Can diffusion weighted MR spectroscopy be used in differentiating acute MELAS and acute stroke?

Dandan Zheng[1], Bing Wu[1], Jiangxi Xiao[2], Zhenghua Liu[2], and Zhenyu Zhou[1]
[1]GE Healthcare China, Beijing, Beijing, China, [2]Radiology Department, Peking University First Hospital, Beijing, China

Target audience MR researchers who are interested in differentiating acute MELAS and acute stroke.

Introduction The underlying mechanism of neurological symptoms in patients with mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) is still controversial [1]. Signal abnormalities in conventional MR contrast are indistinguishable from those observed in stroke, especially in the acute stage. In this study, diffusion weighted MR spectroscopy was used to differentiate acute MELAS from acute stroke and also to probe the mechanisms underlying the pathogenesis of MELAS.

Method Two groups of subjects were recruited in this study: 1) eight patients diagnosed with MELAS (5 males and 3 females, mean age 20.3±4.2 years) in the acute stage (within one month) with eleven age matched healthy controls (7 males and 4 females, mean age 18.6±2.9 years, group1) ; 2) twelve patients (18 males and 4 females, mean age 53.3± 3.7 years) in the acute stage of stroke (between 24 and 48 hours from onset of symptoms) with fifteen age matched healthy controls (10 males and 5 females, mean age 53.3±4.9 years, group 2). Written consent forms were obtained prior to the study. Diagnoses of MELAS syndrome were based on the clinical symptoms and the finding of a mutation at the nucleotide position 3243 in the mitochondrial DNA by blood examination [2]. The DW-MRS sequence used is based on point resolved spectroscopy (PRESS) sequence with a pair of single polar diffusion gradients prior to the MRS preparation. The MR scanner used was a 3.0T clinical whole-body system (Signa EXCITE HD, GE). Parameters for the DW PRESS were as follows: TR = 2000 ms, TE = 288 ms, voxel size = 2×2×2 cm^3, spectral band width = 5000 HZ and data points = 4096. MRS data without diffusion weighting and a b-factor of 1000 s/mm^2 were acquired. Post-spectral processing was performed using SAGE software. The ROIs used were placed based on the T2 flair image (healthy controls) or DWI image (patients). Pure water subtraction was performed to reduce residual water signal in each suppressed frame. Phase corrections were performed prior to the summation of FIDs. Since the integral peak area was more sensitive to the random noise, height of spectral peak was used to as a metric to determine the metabolites contents in this study. The apparent diffusion coefficients (ADCs) values were estimated in the conventional way and used for statistical analysis.

Results The obtained spectral with and without diffusion weightings for acute MELAS, acute stroke patients and the healthy volunteers are shown in Fig.1. For the patients, the ROIs were placed in the lesion regions. And for the healthy controls, the ROI was placed at the frontal lobe. The ADCs of choline-containing compounds (Cho), creatine (Cr) and N-acetyl-aspartate (NAA) in all the subjects are listed in Table 1. Comparing to the age-matched healthy controls, the ADC of Cr and Cho obtained in acute MELAS patients were statistically higher ($P<0.05$). However, the ADCs of the metabolites of acute stroke patients were statistically lower compared to those of age-matched healthy controls ($P<0.05$). Among the four, the ADC of Cho showed highest level change. Despite the fact that the two patient groups were not age-matched, it is obvious that the ADCs of metabolites in acute MELAS patients were significantly higher than those in acute stroke patients (Fig.2).

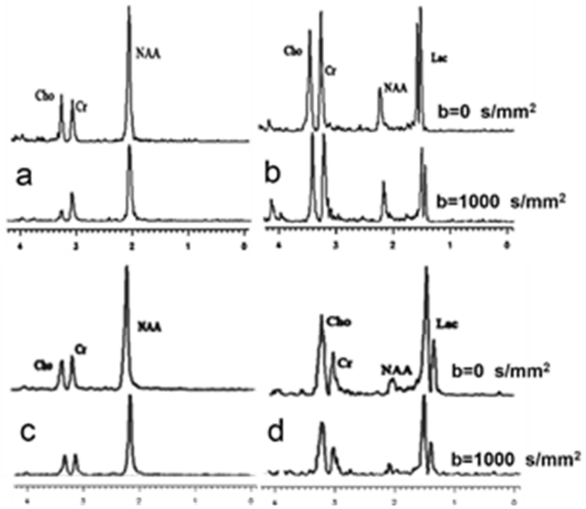

Fig.1 Spectral plots of ROIs without and with diffusion weighting for (a) healthy volunteer group1 (b) acute MELAS patient (c) healthy volunteer group 2 (d)acute stroke patient.

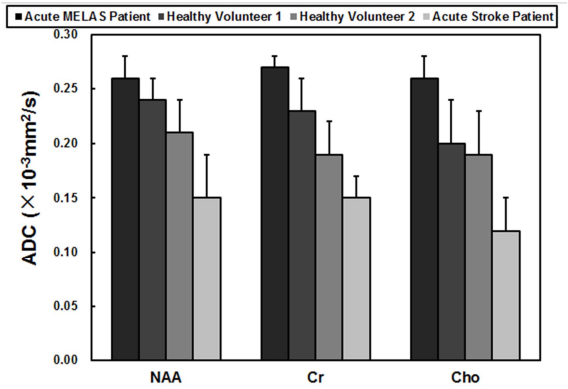

Fig.2 Mean metabolite ADCs for regions of interest across subjects with acute MELAS and stroke and the healthy volunteer groups, respectively.

Discussion and Conclusion Cho concentration in astrocytes was twice that of neurons [3], the increased ADC of Cho suggests that the astrocytes may also be involved in the pathologic changes of MELAS. Degeneration pycnosis neurons, mitochondrial swelling and the neurons with strange shapes can be found in the acute stage of MELAS [4], which lead to increased ADC of the metabolites. The percentage of shrunken neurons in the lesion increases and the sizes of these neurons decrease within the development of the acute stroke [5], which leads a decrease of the metabolites ADC. DW-MR spectroscopy was demonstrated to be able to differentiate MELAS from the stroke in the acute stage, and may be a viable tool to reveal the intracellular pathophysiologic information.

Reference

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[2] de Toledo M, et al. Rev Neurol. 2001
[3] Hajek M, et al. Eur J Radiol 2008
[4] Gilchrist JM, et al, Stroke 1996
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Table 1 ADCs of metabolites in the patients and health volunteers

Population	Age	n	NAA	Cr	Cho
Acute MELAS Patient	12-35	8	0.26±0.02	0.27±0.01[a]	0.26±0.02[a]
Healthy control 1	11-38	11	0.24±0.02	0.23±0.03[a]	0.20±0.04[a]
Healthy control 2	41-71	15	0.21±0.03[b]	0.19±0.03[b]	0.19±0.04[b]
Acute Stroke Patient	48-62	12	0.15±0.05[b]	0.15±0.06[b]	0.12±0.03[b]

[a]$P<0.05$. (Two-sided, unpaired and unequal variance)
[b]$P<0.05$. (Two-sided, unpaired and unequal variance)