Changes of Cerebral Phosphate Metabolism in Human Primary Visual Cortex during Functional Activation Observed by in vivo ^{31}P MRS at 7T

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Introduction

Information provided by in vivo ^{31}P MRS such as phosphocreatine (PCr), adenosine triphosphate (ATP) and inorganic phosphate (Pi) concentrations and their ratios, intracellular pH, and forward rate constant (k_f) of the creatine kinase reaction is useful in studying functional energetics of the brain [1-3]. Previous studies have shown that intracellular pH [1,2], PCr/Pi ratio [1,2] and k_f [3] in the activated brain areas change significantly during functional stimulation, suggesting altered cerebral energy metabolism. However, limited by the low detection sensitivity of in vivo ^{31}P MRS at low fields, the previous studies were carried out either with only surface coil localization or large single-voxel localization [1-3], and the results obtained thus are susceptible to partial volume effect and signal contamination. In a recent study, the feasibility of performing in vivo ^{31}P MRS on human brain with high detection sensitivity was demonstrated at 7T [4]. In this study, we extended the previous efforts and studied at 7T the changes of cerebral energetics in the human primary visual cortex (V1) during functional activation using 3D ^{31}P chemical shift imaging (CSI).

Methods

Eight normal subjects (age range: 20-28 yrs; 4M:4F) were recruited for this study. All procedures were approved by the institutional review board at University of Minnesota. Studies were performed on a 90 cm bore 7T magnet with a Varian INOVA console. A linear saddle proton surface coil was used for shimming and imaging, and a 5 cm single-loop surface coil, passively decoupled from the proton coil, was used for ^{31}P spectroscopy. Localized shimming was performed on a 3×3×3 cm^3 voxel placed in the V1 area using a FASTMAP algorithm [4].

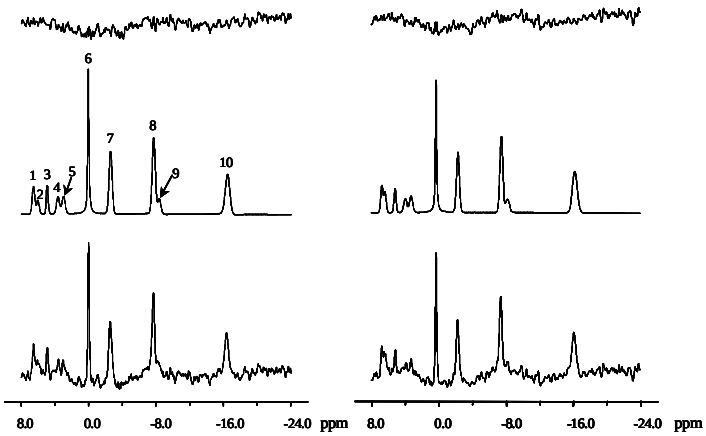

Figure 2a. Averaged ^{31}P spectra (bottom row) from a typical subjec over selected voxels acquired during the rest periods (left column) and functional activation (right column). The middel and top rows show the fitted spectra by MRUI and the residues, respectively. 1. phosphoethanolamine (PE); 2. phosphocholine (PC); 3. Pi; 4. glycerophosphoethanolamine (GPE); 5. glycerophosphocholine (GPC); 6. PCr; 7. γ-ATP; 8. α-ATP; 9. nicotinamide adenine dinucleotides (NAD); 10. β-ATP.

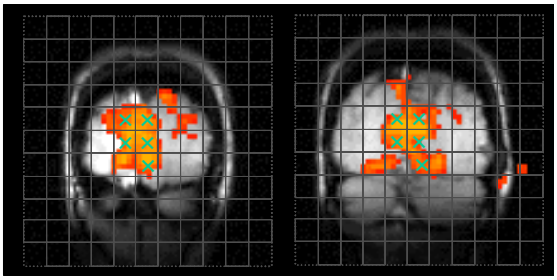

Figure 1. fMRI activation maps of 2 V1 slices from a subject. "X" indicates the voxels from which the spectra were selected, averaged, and quantified.

