Effectiveness of four different clinical language paradigms for language lateralization: a ROI analysis

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Introduction: Presurgical mapping of patients with tumors affecting eloquent language cortex aims to determine not only the eloquent areas at risk of being resected during the lesion resection, but also the hemispheric language dominance, because these factors can influence the extent or even the feasibility of resection (in cases of dominant hemispheric lesions). fMRI has essentially replaced the invasive gold standard intracarotid sodium amobarbital (Wada) test for preoperative determination of language lateralization, primarily due to extensive validation across multiple studies that have consistently demonstrated concordance of lateralization between the two methods ranging from 71-100% (1-3). However the choice of the paradigm performed by a patient for language mapping as well as the region of interest (ROI) where the lateralization index (LI) is calculated has been demonstrated to affect the hemispheric dominance determination. In this paper we present the results of a retrospective study in a series of brain tumor patients referred for presurgical language mapping in order to compare the effectiveness of lateralization of different expressive, receptive and semantic clinically used fMRI paradigms in anatomically and functionally defined language ROIs.

Materials and Methods: 41 right handed patients with brain tumors were included in the study approved by our Institutional Review Board. Patients were imaged at 3.0T on a Siemens Trio MRI system. For BOLD fMRI axial slices were acquired using T2* EPI sequence (33 slices, 4 mm thick with 1-mm gap between slices). In-plane spatial resolution was 3.75×3.75 mm^2; TR=2000 ms; TE=30 ms. A volumetric T1-weighted MPRAGE acquisition was acquired and used as high-resolution anatomic reference frame (matrix=256×256) for overlay of functional activation maps. Prism Acquire system was used for fMRI paradigm presentation. Four block design paradigms-- rhymimg (R), silent word generation (SWG), sentence completion (SC) and listening comprehension (LC)-- were included for the purposes of this study from a battery of clinically used language mapping tasks. Images were processed and analyzed by using Analysis of Functional NeuroImages (AFNI) software. For each task activation maps (t-score) were generated using General Linear Model (GLM) analysis. Dual rater ROI analysis was performed for LI calculation. Two functional and two anatomical ROIs were manually drawn for each paradigm per patient. The functional ROIs were defined for each paradigm by the activation cluster which most closely approximated the position of Broca's area (BA) and Wernicke's area (WA) [Figure 1]. Anatomical ROIs were then defined by the boundaries segmenting the frontal lobe as one volume and then the temporal and parietal lobes as the second, using the central sulcus as the posterior margin of the frontal ROI in an effort to encompass expressive and receptive activation clusters based on anatomy rather than activation centers [Figure 2]. Contralateral ROIs were also defined both for the functional and anatomical ROIs. A threshold-independent lateralization index (LI) was determined in each ROI for each paradigm (4). An ANOVA test with specific post hoc test was performed using SPSS software in each ROI for 4 different groups (the paradigms) to determine significant differences among the paradigms to express language lateralization including multiple factors (tumor grade, tumor lobar location and hemisphere). Statistical significance was considered at $p<0.05$ level.

Figure 1

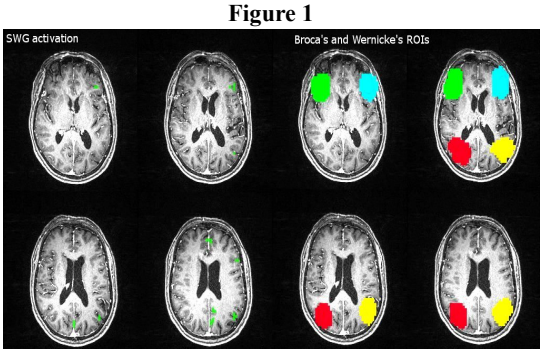
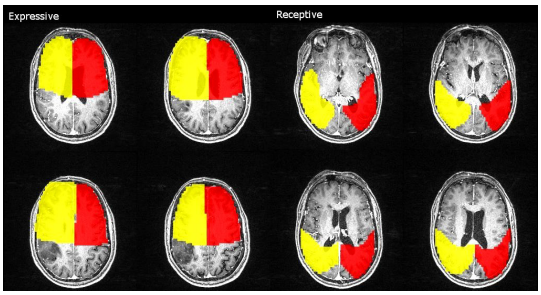


Figure 2



Results: Intraclass Correlation Coefficient was very good (82%) and mean values among the two raters were used in the ANOVA. A main effect was found for the paradigms ($p<0.04$) in BA with significantly higher LI value for SWG (0.36439±0.247377) compared to LC (0.15980±0.242726), p=0.009, and for R (0.39985±0.219774) compared to LC (0.15980±0.242726), p=0.001. No main effect was found for any of the factor included in the ANOVA or significant interaction among them. In the WA ROI the analysis did not reveal any main or interaction effect. A main paradigm effect was present in the expressive ROI ($p<0.04$) with SWG LI (0.28343±0.187000) higher than LC LI (0.12007±0.159014), p=0.01. In this ROI the analysis reported also a main effect on tumor grade; specifically LI in low grade tumors (0.270±0.187) was significantly higher than LI in high grade tumors (0.147±0.161), p=0 .001.

Comparison of the two populations at a single paradigm level demonstrated higher LI for SWG in low grade lesions (0.353±0.165) compared to high grade (0.201±0.182), p=0.01 as well as higher LI for R in low grade lesions (0.257±0.128) compared to high grade lesions (0.148±0.151), p=0.02. No interaction effects were present among the ANOVA factors except for a trend in the interaction lobe grade (p=0.055). A main effect for the paradigms was present in the receptive ROI (p=0.03) but post-hoc tests did not reveal any significant pair effect difference. No other main or interaction effects were found for the remaining factors.

Discussion and Conclusions: The results of this study demonstrate that expressive paradigms, such as SWG and R, are optimal lateralizing tasks in the expressive ROIs and this confirms the findings of previous studies in which a holohemispheric approach was used (5). Receptive and semantic tasks do not perform better than SWG and R for lateralization in receptive ROIs such as WA. Therefore new paradigms need to be designed for improved determination of lateralization in language receptive areas.

References:

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