Comparison analysis between patients with seizures and developmental delay: a multiple modality study

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Introduction: Diffusion tensor imaging (DTI) measures the diffusivity properties of water molecules in a series of directions, which provides information about the microstructure of the tissue in-vivo [1]. Proton MR spectroscopic imaging (MRS) measures concentrations of several metabolites, including N-acetylaspartate (NAA), Choline-containing compounds (Cho) and creatine-phosphocreatine (Cr) [2]. Some studies suggested that a combination of DTI and NAA yield better diagnostic information than either measure alone [3]. In this study we demonstrate that DTI and MRS reveal useful and consistent information about the microstructure of the basal ganglia and thalami.

Material and Methods: This IRB approved study includes 23 patients (mean age of 2.9 ± 2.8, range of 0.1-3.1) with seizures (SZ) and 20 patients (mean age of 2.1 ± 0.8; age range of 1.1-3.4) with developmental delay (DD). All imaging was performed on Philips Intera 1.5T scanners at Texas Children's Hospital. For the DTI, an axial spin echo, single shot, echo planar imaging sequence was used with the following parameters: FOV=256 mm; TR,=70150 ms; TE=90 ms; measured voxel size=2.0 × 2.0 × 2.7 mm^3 with a reconstructed voxel size of 2.0 × 2.0 × 2.7 mm^3. Diffusion gradient was encoded in 15 directions with two b-values, low b-value of 0, and high b-value of 860 s/mm^2. To improve signal to noise ratio, high-b images were acquired twice and averaged. Each acquisition took approximately 5 minutes 45 seconds, and 55 slices were be acquired. Proton magnetic resonance spectroscopic (MRS) data were collected using 2D chemical shift imaging (CSI) technique with the region of interest preselected by means of point-resolved spectroscopy (PRESS) through a plane of 15 mm thick at the basal ganglia level. Short echo time (TR/TE 1500/31 ms) was used. The FOV for the 2D CSI is 160 x 160 mm, with 16 x 16 phase encoding steps, yielding 10-mm in-plane resolution. The MRS and DTI analysis included four regions, the right and left basal ganglia (ROI1 and ROI2), and the right and left thalami (ROI3 and ROI4), see figure. In MRS analysis, the four regions were manually selected and averaged using Philips spectool 4.2, and the subsequent analysis by LCModel 6.1 [4] yielded the NAA/Cr and Cho/Cr ratios. The corresponding measurement of fractional anisotropy (FA), apparent diffusion coefficient (ADC),, and axial and radial diffusivities were calculated using Philips PRIDE fibertracking tool 4.2, on the same ROIs as in the MRS analysis. Data were analyzed using statistical software (SPSS, 15.0 version; SPSS, Chicago, IL). A general linear model analysis was used to examine group differences for DTI (FA, ADC, axial and radial diffusivities) and MRS measures (NAA/Cr, NAA/Cho, Cho/Cr) after controlling for the patient age. The same statistical analysis was repeated after controlling for the NAA/Cr in addition to age.

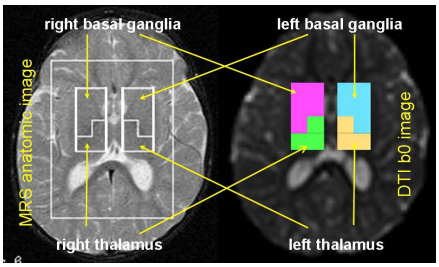

Figure: four ROIs on the anatomic image of MRS and the b0 image of DTI.

Results and Discussion:

NAA/Cr was significantly higher in the DD group in the left basal ganglia, and there was a trend toward significance in the right thalamus and right basal ganglia. Consistent with group differences in NAA/Cr, the FA changes show the same trend (higher in DD) in the direction between groups, while the radial diffusivity and ADC change in the opposite direction, as expected. There was no difference in axial diffusivity between groups. After controlling for NAA/Cr and age, none of the measures show significant differences between groups. Among diffusivity measures, the change in the radial diffusivity is more consistent with the NAA/Cr than any other measures but in the opposite direction. Because the NAA is mostly present in the neuron, the lower NAA concentration indicates the presence of less neurons or a less healthy neuron concentration in the SZ group. This analysis also suggests that radial diffusivity more likely reflects micro-structural change induced by a change in neuron density. After controlling for NAA/Cr in addition to age, group differences disappear on statistical analysis, supporting our hypothesis that the difference between the DD and SZ groups result from neuron density.

	Left Basal Ganglia			Right Basal Ganglia			Left Thalamus			Right Thalamus		
	Effect size	t-value	p-value	Effect size	t-value	p-value	Effect size	t-value	p-value	Effect size	t-value	p-value
NAA/Cr	0.63	3.48	0.00	0.35	1.92	0.06	0.21	1.19	0.24	0.35	1.95	0.06
Axial Diffusivity	0.23	-1.30	0.20	0.31	-1.73	0.09	0.04	0.02	0.83	0.26	-1.44	0.16
Radial diffusivity	0.37	-2.08	0.05	0.38	-2.14	0.04	0.17	-0.97	0.34	0.42	-2.32	0.03
FA	0.42	5.38	0.03	0.33	1.83	0.08	0.36	2.00	0.05	0.51	2.83	0.01
ADC	0.33	-1.81	0.08	0.36	-2.01	0.05	0.13	-0.71	0.48	0.37	-2.06	0.05

Table: Effect size, t-value, p-value of DTI and MRS measures on all four regions. The positive t-value indicates that the corresponding measure on the DD group is higher than that on the SZ group. Effect size of 0.1 is small, 0.25 is moderate, and 0.4 is large.

Conclusion:

We used a multi-modal approach to study regions likely affected by seizures and developmental delays. The complimentary information of MRS and DTI provide some insight about potential microstructure differences between those two groups. Hopefully further study can provide useful information about the pathology of these disorders. In the future, we will include a control group in this study and also increase the sample size.

Reference: 1. Basser PJ, et al, J Magn Reson B 103:247-254 (1994); 2. Castillo M, et al, AJNR AM J Neuroradiol 17:1-15 (1996); 3. Yin H, et al, J Neurol 251:1249-1254 (2004); 4. Provencher SW, Magn. Reson. Med. 30:672-679 (1993)