Differentiating High-energy Phosphate Metabolites and pH in Human Gray and White Matters by using 3D ^{31}P Chemical Shift Imaging of Entire Brain at 7 Tesla

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INTRODUCTION

In vivo ^{31}P MRS can be used to assess bioenergetics of human brain non-invasively, and it is useful for studying brain function and neurological diseases. Large gains in both NMR sensitivity and spectral resolution at 7 Tesla significantly improve the quality of *in vivo* ^{31}P MRS in the human brain for providing rich information including phosphocreatine (PCr), adenosine triphosphate (ATP) and inorganic phosphate (Pi), intracellular pH, and forward rate constant of the creatine kinase (CK) reaction, as well as the ATP synthesis rate [1,2]. It is well known that the cerebral metabolic rates (e.g., glucose and oxygen utilizations) and blood flow are significantly higher in the gray matter than that in the white matter. It has been demonstrated that the CK activity in the human gray matter is also higher than white matter indicating a high phosphate metabolism in the gray matter in the human brain [3]. In this study, we systematically analyzed the i*n vivo* 3D ^{31}P chemical shift imaging (CSI) data acquired from the entire human brain at 7 Tesla for quantifying ATP, PCr and other phosphate metabolites, pH and magnesium (Mg^{2+}) between the gray and white matters. Significant differences in most measured parameters were found in this study.

METHODS

3D ^{31}P CSI data were acquired on a 90-cm bore 7 T Magnex magnet with a Varian INOVA console. A ^{1}H/^{31}P double-tuned TEM volume coil using quadrature driving was designed and constructed for MR applications at 7 Tesla. Three dimensional ^{31}P CSI was acquired using a Fourier series window imaging technique [4] with spectral bandwidth of 5000 Hz, 45^{o} Ernst angle for optimal spin excitation, FOV of 20×20×22 cm^3, matrix size of 15×15×13, TR = 0.5 s, cylindrical voxel shape, 10.9 ml voxel size and the total acquisition time of 51 minutes. Two grouped ^{31}P spectra were used for quantification and they were the summation of 8-10 ^{31}P spectra from the multiple voxels either dominated by the gray matter or white matter brain tissue. Spectral processing was carried out using the software package MRUI, and the AMARES method of MRUI was used for quantification. Due to the closed chemical shifts between phosphoethanolamine (PE) and phosphocholine (PC), these two resonance peaks were treated as a single resonance peak and was assigned to PME. However, both glycerophosphoethanolamine (GPE) and glycerophosphocholine (GPC) were treated as a single resonance peak. Intracellular pH was calculated from the chemical shift difference between the PCr and the Pi resonances. The magnesium concentration was calculated from the chemical shift difference between the α-ATP and β-ATP resonance peaks and other constants [5]. Paired *t*-test was used for statistical analysis and a $p<0.05$ was considered statistically significant. The results were presented by mean±std.

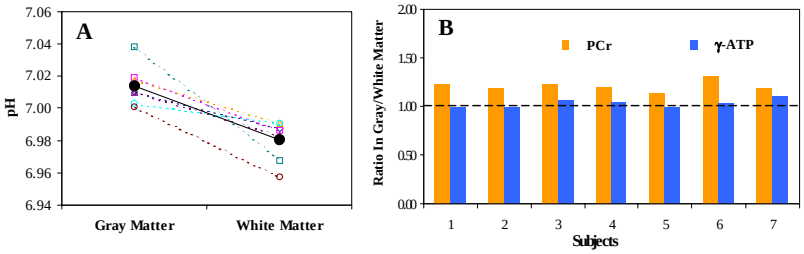

Figure 1. (A) pH values and (B) PCr and ATP metabolites ratio in gray and white matter dominated voxels in human brain obtained form 7 subjects on 7T.

RESULTS AND DISCUSSION

Figure 1A shows the paired results of pH values measured in the gray and white matter, respectively, from seven subjects. Each subject has a relatively low pH (or more acidic) in the white matter compared to that in the gray matter, though the difference was small. The pH value was 6.980±0.013 and 7.014±0.013 in the white and gray matter, respectively, with a pH difference of 0.034±0.019. The pH difference is statistically significant (P = 0.003). Figure 1B summarizes the comparison results of the PCr and γ-ATP concentrations ratios between the gray and white matters. It indicates that there is no statistical difference in the ATP concentrations between the gray and white matter (P = 0.14). In contrast, the PCr concentration in the gray matter is statistically higher than that in the white matter ($P = 3.4\times10^{-5}$). This result is consistent with the fact of high bioenergetics in the gray matter. Table 1 summarizes the results of PCr and ATP concentration ratio and other phosphate metabolite as well as Mg^{2+} concentration ratio. Based on this preliminary study, the concentrations of PME, GPE and Mg^{2+} don't have statistical differences between the gray and white matters. Nevertheless, the GPC concentration in the white matter is significantly higher (31%) than that in the gray matter. This difference may be linked to the membrane phospholipid metabolism between two different brain tissue compartments. One potential impact of GPC is on the schizophrenia patient, which shows a decreased GPC content in the prefrontal region [6].

The differences measured in this study present low-limit values because of the significant contaminations of the white matter tissue in the grouped gray matter compartment used in our analysis. It is expected that the use of more precise tissue segmentations between the gray and white matters based on T_1-weighted images should increase the differences.

Table 1. Summary of phosphate metabolites and Mg^{2+} concentration ratio in gray and white matter dominated voxels in human brain.

	Mg^{2+}	GPC	PME	GPE	PCr	ATP
Ratio(GM/WM)	1.19±0.33	0.69±0.18	1.02±0.42	1.03±0.34	1.21±0.05	1.03±0.05
p_value	0.15	0.001	0.86	0.81	0.00034	0.14

CONCLUSION

Excellent ^{31}P NMR sensitivity and improved spectral resolution achieved at 7 Tesla are capable of determining small differences of the measurable parameters between the gray matter and white matter reliably. This study suggests that ultra-high field strength is significantly advantageous for performing *in vivo* ^{31}P spectroscopy on human brain for better quantification, thus, it provides a great opportunity for noninvasive study of phosphate bioenergetics related to brain function and neuropathology.

ACKNOWLEDGEMENTS NIH grants NS38070, NS39043, NS41262, EB00329, EB00513 and P41 RR08079, the W.M. Keck Foundation, and the MIND institute.

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