

Abstract: P2-213

Citation: NeuroBiology of Aging, Volume 25, Number S2 , July 2004, Page 291

Selective Reduction of Medial Temporal Lobe NAA in Cognitively Impaired but Non-Demented Elderly Subjects

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Background: Previous MR spectroscopic imaging (MRSI) studies have shown that Alzheimers disease (AD) is associated with a characteristic pattern of diminished N-acetylaspartate (NAA) concentration in the medial temporal lobe (MTL), encompassing the hippocampus and adjacent regions (e.g., Schuff et al., 2002). Because NAA is a marker of neuronal integrity, a selective reduction of NAA in MTL could be a sign of incipient AD pathology in non-demented individuals at risk for AD. Moreover, NAA reduction is more specific to neuron loss than MRI-measured atrophy. Thus, NAA may be a more sensitive measure of AD pathology than hippocampal volume in non-demented subjects at risk for AD. **Objectives:** To determine whether cognitively impaired but non-demented (CIND) individuals at risk for dementia exhibit a similar pattern of reduced NAA in the MTL as AD patients. To compare regional NAA patterns and hippocampal volumes in CIND patients who remained stable and who subsequently become demented. **Methods:** Seventeen CIND patients with a CDR of 0.5 and clinically determined to be non-demented (mean age: 75.4; mean MMSE: 26.6) were compared with 24 AD patients meeting NINDS-ADRDA criteria for probable AD (mean age: 74.8; mean MMSE: 17.4; CDR 1), and 24 age-matched cognitively normal controls (mean age: 76.0; mean MMSE: 29.0; CDR = 0). Of the CIND patients with clinical follow-ups, 6 became demented while 6 remained stable over 3.6 years. Acquisition and processing of MRSI data have been described in Schuff et al. (2002). Data were analyzed with MANCOVAs and pair-wise group comparisons. **Conclusions:** MTL NAA was significantly reduced in CIND patients relative to controls ($p < 0.02$). In contrast, hippocampal volume and MMSE score differences were not significantly different between CIND patients and controls. CIND patients who later converted to dementia had lower MTL NAA than control subjects ($p = 0.01$) while there were no significant MTL NAA differences between stable CIND patients and controls. Together, these results suggest that MTL NAA reduction can be detected before development of dementia. Thus, MTL NAA may potentially serve as an early marker for AD.