Reliability of Language Paradigms in fMRI for Pre-operative Mapping

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Introduction: BOLD functional MRI (fMRI) has demonstrated usefulness in presurgical planning of tumor resection and for epilepsy surgery. The goal in these cases is to map important functional cortex (e.g. motor, language and memory) in the area of the resection to minimize postoperative deficits. The extant clinical standards, the Wada test and electro cortical mapping are invasive and not without significant limitations. Despite several groups and much published data demonstrating the utility of fMRI in presurgical mapping, the methods remain unstandardized and are not yet reimbursable by insurance. With the Wada test, which lateralizes language, being gradually phased out, the opportunity exists for fMRI to play an increasingly larger role in presurgical mapping. To become a clinically valid method, fMRI needs to demonstrate reliability of lateralization and sensitivity and specificity for localization. FMRI will never attain the degree of specificity of deficit-based methods (i.e., Wada and ECM) which simulate cortical ablation, since fMRI reveals brain regions involved in but not necessarily indispensable to a function. The aim of this paper is to provide evidence for the reliability of some of the language paradigms through analysis of fMRI data from a group of pre-surgical patients and comparing it with individual brains that have contributed to the group. These components include reading words, syntactic, semantic and phonological processing and in combination are predicted to activate the entirety of the perisylvian language network. The ability to activate the entire perisylvian language network with a set of paradigms is important, since brain lesions can and do occur anywhere within the brain parenchyma. Therefore, matching the target brain area with language tasks is vital.

Methods: We report results from 4 female right-handed patients (3 epileptics and 1 tumor). All MRI scanning was performed on a Siemens Sonata 1.5T scanner. Structural images included T1, T2 and FLAIR scans and were coplanar with gradient echo EPI functional scans. Functional imaging used a 64x64x27 matrix (TR=2 s, FOV=256*256 mm^2, 3.75*3.75*5 mm^3) with blocked paradigms lasting 4-7 minutes. A head mold was used to limit head motion and to increase comfort and video goggles and earmuff headphones were used to convey the stimuli (Resonance Technology, Inc.) The paradigms used included visual tasks--1) Verb generation to noun vs. fixation; 2) Object naming vs. nonsense objects; 3) Sentence generation vs. consonant strings. Patients gave only covert responses so as to minimize motion and susceptibility artifacts. Image processing used SPM2 (Wellcome Department of Cognitive Neurology) and MEDx (Medical Numerics Inc.). Images were motion corrected, smoothed with a Gaussian (6 mm in-plane only) and detrended before statistical parametric maps were created using regression of time series data with a square wave convolved with a hemodynamic response function of 4.8 sec delay and 1.8 sec dispersion. The functional maps obtained were all spatially normalized to standard MNI space of 2*2*4 mm using the EPI image. Maps were then averaged across patients by paradigm.

Results: Regions of interest were extracted from group-averaged (N=4) t-maps using a voxel-wise Z-threshold of 3.5 and 3-D masks created from clusters were used to interrogate individual patient t-maps. The number of suprathreshold voxels in each cluster ($Z \geq 3.5$) from each patient and task paradigm was assessed. A percentage score of individual suprathreshold voxel count relative to the total cluster voxel count was used to indicate inter-individual variability of activation for a given ROI.

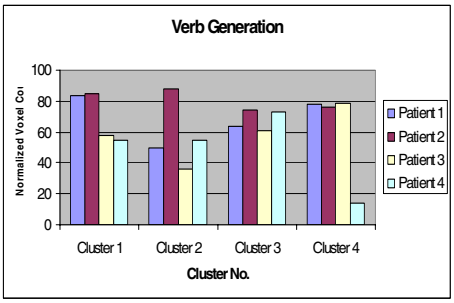

Fig I. Normalized Suprathreshold Voxel count plotted for each cluster on each patient for Verb Generation paradigm.
Cluster 1 - Right Extrastriate
Cluster 2 - Left Temporal
Cluster 3 - Left Frontal+Ant. Cingulate
Cluster 4 - Right Frontal

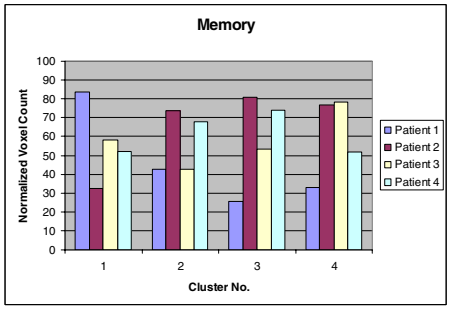

Fig II. Normalized Suprathreshold Voxel count plotted for each cluster on each patient for Memory paradigm.
Cluster 1 - Right Extrastriate
Cluster 2 - Left Temporal
Cluster 3 - Left Frontal
Cluster 4 - Anterior Cingulate

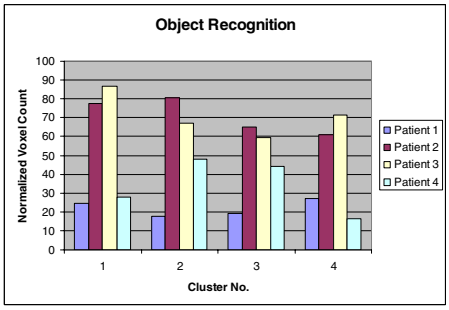

Fig III. Normalized Suprathreshold Voxel count plotted for each cluster on each patient for Object Recognition paradigm.
Cluster 1 - Right Extrastriate
Cluster 2 - Left Extrastriate
Cluster 3 - Left Frontal
Cluster 4 - Anterior Cingulate

Discussion & Conclusion: There were 4 distinct clusters each in verb generation, memory and object naming paradigms, which showed high inter-individual variability for activated volume. Only the left frontal and a small left temporal region constituted regions within classical language cortex. Verb generation clusters ranged from 14-88% of total volume with the left frontal cluster being least variable (61-75%) and left temporal with moderate variability (36-88%). Working memory showed more variable (26-81%) left frontal activation and no hippocampal activation.

This preliminary study demonstrates the continuing need to systematically evaluate the inter-subject reliability of multiple language paradigms in order to improve the clinical utility of fMRI in preoperative mapping. This pilot study shows the feasibility of the method to evaluate these essential paradigms. Further investigation through greater population of subjects and extending the method to several other paradigms gives enough promise for research into improving the clinical utility of fMRI.