Proton Magnetic Resonance Spectroscopic Imaging in Mild Cognitive Impairment

A. Horska[1], C. Munro[2], A. Arslanoglu[1], J. Brandt[2], P. Barker[1]

[1]Department of Radiology, Johns Hopkins University, Baltimore, MD, United States, [2]Department of Psychiatry and Behavioral Sciences, Johns Hopkins University, Baltimore, MD, United States

INTRODUCTION

Mild cognitive impairment (MCI) may be viewed as a preclinical condition to Alzheimer's disease. Since it is possible that neuropathologic changes to brain tissue may be present many years before any clinical symptoms occur, early detection of preclinical disease is of great importance. In vivo single voxel proton magnetic resonance spectroscopy (^{1}H MRS) detected biochemical abnormalities in patients with MCI (1-4), including elevated ratio myo-inositol/creatine (mI/Cr) and decreased ratio N-acetyl aspartate (NAA)/Cr. However, the published results are somewhat discordant in terms of detection and location of metabolic abnormalities. To evaluate the extent of metabolic abnormalities and to identify brain regions with abnormal metabolism in MCI subjects, we employed multi-slice high-resolution ^{1}H magnetic resonance spectroscopic imaging (MRSI). We hypothesized that in MCI subjects a) the metabolite ratios involving the neuronal marker NAA will be low, b) metabolic abnormalities will be more pronounced in older subjects, and c) lower metabolite levels will be associated with impaired neuropsychological performance (in particular on tests of memory, attention, motor speed, and verbal ability).

MATERIAL AND METHODS

We examined 8 subjects (4 men) with a clinical diagnosis of MCI, aged 65 – 80 years. Twenty healthy elderly adults over age 65 years (10 men, age range 65 – 87 years) comprised the control group (5).

Routine brain MRI and ^{1}H MRSI were performed at 1.5 Tesla. ^{1}H MRSI was performed using a multi-slice spin-echo sequence with outer volume suppression (6), with TR/TE=2300/280 ms and nominal voxel size 0.8 ml. Four supratentorial oblique slices were measured with a 15 mm thickness and a gap of 2.5 mm. Metabolite ratios NAA/Cho, NAA/Cr, and Cho/Cr were evaluated from both hemispheres in the following regions: hippocampal and parahippocampal regions, midbrain, temporal cortex and temporal white matter, thalamus, putamen, insula, dorsolateral frontal cortex, visual cortex, premotor/motor white matter, parietal white matter, posterior prefrontal cortex, inferior parietal cortex, medial premotor cortex, motor cortex, and dorsal parietal cortex.

The results of the following tests were included in the analyses: Hopkins Verbal Learning Test-Revised (total learning), Trail Making Test (parts A and B), and Verbal Fluency (combined parts S and P; animal and supermarket). Ratios NAA/Cho and Cho/Cr were used in these analyses.

Statistical analyses were performed using ANOVA with the Fisher's PLSD method as a post-hoc test. Regression analysis was applied to examine the effect of age on metabolite ratios and the relationship between the neuropsychological test scores and metabolite ratios. Statistical significance was set to $p<0.05$. Data are presented as means (and standard deviations).

RESULTS

High resolution spectra were obtained in all subjects. An example of a spectrum of the hippocampus in a 73 year old man with MCI is shown in Fig. 1. No differences in average regional metabolite ratios NAA/Cr, NAA/Cho and Cho/Cr between MCI and control groups were detected (Table 1).

Mean NAA/Cr (averaged from 17 regions) decreased linearly by 13% ($p<0.07$) over the examined age range (22 years) with no difference between groups (Fig.2, note data overlap of three MCI subjects aged 80.3 years). The relationship between NAA/Cho and age was best modeled by a second order polynomial function ($p<0.05$), with relatively stable levels between the ages 65-72 years and a 14% average decrease over the following 15 years.

