Assessment of Automated Brain Region Directed 3D Proton Spectroscopy Data Analysis Pipeline

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Introduction

While many fast 3D magnetic resonance spectroscopic imaging (MRSI) methods have been developed, analysis of massive amounts of data still remains a challenge. Considerable effort has been directed to developing automated spectral analysis and display methods for MRSI data [1-3]. All of those methods include a correction for partial volume effects and allow for correlation of metabolite values with contributions from different tissue types obtained from tissue segmentation. However, if an abnormalilty is not tissue specific but brain region specific, partial volume effects of the particular brain region of interest may decrease sensitivity to such changes. Therefore, a fully automated analysis taking into account the amount of each brain structure contributing to a particular spectrum is essential to increasing sensitivity of MRSI techniques to such metabolite changes.

Materials and Methods

The MRSI data analysis process includes: (i) brain region segmentation and registration, (ii) brain region mask formation, (iii) spectral fitting of MRSI voxels containing a specific masked brain region using LCModel [6], (iv) calculation of weighted average concentrations for a particular brain region/brain structure, (v) metabolite image formation and study analysis. The weighted average metabolite concentration (or ratio) for a particular brain region j was calculated as

$$conc_j = \frac{\sum_i (conc_i \times w_{i,j})}{\sum_i w_{i,j}}$$

with i counting over all MRSI voxels containing brain structure j, and w being the weight (obtained form the brain-structure masks registered to the 3D MRSI data) of brain structure j in a particular voxel i.

MRI and MRSI data of human brain were acquired from 20 subjects on a 3.0T Tim Trio MR scanner (Siemens Healthcare) equipped with a standard 12-channel head coil array. MRI acquisitions include a T_1-weighted MPRAGE sequence (1.0x1.0x1.2 mm resolution) and T_2-weighted axial images for MRSI data acquisition planning. A standard 3D MRSI spin echo sequence was used for obtaining MRSI data (TR/TE = 1500ms/30ms; field of view = 120 x120 x 96mm^3; matrix size = 12 x 12 x 8 interpolated to a nominal voxel size of 7.5 x 7.5 x 6 mm^3). Voxels within a brain-region mask were then fed into LCModel [4] to obtain metabolite values for each voxel. To compare the sensitivity of this weighted approach to brain-region-specific metabolite changes to conventional methods (normalized sum of metabolite values over all voxels containing a particular brain region, but without taking into account the weight of the brain region in each voxel), three groups of "patient data" were constructed from the original data with hippocampus-specific increases in metabolite ratios by 5%, 6% and 10% respectively. This simulation of patient data was accomplished by changing the metabolite values $conc_i$ for each voxel i containing hippocampus with weight j according to (Example for a 5% increase of concentration in hippocampus only)

$$conc_{i,new} = (1.05 \times conc_i \times w) + conc_i \times (1 - w)$$

Average concentrations with and without considering brain region contributions were then calculated for controls as well as the three simulated patient groups. The difference was explored using paired Student t-tests and one-way analysis of variance (ANOVA).

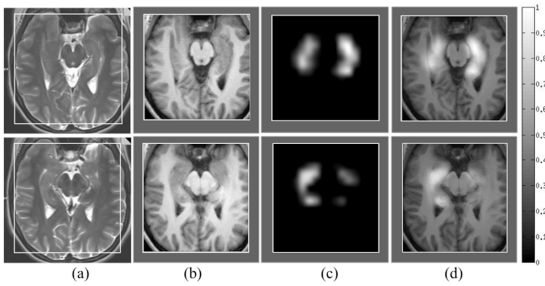

Figure 1. Results of hippocampus registration process for one subject. (a) T2-weighted images with MRSI FOV indicated as white box; (b) registered T1-weighted images; (c) brain region masks in MRSI resolution for hippocampus; (d) overlay on b).

