Cerebrovascular reactivity (CVR) mapping in patients with low grade gliomas undergoing presurgical mapping with BOLD fMRI

Domenico Zacá[1], and Jay J Pillai[1]
[1]*Division of Neuroradiology, Johns Hopkins University School of Medicine, Baltimore, MD, United States*

Introduction: The coupling mechanism between neuronal firing and regional hemodynamic changes, which constitutes the basis of the Blood Oxygen Level Dependent (BOLD) contrast for detection of eloquent cortex, is often impaired in patients with brain tumors or other resectable brain lesions, and this impairment is referred to as neurovascular uncoupling (NVU). The presence of NVU may result in misinterpretation of functional MRI (fMRI) activation maps secondary to false negative activation, thus potentially increasing the risk of postoperative neurologic deficits related to the inadvertent resection of "BOLD-silent" eloquent cortex. NVU has been documented in multiple studies including patients with high grade gliomas (1, 2) where decreased motor activation in tumor ipsilateral hemisphere compared to homologous areas in the contralateral hemisphere has been reported. These findings have been attributed to tumor angiogenesis characterized by impaired cerebrovascular reactivity (CVR) and abnormal hyperperfusion, as detected by T2* DSC perfusion imaging (3). There is lack of similar studies in the literature investigating the prevalence of NVU in patients with low grade gliomas. Although these lesions are not associated with changes in basal perfusion, they are characterized by impaired CVR (4). Furthermore, discordance between the results of preoperative fMRI and intraoperative cortical stimulation mapping due to NVU has been documented in low grade gliomas (5). In this study we used BOLD CVR mapping utilizing a breath hold (BH) task along with standard fMRI activation studies for presurgical mapping in order to determine the prevalence of NVU in a cohort of patients with low grade gliomas.

Materials and Methods: 8 patients with perirolandic low grade gliomas, referred by neurosurgeons for presurgical mapping of primary sensorimotor cortex by fMRI, participated in this study that was approved by the Institutional Review Board. Images were acquired on a 3T Siemens Trio scanner. Structural imaging included a 2D T2 FLAIR (TR=9000 ms, TE=115 ms, TI=2500 ms, voxel size 1.0x1.0x3.0 mm^3) sequence. A T2* GRE single shot EPI BOLD sequence (TR=2000 ms, TE=30 ms, voxel size 3.75x3.75x4.0 mm^3) was used for functional imaging. Patients performed multiple block design, 3 or 4 minute long , motor paradigms in addition to a BH task (40 seconds normal breathing alternating with 16 seconds of BH repeated 4 times) for CVR mapping. Activation maps for each paradigm and BOLD percentage signal change (PSC) maps following a BH task were created using GLM analysis. Composite motor activation maps were created selecting the tasks and applying the thresholds cited in the clinical report of each exam that was available in the electronic medical record. A dual rater Region of Interest (ROI) analysis was performed using MIPAV software on composite activation maps co-registered and overlaid on the T2 FLAIR images. ROIs were drawn on slices containing significant motor activation in the hemisphere contralateral to the tumor ("contralesional") and included the hyperintense portion of the lesion on the T2 images and clusters of activation distant up to two gyri from the margins of the tumor (defined as "ipsilesional ROIs"). Mirror contralesional ROIs were automatically generated. The number of activated voxels and the average PSC were computed and compared in the ipsilesional and contralesional ROIs.

Results: Figure 1A demonstrates how activation in the ipsilesional ROI was decreased compared to the contralesional ROI in all patients both for rater 1 and rater 2. Similarly in all but one patient (Figure 1B) reduced CVR (average PSC) is present in the ipsilesional ROI compared to the contralesional ROI. In figure 2A and 2B paired comparisons demonstrate both decreased number of active voxels as well as CVR at a group level both for rater 1 and rater 2.

Discussion and Conclusions: Our findings demonstrate that NVU can adversely affect the results of presurgical BOLD fMRI activation maps in patients with low grade gliomas, similar to previously described findings in higher grade gliomas. NVU within and in the vicinity of these lesions is likely due to factors other than tumor angiogenesis, such as altered PH levels, abnormalities involving astrocytes, neurotransmitters and chemical mediators involved in regulating the vascular response. We also demonstrated the utility of CVR mapping using a BH task in assessing NVU potential. This technique should be routinely used in clinical fMRI studies as an essential quality control tool for proper interpretation of fMRI results.

References:

(1) Holodny *et al*. AJNR 2000; 21:1415. (2) Hou *et al*. Neuroimage 2006; 32:489. (3) Ludemann *et al*. JMRI 2006; 23:435. (4) Hsu *et al*. JMRI 2004; 19:160. (5) Ulmer *et al*. AJNR 2003; 24:213.