Neurochemical profiling of the hippocampus in Alzheimer's disease with short echo time ^{1}H MRS

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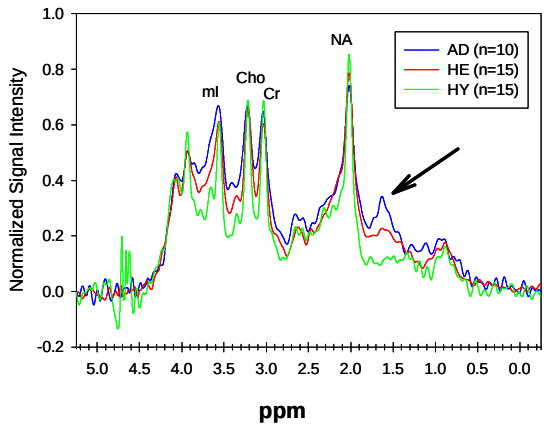
Abstract
Proton magnetic resonance spectroscopy (^{1}H MRS) holds promise in the study of Alzheimer's disease (AD). The anteromedial temporal brain regions are of particular interest because of their early involvement in the disease. This study examined short echo time data (20 ms) from the hippocampus of 10 patients with probable AD and 30 healthy adults. *Myo*-inositol concentrations were significantly higher in the AD patients compared to the healthy young adults ($p<0.05$). In addition, we observed a significant shortening of the brain water spin-spin relaxation time with AD ($p<0.01$) and age ($p<0.05$). Finally, we observed a region of large difference in signal intensity among the three groups at 1.63 ppm not previously reported in the literature.

Introduction
Alzheimer's disease (AD) is the most common form of dementia in the elderly. The clinical stages of AD correlate well with hierarchical neuropathological changes in the brain, progressing from the transentorhinal cortex to the limbic system, and finally invading the isocortex (1). The hippocampus is therefore a critical target region in AD research. Spectral distortions from strong magnetic field susceptibility gradients have limited the advancement of short echo time ^{1}H MRS in hippocampal studies. In this study, we employed a multiple inversion recovery water suppression method to minimize spectral distortions from residual water (2). This allowed us to examine hippocampal tissue in AD at TE=20 ms.

Method
Participants were 10 patients fulfilling the NINCDS-ADRDA criteria for probable AD (5 women, 5 men; mean age 75 ± 7 years) and 30 healthy volunteers (17 women, 13 men) separated into two age groups: young (mean age 21 ± 3 years, N=15), and elderly (mean age 71 ± 9 years, N=15). All spectroscopy data were collected from the right hippocampal region on a 1.5T MR system using a STEAM sequence (TE/TM/TR = 20/10/4000 ms, 128 excitations, mean voxel-of-interest ~ 6 cm^3). Metabolite concentrations were reported in millimoles per kilogram of brain water (3).

Figure 1.



Results and Discussion
Similar to previous short echo time ^{1}H MRS studies of AD (4-5), we observed elevated *myo*-inositol (mI) concentrations in the AD patients, an average increase of 17% relative to the healthy elderly adults, and 42% relative to the young adults. However, only the differences between the AD patients and the healthy young adults reached statistical significance ($p<0.05$). We also observed a significant shortening of the brain water spin-spin relaxation time with AD ($p<0.01$) and age ($p<0.05$) (6). These differences are consistent with documented age-related decreases in brain tissue water content (7-10) and suggestive of an increase in cerebral tissue density in AD.

An interesting and unexpected finding of this study was the detection of a large and previously unreported peak at 1.63 ppm (Fig. 1). The average intensity of the peak was nearly 150% greater in the AD spectra relative to spectra from the healthy young adults, and nearly 75% greater when compared to spectra from the healthy elderly adults. A search of the literature yielded no insights as to which chemical(s) might be the contributing source; although animal studies show a resonance around 1.63 ppm, the peak is unidentified (11). The high frequency of this peak, the depth of the voxel position, the specificity of the peak to AD, and its near absence in the healthy young adults' spectra, makes it highly unlikely that the peak results from lipid contamination. Additional studies are needed to determine the chemical source of the resonance, and to characterize the peak in terms of its coupling constants and relaxation rates.

References
(1) Braak H, Braak E. Acta Neuropathol 1991; 82:239-259. **(2)** Knight-Scott et al. ISMRM 9th Annual Meeting 2001, Glasgow, Scotland. **(3)** Knight-Scott J et al. Magn Reson Imaging 2003; 21:787-797. **(4)** Miller BL et al. Radiology 1993; 187:433-437. **(5)** Moats RA et al. Magn Reson Med 1994; 32:110-115. **(6)** Haley AP et al. Neurosci Lett 2004; 362:167-170. **(7)** Bondareff W, Narotzky R. Science 1972; 176:1135-1136. **(8)** Desbordes P, Cohadon F. J Gerontol 1987; 42:655-659. **(9)** Chang L et al. Life Sci 1996; 58:2049-2056. **(10)** Zs.-Nagy I. J Mol Med 1997; 75:703-71. **(11)** Pfeuffer J et al. Magn Reson 1999; 141:104-120.