Investigation by Means of Absolute Quantification of Proton MR Spectroscopy in Adolescent with Attention-Deficit/Hyperactive Disorder

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Introduction

Prefrontal dysfunction has been considered as one of the contribution to the behavior and cognitive deficits associated with attention-deficit/hyperactivity disorder (ADHD) in children [1]. Recently proton MR spectroscopy (MRS) is regarded as a powerful tool to observe cerebral metabolism in brains of ADHD subjects [2]. Unfortunately, the findings at present are not clear enough to have an interpretation of metabolism alternations for ADHD subjects. In this study, we investigated the absolute concentrations of metabolite in prefrontal cortex for ADHD patients in adolescents. Results including absolute concentration and metabolic ratios were also compared with previous findings of literatures [2].

Materials and Methods

A total number of 23 children (age: 13.0±3.1 y/o, 4 female and 19 male) with a diagnosis of ADHD and 15 healthy control subjects (age: 15.5±1.8 y/o, 8 female and 7 male) were included in this study. All studies were performed on a 1.5T MR system (General Electric, Milwaukee, WI) with conventional single-voxel MR spectroscopy protocol (PRESS, TR/TE = 1600/35 ms, Average=128). The voxel size was adjusted ranging from 4 to 8 cc in order to fit the area of prefrontal white matter. Two spectra acquired from right and left prefrontal cortex for each subject were afterward analyzed by LCModel. Absolute concentrations of NAA+NAAG, Cr, Cho, Myo-Ino and Glx were quantified using water scaling approach and metabolic ratios over Cr (/Cr) signal were also calculated. Student-t test was used to test the hypotheses and a result of $p<0.05$ was considered significant.

Results

Absolute metabolic concentrations of both groups in right prefrontal were compared in terms of Creatine, Myo-Inosital, Choline, NAA+NAAG, and Glx, as shown in Figure 1. Table 1 summarizes the mean and standard deviations (SD) of absolute concentrations in left and right prefrontal cortex for patients with ADHD and normal subjects respectively. T-tests reveal the significant difference of Cr concentration ($p=0.03$) in right prefrontal cortex between two groups. Metabolic ratios (Table 2) showed the difference of (NAA+NAAG)/Cr ($p=0.02$) as well as Myo-Ino/Cr ($p=0.04$) are significant in the right prefrontal cortex between two groups. No significant difference is found in the left prefrontal cortex for absolute concentration and metabolic ratio.

Discussion

Our result indicated the metabolic alternations between ADHD patients and normal subjects in the right prefrontal cortex while no significant difference was found in the left prefrontal cortex, which is consistent with findings in the previous literature [2]. Since significant concentration enhancement was found in Cr in our study, the metabolic ratio using Cr as the normalized level may not be a proper index to evaluate the neurometabolic changes of ADHD patients. In many clinical studies, Cr has been regarded as a normalized level for other metabolites. For ADHD studies, however, Cr could be a potential index for evaluation. As demonstrated in this study, significant difference of metabolic ratio found in Myo-Ino and NAA+NAAG is probably biased by Cr. Thus, the importance of absolute quantification to investigate metabolism of ADHD was also demonstrated in this study.

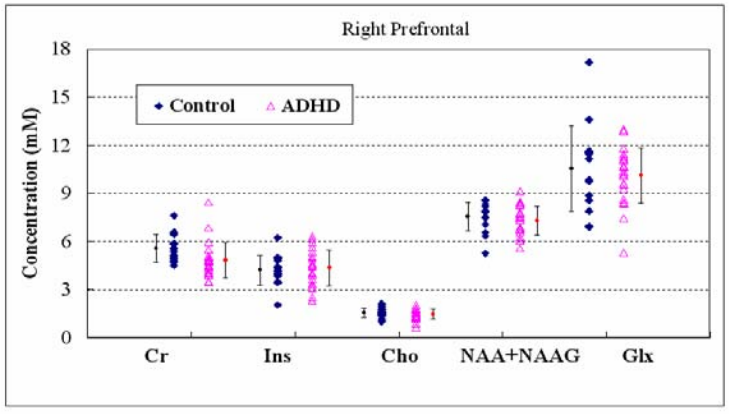

Figure 1. The absolute concentrations of metabolites in right prefrontal cortex for normal controls and ADHD patients.

Table 1. Absolute concentrations of metabolites for ADHD and normal subjects and T-Test results

Metabolite Conc.	ADHD		Normal Control		T-test
(mM)	Mean	SD	Mean	SD	p- value
Left Prefrontal					
NAA+NAAG	7.66	1.03	7.80	0.55	0.62
Cr	4.94	0.68	4.88	0.76	0.83
Cho	1.52	0.26	1.69	0.27	0.05
Myo-Ins	4.44	0.97	4.04	1.11	0.25
Glx	10.59	2.40	9.85	1.93	0.32
Right Prefrontal					
NAA+NAAG	7.31	0.89	7.56	0.91	0.41
Cr	4.84	1.10	5.59	0.89	**0.03**
Cho	1.48	0.32	1.56	0.28	0.42
Myo-Ins	4.35	1.12	4.22	0.92	0.71
Glx	10.11	1.71	10.55	2.66	0.54

Table 2. Metabolic ratio of ADHD and normal subjects and T-Test results

Metabolic Ratio	ADHD		Normal Control		T-test
	Mean	SD	Mean	SD	p- value
Left Prefrontal					
(NAA+NAAG)/Cr	1.57	0.23	1.64	0.30	0.45
Cho/Cr	0.31	0.07	0.35	0.06	0.07
Myo-Ins/Cr	0.92	0.20	0.84	0.29	0.32
Glx/Cr	2.21	0.63	2.03	0.48	0.36
Right Prefrontal					
(NAA+NAAG)/Cr	1.56	0.26	1.37	0.19	**0.02**
Cho/Cr	0.31	0.07	0.28	0.03	0.12
Myo-Ins/Cr	0.92	0.24	0.76	0.16	**0.04**
Glx/Cr	2.19	0.59	1.91	0.55	0.15

Reference

[1] R.A. Yeo et al., J. Am. Acad. Child Adolesc. Psychiatry, 42: 303 (2003).

[2] V.A. Russel et al., Behavioral and Brain Functions, 2: 30 (2006).