Basal Ganglia NAA/Cr ratio in Gulf War Syndrome at 3T

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Introduction

Abnormalities in ratios of brain metabolite peak areas were previously measured via magnetic resonance spectroscopy (MRS) at 1.5T in the pons and basal ganglia [1,2] and in bilateral hippocampus [3] of Gulf War Syndrome patients. The original veterans of the Seabees cohort studied in [1] recently participated in a follow-up study at 3T. A part of the protocol used single voxel spectroscopy (SVS) ^{1}H MR to study metabolite concentrations in the left and right basal ganglia of normal controls and Syndrome II ("confusion-ataxia") [4] patients. Personnel performing the data acquisition and initial analysis were blinded with respect to the group memberships. The blind was then partially lifted to split the subjects into two unidentified groups A and B. The group comparison indicates significantly lower N-acetylaspartate-to-creatine (NAA/Cr) ratio in group A compared to group B. We hypothesize that group A is Syndrome II and group B is normal controls. This pilot study helps to improve the understanding of the chemical changes in the brain in Gulf War Syndrome and possibly in other related neurodegenerative conditions.

Methods

Twenty Gulf War veterans (9 members of group A and 11 members of group B) were studied with the same SVS left and right basal ganglia protocol. A standard single voxel spectroscopy sequence (SVS PRESS) was used on a Siemens 3T Trio TIM with the following parameters: TR/TE/NS = 2500ms/30ms/96, voxel (centered in the basal ganglia, bilaterally) volume = 12.0 mL (20 mm x 30 mm x 20 mm), spectral width = 2000 Hz, water suppression bandwidth = 50 Hz, data points = 1024, acquisition time = 4:10 min. An unsuppressed water spectrum was also acquired for eddy current compensation and quantitation. Good quality high-resolution and high-contrast localizer images were used for proper voxel positioning to ensure its reproducibility. Reproducibility and quality of the single voxel spectroscopy (SVS) methods used was previously demonstrated [5]. Post-processing of the MRS data was performed using LCModel [6]. Group and hemispheric differences were studied with unbalanced 2-way Analysis of Variance (ANOVA).

Results and Discussion

Manual adjustment of the shim currents produced metabolite half-height line width of 9-14 Hz in most sessions. An example of the basal ganglia spectrum processed with LCModel is shown in Figure 1. Although a water reference spectrum was collected for metabolite quantitation, the NAA/Cr ratio is reported for comparison with the original 1997-8 study and because it is less sensitive to individual shim variations and possible metabolite relaxation time differences [7]. The NAA/Cr ratio in the basal ganglia was significantly lower in group A than in group B (group effect p=0.0125, unbalanced 2-way ANOVA). The group difference is greater in the right basal ganglia (10% difference, p=0.022) than in the left (8% difference, p=0.15). See also Table 1 and Figure 2. In the original study [1], Syndrome II patients had lower, highly statistically significant NAA/Cr in the right basal ganglia than controls (18% difference, $p < 0.001$) and lower, but less significant NAA/Cr in the left basal ganglia (9% difference, $p < 0.09$). Additionally, the NAA/Cr ratio is significantly higher in the left basal ganglia than the right in both groups (overall hemispheric effect significance of p=0.0001).

Conclusion

N-acetylaspartate is widely regarded as a marker of neuronal viability and any changes in disease are important. Our preliminary findings show differences in this ratio between controls and Gulf War syndrome II patients. However, to transition from metabolite ratios (or "institutional units", if water reference is used) for metabolite concentrations to absolute metabolite concentrations, relaxation time measurements in vivo are needed [7,8] as well as determination of the compartmentation in the human brain [9].

Acknowledgments

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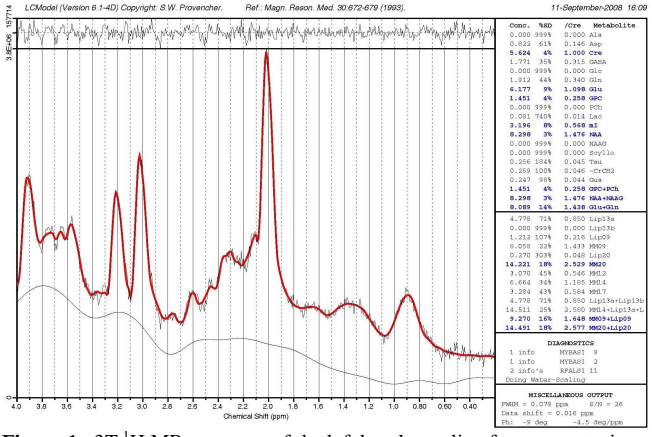

Figure 1. 3T ^{1}H MR spectrum of the left basal ganglia of a representative subject processed using LCModel. Metabolites detected with acceptable reliability are shown in blue.

	Left BG NAA/Cr (STDEV)	Right BG NAA/Cr (STDEV)
Group A	1.29(0.13)	1.09(0.13)
Group B	1.41(0.19)	1.21(0.09)
p-value	0.15	0.022

Table 1. Mean basal ganglia NAA/Cr ratio (and group standard deviation) by group and hemisphere.

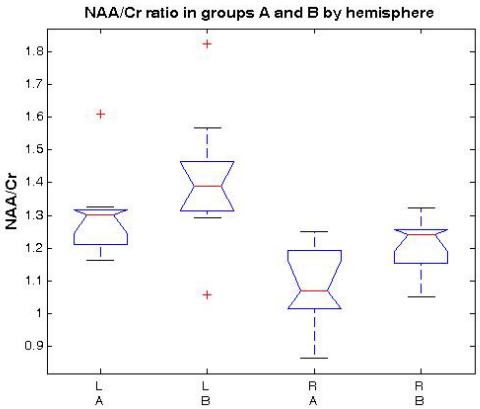

Figure 2. Group and hemispheric differences in the NAA/Cr ratio. Red lines represent median values. Non-intersecting notches indicate significance (here in median values, better than 0.05). Plus signs represent outliers (outside of 1.5 inter-quartile range).