

The Reliability of Presurgical fMRI Language Lateralization in Patients with Primary Brain Tumors and Prior Surgery

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Introduction

The Intracarotid Amobarbital Procedure (IAP) also known as the WADA test is currently the gold standard for establishing hemispheric dominance for language (1). However, due to its invasive nature, it is hoped that functional magnetic resonance imaging (fMRI), a non-invasive, repeatable imaging method, will replace the WADA test. While fMRI has been shown to lateralize language reliably in healthy subjects (2), more needs to be known about the reliability of the fMRI result in patients with pathologic conditions including tumors. Our group has recently shown that previous surgery can affect the sensitivity of the fMRI map within the motor cortex in tumor patients (3). However, due to the nature of the hemispheric laterality measurement, it may be less susceptible to interference from localized surgical artifact including the presence of titanium plates to secure skull flaps, metallic staples to close surgical incisions, hemorrhage from surgery. We investigated data obtained from glioma patients with and without prior surgery and characterize the effects of such on the laterality index (LI). Our results were, when available, compared with the results of intraoperative electrocortical mapping during surgery. We hypothesized that the effects of the tumor and of the surgical artifact would not be sufficient to affect the overall hemispheric measurement of language laterality.

Subjects and Functional Tasks

21 brain tumor patients (14 patients with prior surgery, ranging in age from 29 to 69 years, and 7 patients without prior surgery, ranging in age from 43 to 66 years) with a glioma in the left hemisphere were included in this study. All patients were right handed native speakers of English. The patients were asked to perform two different language tasks including phonemic fluency and verb generation. In verb generation, patients were presented with a noun and asked to silently generate action word associated with the noun. For the phonemic fluency task, a letter appeared on the screen, and patients were asked to silently generate words that began with that letter. The baseline was a resting state and consisted of a fixation on a cross-hair. The paradigm was presented as a block paradigm, consisting of 60 images with 5 images of paradigm execution alternating with 5 images of rest.

Method and data Analysis

T1-weighted images (21 contiguous axial slices) were acquired for the anatomical images. Functional images were acquired with a gradient echo EPI sequence (TR/TE=4000/40 ms; 128x128 matrix; 240 mm FOV; Thickness=4.5 mm) using 1.5T GE scanner. 3D T1-weighted anatomical images were acquired with a spoiled GRASS sequence. Images were processed and analyzed using AFNI software (4). The map used for the calculation of the LI was the result of a combined task analysis in order to isolate the essential language cortex (5). 3D motion correction and spatial smoothing (4mm) were applied. Functional activity was generated using cross-correlation. Region of interest (ROI) was defined based on the T1-weighted or T2 weighted anatomical images. The ROIs were both hemispheric and Broca's area in both hemispheres. The number of activated voxels included in each ROI was determined. LI were calculated in each ROI using the formula: $LI = (L+R)/(L-R)$. Activation volume in the left and right side was defined as L and R. The output was compared for patients with and without prior surgery. Consequently, LI ranged from -1 (lateralized to the right) to +1 (lateralized to the left). Subjects were defined as having bilateral language representation if the LI ranged from -0.2 ~ 0.2 (2).

Results

Activation map shows language areas including inferior frontal gyrus (Broca's area), superior temporal gyrus, middle frontal gyrus, supplementary motor cortex of both groups. Figure 2a and 2b shows scatter plots for LI for both groups. Using a chi-squared test with 2 degrees of freedom, we found no differences in LI based on whether or not a patient had a prior surgery ($p=0.93$ using hemispheric ROI (Figure 2a) and $p=0.41$ using Broca's area ROI (Figure 2b)). Additionally, when looking at the ratio in a continuous fashion, we tested to see whether the median of the surgery group was higher than the median of the non surgery group using a Wilcoxon two sample test. For Broca's area ROIs, the median ratio for the surgery group was 0.59, while the median ratio for the non surgery group was 0.31. However, this difference was not statistically significant ($p=0.76$). For hemispheric ROIs, the median for the surgery group was 0.40 and the median for the non surgery group was 0.32, again not significant $p=0.23$. The language lateralization of 11 patients who underwent intraoperative electrocortical mapping was 100% concordant with fMRI prediction.

Discussion

We contribute evidence toward the goal of replacing the invasive WADA test with fMRI for the purpose of hemispheric language dominance. Despite the presence of tumor and artifact from previous surgery (Figure 1), the effects of tumor and surgical MR artifact were not sufficient to affect the overall hemispheric measurement of LI and fMRI revealed the expected left hemispheric dominance from both groups. It is reasonable to expect that patients with a prior surgery could demonstrate a decrease in the BOLD signal and a subsequent incorrect estimation of the LI, but the determination of left hemispheric language dominance was not affected. Additionally, in those cases where surgical artifact and/or de-coupling may have slightly affected the LI (but not enough to change the determination of left-dominant) using a Broca's Area ROI further clarified the hemispheric dominance. Direct cortical stimulation also supported the above results. 3 of 21 subjects (using hemispheric ROI) and 4 of 21 subjects (using Broca's ROI) showed language dominant in the right hemisphere and this might reflect real compensatory language processes or may be a result of tumor induced de-coupling in the left hemisphere, but to confirm this, other methods like TMS (transcranial magnetic stimulation) are required.

References

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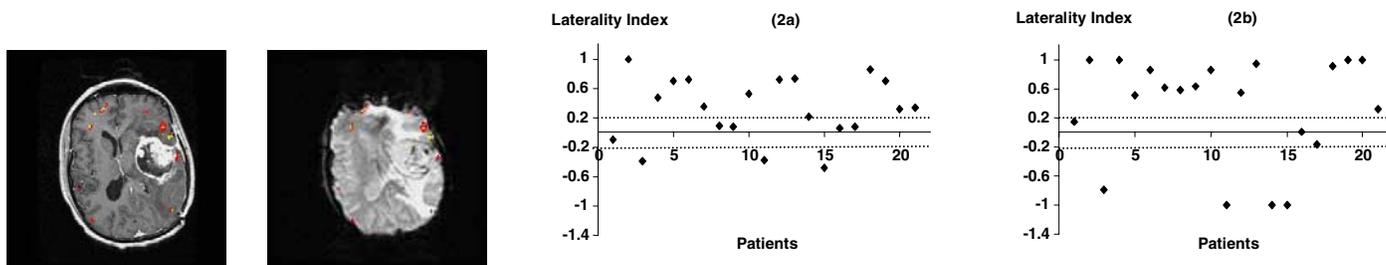


Figure 1. fMRI scan of a GBM patient with a prior surgery (T1(left) and T2* (right) images)

Figure 2a and 2b. Scatterplot of language LI obtained using hemispheric ROIs (2a) and Broca's area ROIs (2b) in 21 patients (1-14: patients with prior surgery, 15-21: patients with no prior surgery). A range (dot line) for bilateral lateralization is shown between -0.2 ~ +0.2.