Metabolic Changes in Juvenile Myoclonic and Frontal Lobe Epilepsy by ^{1}H MR Spectroscopy

H-M. Baik[1], B. Swartz[2], L. Vu[1], H. Liu[1], O. Nalcioglu[1], M-Y. Su[1]

[1]Tu & Yuen Center for Functional Onco-Imaging, University of California-Irvine, Irvine, CA, United States, [2]Epilepsy Center, Haog Hospital, Newport Beach, CA,

United States

Introduction

Non-invasive proton magnetic resonance spectroscopy (^{1}H-MRS) offers the opportunity to investigate regional changes in the metabolite composition of different brain regions in vivo. The electrophysiological study has suggested that the thalamo-cortical connection is impaired in patients with juvenile myoclonic epilepsy (JME). Savic et al. reported reduced *N*-acetyl aspartate (NAA) concentrations in the frontal lobe of JME patients using ^{1}H-MRS [1-2]. More studies are needed to confirm this observation. The purpose of this study was to evaluate the metabolic changes from the anterior cingulate in JME patients and patients with frontal lobe epilepsy (FLE) compared to normal age-matched controls, to investigate whether metabolic abnormalities are associated with thalamo-cortical loop dysfunction.

Methods

This study included 26 subjects, 9 JME patients (4 men and 5 women; mean age 31 years), 8 FLE patients (4 men and 4 women; mean age 38 years) and 9 age-matched healthy controls (5 men and 4 women; mean age 32 years). The examinations were performed on a Philips Eclipse 1.5 T MR system with the standard quadrature birdcage head coil. For T_1-weighted MRI, a 3D SPGR (RF-FAST) pulse sequence was employed to acquire brain anatomic images, with TR= 20 ms, TE= 4.47 ms, 1.5 mm slice thickness, flip angle= 20°, matrix size= 256x256, FOV= 25.6 cm. After the MR study was completed, single-voxel MR spectroscopy was performed using a STEAM sequence. In JME patient and control cases, the spectroscopic voxels were placed over the right dorsal prefrontal cortex, right thalamus, and the anterior cingulate. In FLE cases, the voxels were positioned on the same side of the seizure focus and the anterior cingulate. Shimming was performed automatically on the water resonance for optimization of the homogeneities in each selected volume. After shimming procedure water suppression was accomplished with three chemical-shift-selective saturation (CHESS) pulses, and the bandwidth of each CHESS pulse was 60 Hz. The acquisition parameters were TR/TE 1600/20 ms, 192 averages, 2500 Hz spectral width, and 2048 data points. An unsuppressed spectrum was also measured for phase correction (16 averages). The spectroscopic data were processed by Fourier transformation, Exponential line broadening of 1.5 Hz, zero-filling to 16384 data points, and a high-pass filter to reduce the residual water signal in the time domain. After automatic phase and baseline corrections, the peak area was obtained from the spectrum by employing the Levenberg-Marquardt algorithm to fit Gaussian to Lorenzian type. The metabolite ratios of NAA/creatine (Cr), choline (Cho)/Cr, myo-inositol (ml)/Cr, $(NAA/H_2O) \times 10^3$, $(Cr/H_2O) \times 10^3$, and $(Cho/H_2O) \times 10^3$ were calculated for analysis. Ratios are given as the mean ± SD. Statistical significance was determined using Student's *t*-test (independent) between control subjects and patients with JME or FLE, where $p < 0.05$ was considered significant.

Results

No patients showed morphological abnormalities on the anatomical MRI. The typical T_1-weighted axial MR image, with the overlaid ^{1}H-MRS from the anterior cingulate is shown in Figure 1. [1]H MR spectra measured from FLE, JME, and control are demonstrated. The metabolite ratios (mean ± SD) measured from the anterior cingulate in different groups are summarized in Table 1. JME patients showed significantly lower NAA/Cr and $(NAA/H_2O) \times 10^3$ compared to controls (1.12 ± 0.21 vs. 1.58 ± 0.59, $p = 0.04$; 0.56 ± 0.12, vs. 0.75 ± 0.16, $p = 0.01$). The FLE patients also had significantly lower NAA compared to controls (1.00 ± 0.32, $p = 0.04$; 0.55 ± 0.21, $p = 0.04$). This result indicates that significant reduction of NAA metabolite in anterior cingulate of JME and FLE. However, there is no significant difference between these two groups. Except NAA, no other metabolites, Cho/Cr, ml/Cr, $(Cr/H_2O) \times 10^3$, and $(Cho/H_2O) \times 10^3$, showed significant alterations. The other two analyzed regions (i.e., dorsal prefrontal cortex and thalamus) in JME and FLE showed comparable NAA to controls.

Discussion

The main observation in this work was the significant NAA reduction in anterior cingulate of patients with JME and FLE compared to control subjects. This result is consistent with the previously reported finding by Savic et al. [1-2]. Hence, the present study demonstrated that ^{1}H-MRS can be used to detect the metabolic changes not visible with structural MR imaging. The physiological role of NAA is still not well understood, but since NAA is exclusively expressed in neurons, it is accepted as a neuronal and axonal marker [3]. Moreover, previous studies have shown that reduced NAA was observed in many neurological diseases that cause neuronal and axonal degeneration (epilepsy, dementias, multiple sclerosis, etc.) [4]. Therefore, our result of NAA reduction may reflect neuronal loss or dysfunction in the anterior cingulate of patients with JME and FLE.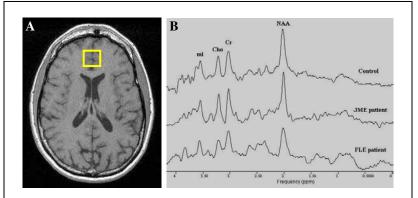 ^{1}H-MRS may provide information for a better understanding of pathophysiologic process in epilepsy patients, and may also for post treatment follow-up.

Figure 1. **A:** axial T_1-weighted MR image showing the spectroscopic voxel in the anterior cingulate. **B:** MR spectra measured from one FLE one JME and a control.

Table 1. Comparison of metabolite ratios obtained by in vivo ^{1}H-MRS

Metabolite Ratio	Controls (n = 9)	JME patients (n = 9)	FLE patients (n = 8)	p^1 Value	p^2 Value
NAA/Cr	1.58 ± 0.59	1.12 ± 0.21	1.00 ± 0.32	0.01*	0.04*
Cho/Cr	0.86 ± 0.42	0.93 ± 0.23	0.82 ± 0.32	0.66	0.42
ml/Cr	0.68 ± 0.29	0.78 ± 0.39	0.70 ± 0.33	0.45	0.41
$(NAA/H_2O) \times 10^3$	0.75 ± 0.16	0.56 ± 0.12	0.55 ± 0.21	0.04*	0.04*
$(Cr/H_2O) \times 10^3$	0.53 ± 0.22	0.50 ± 0.19	0.52 ± 0.09	0.84	0.78
$(Cho/H_2O) \times 10^3$	0.42 ± 0.09	0.39 ± 0.18	0.43 ± 0.09	0.72	0.66

* JME (p^1) and FLE (p^2) compared to controls, significant with $p < 0.05$.

References 1. Savic et al. Epilepsia 41:290-296 (2000). 2. Savic et al. Neuroimage 21:163-172 (2004). 3. Pioro et al., Neurology 44: 1933-1938 (1994). 4. Ross et al. Magn Reson Q 10:191-247 (1994)