A Longitudinal Study of the Cortical Reorganization of Language Function in Brain Tumor Patients

K. K. Peck[1], N. Brennan[2], B. Hou[3], and A. Holodny[4]

[1]Medical Physics, Memorial Sloan-Kettering Cancer Center, New York, New York, United States, [2]Radiology, Memorial Sloan-Kettering Cancer Center, [3]Medical Physics, Memorial Sloan-Kettering Cancer Center, [4]Radiology, Memorial Sloan-Kettering Cancer Center, New York, New York, United States

Introduction

Until recently, it was believed that once damaged, the brain could not recover lost function. Previous functional imaging studies of stroke patients with aphasia suggest that recovery of language function may occur via the recruitment of ipsilateral perilesional tissue and/or homologous right hemispheric language areas (1, 2, 3). In addition, recent studies in brain tumor patients have demonstrated a capacity for cortical reorganization of function previously performed by damaged areas (4). However, these studies are based on single examinations in an effort to document possible atypical language organization that has already occurred. Thus, in these studies, fMRI activation patterns represent the reorganized language network rather than the dynamics of reorganization. The purpose of this longitudinal study is to measure the dynamic changes in language organization in brain tumor patients over time in an effort to better understand the mechanism underlying cortical reorganization.

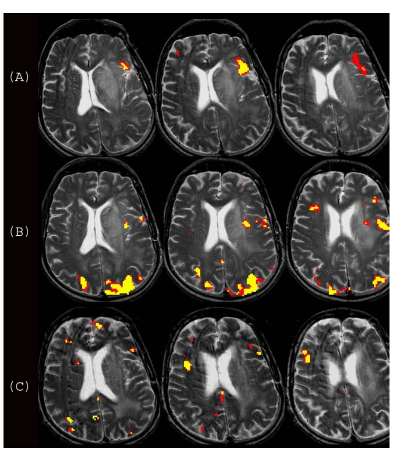
Subjects and Functional Tasks

Five right-handed brain tumor patients with a low-grade tumor directly adjacent to the frontal language areas (Broca's area), were prospectively studied. Three language paradigms were applied: 1) verb generation to specific nouns, 2) category generation, and 3) phonemic fluency (word generation to given letters). The paradigm was presented as a block design, consisting of 60 images, with 6 intervals (5 images) of paradigm execution alternating with 6 intervals (5 images) of rest. The finger-tapping task was performed as a control as it is assumed that a primary sensory response will be stable over time. For the language tasks, the patients were asked to perform the tasks silently, avoiding mouth and tongue movement. Stimulus presentation was performed using Brainwave software (Medical Numerics) and the stimulus was projected onto a LCD goggles. Three fMRI scans were acquired (1 presurgically and two postoperative follow-up scans at 3-6 month intervals) using the same functional paradigms. Formal neuropsychological evaluations were paired with each fMRI examination.

Method and Data Analysis

The functional studies were performed on a 1.5T GE using echo planner imaging. Functional images were acquired with TR=4000 ms; TE=40 ms; 90^{o} flip angle; 128×128 matrix; 240 mm FOV; 4.5 mm thickness. 26-28 oblique axial slices were acquired parallel to the AC-PC line. 2D and 3D T1 weighted anatomical images were acquired with a spin echo and a spoiled GRASS sequence. Image processing and analysis were performed with AFNI software. The reconstructed fMRI data were aligned using a 3D rigid-body registration. Functional activity was generated using a cross-correlation analysis. Motion parameters generated during slice registration were used as regressors to reduce motion-correlated activation. Functional images with activated pixels were generated at a threshold of $p<0.001$. To reduce additional false positive activity from large venous structures or random signal fluctuations, voxels in which the standard deviation of the acquired time series exceeded 6~8 % of the mean signal intensity were set to zero. Broca's area region-of-interest (ROI) measurements were used to determine the language laterality index (LI). Laterality indices were calculated on the basis of left (L) and right (R) activation volume in the Broca's area ROIs using the formula LI = (L-R)/(L+R). Hemispheric dominance was established on the basis of LI measurements, in conjunction with the results of neuro-psychological assessment and intraoperative electrocorticography (IEC).

Results and Discussion



4 of 5 patients qualitatively demonstrated increased right hemispheric compensation in either Broca's Area, Wernicke's Area or both on the post-operative and subsequent follow-up fMRI scans. Figure 1 shows a representative example. Figure A: pre-surgical baseline fMRI scan, Figure B: 3 months post-surgery and Figure C: 6 months post-surgery. Two post-operative follow-up fMRI scans figure B) and C) demonstrated progressively increasing fMRI activation in Broca's area in the right hemisphere (contralateral to the tumor). Pre-surgical fMRI indicated the expected left-hemispheric dominance for language. This was also suggested intraoperatively with electrocorticography. This lends support to the interhemispheric compensation model proposed by others in stroke patients. Whether or not this pattern of fMRI indicated functional compensation in the right hemispheric language homologues is clinically meaningful (ie. enables the surgeon to be more aggressive in the left assumed dominant hemisphere) is yet unknown. However, there is evidence using transcranial magnetic stimulation (TMS) to suggest that co-dominance or right dominance on fMRI does predict the extent of disruption of speech in the right hemisphere with TMS (5). This study does not rule out the presence of intra-hemispheric cortical compensation. The possibility of tumor induced de-coupling and post-surgical artifacts make reliable measurements in the left-hemisphere difficult. Whether or not tumor invasion of primary language centers can potentially alter functional assessments made at these sites is an important question that could impact pre-surgical planning efforts and needs to be further investigated.

References **1.** Staudt M *et al*., *Neuroimage,* 2002 16:954-967, **2**. Thulborn K *et al*., *Stroke*, 30:749-754, **3**. Crosson B *et al, J Cognitive Neuroscience*, 2005 17:391-406, **4**. Holodny A *et a*l., *J Comput Assist Tomogr*, 2002 26:941-3, 5. Knecht *et al*., Nature Neuroscience, 2002 5:695-699.