Functional imaging of 7 coronal slices covering the entire V1 area was performed using a gradient-echo EPI sequence (FOV = 20×20 cm^2, matrix size = 64×64, TR = 1.5 s). Two task periods, during which a bifocal eye goggle flickered at a frequency of 8 Hz, and two rest periods were used, each containing 20 image sets. Activation maps were generated using the period cross-correlation method and a statistical threshold of 0.35-0.55. 3D ^{31}P CSI was performed using a Fourier series window (FSW) imaging technique [6], a spectral bandwidth of 6000 Hz, a FOV of 15.7×15.7×15.7 cm^3, and a hard excitation pulse of 200 μs for maximum global PCr signal intensity. Two spatial resolutions were achieved by having different matrix sizes: 11×11×11 to give a voxel size of 7.5 ml (high resolution; n=4), and 9×9×7 to give a voxel size of 24.3 ml (low resolution; n=4). TR for high and low resolution 3D CSI was 1.5 s and 4.5 s, respectively. 3D CSI were performed separately and consecutively in the absence of visual stimuli and in the presence of continuous visual stimuli. Spectral processing was carried out using the software package MRUI, and the AMARES method of MRUI was used for quantification. Paired *t*-test was used for statistical analysis and a $p<0.05$ was considered statistically significant.

Results

The fMRI activation maps from a typical subject is shown in Fig. 1. The grids overlaid on the images show the positions of the voxels in ^{31}P CSI (high resolution). Localized ^{31}P sepcetra were taken from a number of selected voxels indicated by the symbol "×" (Fig. 1) and averaged. Those voxels were chosen based on that they were activated by visual stimuli and located in the primary visual cortex. The averaged spectra from the same voxels (bottom row of Fig. 2a) were analyzed and quantified for the rest (left column) and activation (right column) periods. The middel and top rows of Fig. 2a show the fitted spectra by MRUI and the residues, respectively. Chemical shift, integrated signal intensity and linewidth of 10 different resonance were estimated from the fitted spectra (Fig. 2a). Intracelluar pH was calculated from the chemcial shift difference between the PCr resonance and the Pi resonance. There was a significant ($p<0.05$) decrease in the integrated PCr signal intensity (-4±4%) and a significant ($p<0.05$) increase in the integrated phosphocholine (PC) signal intensity (25±11%) during visual stimulation. The integrated signal intensites of γ-ATP and Pi, the PCr/γ-ATP, PCr/Pi and γ-ATP/Pi ratios, the linewdith of all resonance, and intracellular pH did not change significantly during functional activation.

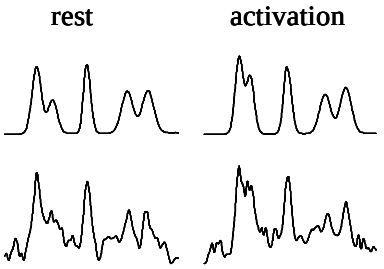

Figure 2b. The amplified spectral regions of the spectra displayed in Fig. 2a, showing the details of the PE, PC, Pi, GPE and GPC resonance. Top: fitted spectra. Bottom: experimental spectra.

Discussion and Conclusion

The results show that there is a small decrease in the PCr concentration in the human primary visual cortex during functional activation. The functional activation induced increase of PC signal has not been reported before. This increase may reflect the change of memberane function elevated by visual stimulation. However, it needs further investigation, since such increase could potentially be confounded by increases in the cerebral contents of glucose 6-phosphate (G6P) and 2,3-diphosphoglycerate (2,3-DPG) during functional activation, which are caused by elevated cerebral glucose metabolism rate and cerebral blood volume, respectively. Finally, this work also demonstrates that high-field ^{31}P MRS is useful for studying bioenergitics during brain activation.

References

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Acknowledgments

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