AGING-RELATED CHANGES IN APPARENT DIFFUSION COEFFICIENT VALUES OF THE CEREBRAL METABOLITES USING DIFFUSION WEIGHTED MR SPECTROSCOPY

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Introduction:

The aging process is characterized by physiological changes which impair numerous organs and systems, especially their functions [1]. Diffusion weighted magnetic resonance spectroscopy (DW-MRS), which introduces pairs of diffusion gradients to MRS, is of fundamental interest because it allows evaluation of the intrinsic diffusion properties of the metabolites, which is more relevant for the understanding of pathphysiological process [2]. With the rapid development of imaging technology, significant change due to aging effect in the apparent diffusion coefficient (ADC) of total cerebral creatine/phosphocreatine (tCr) has been obtained from previous research with animal models [3]. The purpose of this study was using DW-MRS to reveal the aging-related changes in diffusion of metabolites in human brain in vivo.

Methods:

Thirty-six healthy volunteers (24 males and 12 females) were recruited for this study. As the rate of brain shrinkage accelerates most obviously after about age 50 [4], the dividing line of the two age groups in this study is set at 50. Group #1 was consisted of twenty-five volunteers (mean age 27±8.5 years, range 20 - 50 years) and group #2 was consisted of eleven volunteers (mean age 61±7.9 years, range 51–73 years). All subjects gave their informed consent which was approved by the Investigational Review Board at our hospital. The DW-MRS sequence based on point resolved spectroscopy (PRESS) sequence technique was implemented for this study. The equipment used for the MR examinations was a 3.0T clinical whole-body system (Signa EXCITE HD; General Electric, Milwaukee, WI) with gradients with a maximum amplitude 40 mT/m and a maximum slew rate 150 mT/m/ms. Parameters for the proton MRS PRESS were as follows: TR 2000 ms, TE 144 ms, voxel size 2×2×2 cm^3 (8 mL), spectral width 5000 HZ, and data points 4096. Data were acquired at only two different b-factor values: 45 and 1050 s/mm^2. The voxel location for proton MRS and the spectrum were shown in Fig 1.a. The total measurement time for a set of DW-MRS series was about 8 min. Post-spectral processing was carried out by SAGE software (GE Medical Systems). Pure water subtraction was used to reduce residual water from each suppressed frame. Because free induction decay (FID) signal varies with phase shift, the phase correction of individual data traces was used to restore phase coherence and avoid signal loss [5]. Phase corrections were performed before the summation of FIDs. Since the integral peak area was more sensitive to the random noise [5], peak height was used to determine the signal intensity of metabolites in this study. The ADC value was estimated by the following equation:

$$ADC=-\ln\left[S(b_2)/S(b_1)\right]/(b_2-b_1) \quad (1)$$

Where S (b_1), and S (b_2) are the signal intensities for the two b-values, b_1 and b_2.

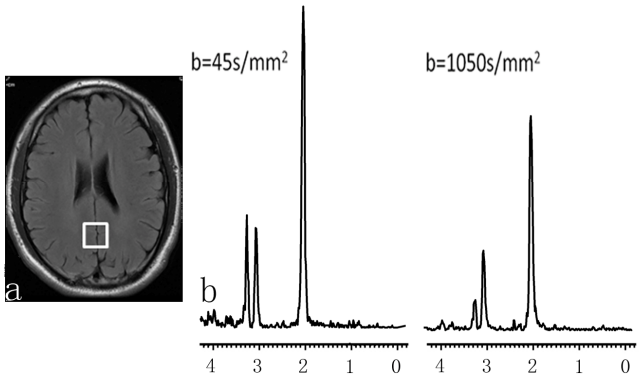

Fig.1 The brain region that was examined and two sample spectra a) Brain region of examination: a 2.0×2.0×2.0= 8cm^3 voxel located in the occipital gray matter (OGM region), b) A sample spectrum taken at low (45 s/mm^2)and high (1050 s/mm^2) b-values from the occipital gray matter.

Table 1: ADCs of metabolites in the health volunteers' brain of different ages

Subject	Age（Y）	n	ADC (mean±SD, ×$10^{-3}$$mm^2$/s)		
			NAA	tCr	Cho
Group #1	20-50	25	0.19±0.06**	0.20±0.05**	0.18±0.06**
Group #2	51-73	11	0.15±0.04**	0.14±0.04**	0.12±0.02**

Statistically significant differences relative to controls: **P <0.01. (Two-sided, unpaired and unequal variance)

Results:

A typical spectrum of the volunteers in this study was given in Fig 1.b. The ADCs of three major metabolites, including choline-containing compounds (Cho), tCr, N-acetyl-aspartate (NAA), in healthy volunteers at different age groups were shown in Table 1. The DW-MRS data revealed an approximately 33.3% decrease ($p<0.01$) in the Cho ADC for group #2 in comparison with group #1. The metabolite signals NAA and tCr show a 21% ($p<0.01$) and 30% ($p<0.01$) decreased in ADC values.

Discussion:

Results show that there were statistically significant differences in ADCs of metabolites between the two different age groups. In fact, previous vivo examination had shown the obvious aging associated changes in geometric shape, gray matter (GM) volume on cortical surface and morphological of neuron. And it had demonstrated a decline in the total brain volume, gray matter volume, cortical thickness, and the surface area of sulcus region due to the increase of apoptotic cell number. [7-9]. Furthermore, it had also been found that all morphometric measures were significantly reduced during aging, in terms of the total dendritic length, total dendritic surface area, total volume, dendritic spine numbers and densities, and dendritic diameter [10]. Therefore, the results of this study could be explained with following explanations: the volume of the apoptotic cell is less than that of the normal cell, and these changes in dendritic morphology may decrease neuronal space, therefore the metabolites in the apoptotic neuron have a smaller diffusion space than those in the normal neuron, leading to lower ADCs of metabolites in elderly people.

Conclusions:

In this study, we demonstrated that the ADC values of the cerebral metabolites of the health people had a significant change in elderly people. The DW-MRS should be helpful to evaluate aging-related changes in the intracellular environment in vivo. These results also indicated that the effect of aging should be taken into account when analyzing the diffusion of brain metabolites by using DW-MRS.

References:

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