G, Haider H, et al: Articulatory/phonetic sequencing at the level of the anterior perisylvian cortex: a functional magnetic resonance imaging (fMRI) study. Brain Lang 75:259–276, 2000
- Rizzolatti G, Craighero L: The mirror-neuron system. Annu Rev Neurosci 27:169–192, 2004
- Roux FE, Boulanouar K, Lotterie JA, Mejdoubi M, LeSage JP, Berry I: Language functional magnetic resonance imaging in preoperative assessment of language areas: correlation with direct cortical stimulation. Neurosurgery 52:1335–1347, 2003
- 29. Ruge MI, Victor J, Hosain S, Correa DD, Relkin NR, Tabar V, et al: Concordance between functional magnetic resonance imaging

and intraoperative language mapping. Stereotact Funct Neurosurg 72:95–102, 1999

- Rutten GJ, Ramsey NF, van Rijen PC, van Veelen CW: Reproducibility of fMRI-determined language lateralization in individual subjects. Brain Lang 80:421–437, 2002
- Souweidane MM, Kim KH, McDowall R, Ruge MI, Lis E, Krol G, et al: Brain mapping in sedated infants and young children with passive-functional magnetic resonance imaging. Pediatr Neurosurg 30:86–92, 1999
- Vlieger EJ, Majoie CB, Leenstra S, Den Heeten GJ: Functional magnetic resonance imaging for neurosurgical planning in neurooncology. Eur Radiol 14:1143–1153, 2004
- Wildgruber D, Ackermann H, Klose U, Kardatzki B, Grodd W: Functional lateralization of speech production at primary motor cortex: a fMRI study. Neuroreport 7:2791–2795, 1996
- Wilkinson ID, Romanowski CA, Jellinek DA, Morris J, Griffiths PD: Motor functional MRI for pre-operative and intraoperative neurosurgical guidance. Br J Radiol 76:98–103, 2003
- 35. Wilson SM, Saygin AP, Sereno MI, Iacoboni M: Listening to

speech activates motor areas involved in speech production. Nat Neurosci 7:701–702, 2004

- Woods RP, Grafton ST, Holmes CJ, Cherry SR, Mazziotta JC: Automated image registration: I. General methods and intrasubject, intramodality validation. J Comput Assist Tomogr 22: 139–152, 1998
- Yetkin FZ, Hammeke TA, Swanson SJ, Morris GL, Mueller WM, McAuliffe TL, et al: A comparison of functional MR activation patterns during silent and audible language tasks. AJNR 16: 1087–1092, 1995

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