No significant relationship between the test scores of Hopkins Verbal Learning Test and ratios NAA/Cho or Cho/Cr in the left hippocampal region were detected. While the performance on the Trail Making Tests A and B improved with increasing ratio NAA/Cho in the white matter (premotor/motor and parietal) of control subjects ($p<0.05$), no improvement was detected in MCI. Verbal Fluency (animals, supermarket) test scores decreased in both groups with increasing white matter Cho/Cr (average data from premotor/motor and parietal regions, $p<0.04$). However, the scores were higher in the control group ($p<0.005$) (Fig.3). No significant relationship between Verbal Fluency (part S, P) test scores and metabolite ratios was detected.

Fig. 1 ^{1}H MR spectrum of the hippocampus (73 year old MCI subject)

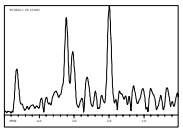


Table 1
Average metabolite ratios

	MCI	Control
NAA/Cr	2.22(0.36)	2.20(0.30)
NAA/Cho	1.75(0.32)	1.72(0.32)
Cho/Cr	1.38(0.27)	1.34(0.22)

Fig. 2

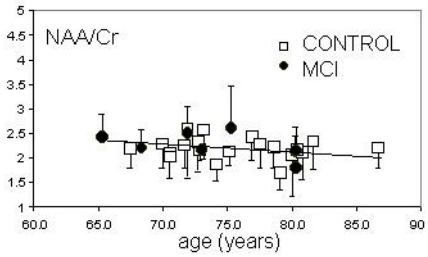
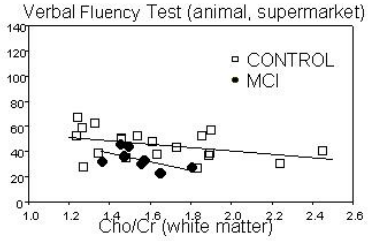


Fig.3



DISCUSSION

No differences in metabolite ratios involving the neuronal marker, NAA, between the MCI patients and control subjects were detected in our study in either gray or white matter despite use of a method providing high resolution data. In contrast, another group has reported a 4.5% lower NAA/Cr in the posterior cingulate gyrus in MCI subjects using single voxel spectroscopy (at 1.5 T with long TE) (4). However, another study by the same group (1) did not reveal any differences in NAA/Cr measured in three gray matter regions including the posterior cingulate gyrus. A lower ratio NAA/Cr (by 5.3% on average) was detected in parietal white matter of MCI patients compared to controls but the difference was not significant (2). Results of a recent longitudinal study may explain the different findings: low NAA/Cr in the occipital cortex was found to be predictive of the development of dementia (7). Our approach was sufficiently sensitive to detect small but significant age-related differences in ratios NAA/Cr and NAA/Cho, similar in both groups of subjects. Age-related differences in metabolite levels in elderly subjects were reported previously using MRSI (8); however, these were not detected by single voxel MRS (3), possibly due to lower resolution compared to MRSI methodology. An interesting observation in our study was a loss of relationship between neuropsychological test scores and metabolite ratios in the MCI group (while present in the control group) in some comparisons, or a decreased performance in the MCI group at the same metabolite levels (Fig. 3), with a similar type of relationship between the test scores and metabolite levels. To evaluate these findings, more data, preferably collected in a longitudinal study (as in ref. 7) are necessary.

REFERENCES

1. K. Kantarci et al. Neurology 55, 210 (2000). 2. M. Catani et al. NeuroReport 12, 2315 (2001). 3. K. Kantarci et al. Denent Geriatr cogn Disord 14, 198 (2002). 4. K. Kantarci et al. AJNR 24, 843 (2003). 5.A. Horská et al. Proc. Intl. Soc. Mag. Reson. Med. 10, 1318, (2002). 6.JH Duyn et al. Radiology 188, 277 (1993). 7. P. Mondrego Ann Neurol 54 (suppl 7),34 (2003). 8. N. Schuff et al. Magn Reson Med 45, 899 (2001).