Results and Discussion

To evaluate the accuracy of the brain structure registration process the volumes of left/right hippocampus and left/right thalamus obtained by the MRSI pipeline were compared to volumes calculated purely from structural MRI volumes. They only differ by about 3% and 4% for hippocampus and thalamus, respectively, which could be due to the registration process. The correctness of positions for the brain region specific MRSI voxels was confirmed by overlaying the interpolated structural brain region masks with registered high resolution T_1-weighted image as shown in Fig.1. The relative average metabolite concentrations calculated with/without weighted brain region contributions show a significant difference when the increase of a metabolite level was specific to the hippocampus. The results for myo-inositol (mI)/ Creatine (Cr) are shown in Fig. 2. The selected ANOVA analysis results for comparing controls and the three simulated patient groups using weighted and unweighted concentrations for left hippocampus are listed in Table 1. Responses to the "abnormal" changes of metabolite levels associated with hippocampal region were more sensitive when the brain-region-weighted approach was used: Changes between simulated patient data at 10% elevated abnormal metabolite levels and normal controls were around 10%, 10%, 9% for mI/Cr, NAA/Cr and tCho/Cr when brain-region-weighted concentrations were used. But only 4%, 3% and 3% changes were found for mI/Cr, NAA/Cr and tCho/Cr when unweighted average concentrations were used. The statistical results also show that the abnormal level of tCho/Cr was significant in the weighted concentration comparison while no attention was drawn to tCho/Cr when the unweighted average concentration was analyzed.

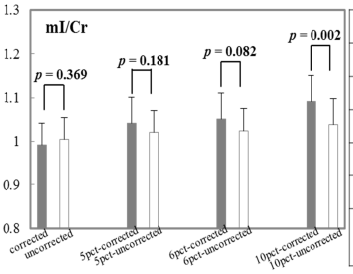

Fig. 4. Comparison between corrected and uncorrected mI/Cr average concentrations for controls and 3 simulated patient groups.

	mI/Cr		NAA/Cr		tCho/Cr	
	Weighted	No weights	Weighted	No weights	Weights	No weights
0pct	0.99±0.05	1.00±0.05	1.20±0.05	1.21±0.05	0.33±0.01 *#	0.33±0.01
5pct	1.04±0.06	1.02±0.05	1.26±0.05	1.23±0.05	0.34±0.01	0.33±0.01
6pct	1.05±0.06	1.02±0.05	1.27±0.05	1.24±0.05	0.35±0.01	0.33±0.01
10pct	1.09±0.06	1.04±0.06	1.32±0.06	1.25±0.05	0.36±0.01 *#	0.34±0.01
statistics	F(3,76) = 0.523 p = 0.668	F(3,76) = 0.064 p = 0.979	F(3,76) = 0.813 p = 0.491	F(3,76) = 0.122 p = 0.947	F(3,76) = 1.853 p = 0.145	F(3,76) = 0.250 p = 0.861

Table 2. One-way ANOVA analysis for average relative metabolite concentrations between controls and simulated patients for left hippocampus with/without considering brain regicn contributions. The relative average concentrations were represented as mean ± SE.

Conclusion

A brain-region-specific 3D proton spectroscopic data analysis pipeline has been developed and tested on human subjects as well as in simulated patient groups. The accuracy of the registration process proved to be accurate enough for correcting/weighting metabolite levels with the calculated brain region content. The statistical analysis indicated that using brain-region-weighted metabolite concentrations increases sensitivity to subtle changes in metabolite levels. The average concentration per unit volume for specific brain regions will make comparisons between different patient groups in clinical studies more readily feasible.

References: [1] Maudsley AA et al. Magn Reson Imaging 1992;10(3):471-485. [2] Doyle TJ et al. J Magn Reson B 1995;106(1):58-63. [3] Maudsley AA et al NM R Biomed. 2006;19(4):492-503. [4] Provencher SW. Magn Reson Med 1993;30(6):672-679

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