Employing Combined Quantitative MRI and MRS Markers to Distinguish Mild Cognitive Impairment

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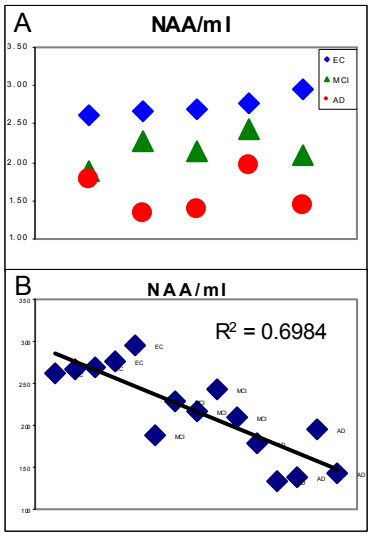
BACKGROUND: Atrophy is the key component in Alzheimer pathology in that it precedes functional decline to dementia [1] and quantitative MRI validate reductions in total hippocampal volume (THV) as biomarkers for progressive mild cognitive impairment (MCI) to Alzheimer's disease (AD) [1]. Quantitative MR spectroscopy (MRS) has also been proposed as an AD/MCI biomarker [2]. We examine whether combining the two in a single MRI examination provide a more sensitive test with increased predictive value.

METHODS/DATA ANALYSIS: Quantitative MRI and ^{1}H MRS were performed on 55 consecutive elderly (age 60-90) subjects (AD n=5, MCI n=5, elderly controls (EC) n=45) and 10 young normal controls (Table 1). Short echo time (TE) MRS employing a 8cm^3 voxel acquired in the posterior cingulate gyrus grey matter assayed (N-acetylaspartate (NAA) and glial marker myo-inositol (mI)), expressed as NAA/mI. Volumetric analyses using 3D-MRI and FreeSurfer [3]. MMSE and neuropsych were applied and a subset of 15 subjects (5 NC, 5 MCI and 5AD) used to test the sensitivity of combining hippocampal volume and NAA/mI.

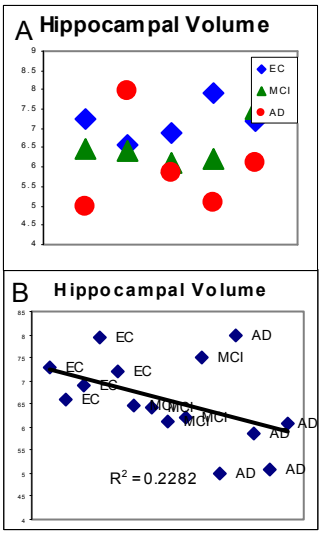
Table 1. Subject Demographics.

	Age	NAA/mI	THV (cm^3)
Young (n=10)	20.4 ± 3.5	2.79 ± 0.3	9.16 ± 0.8
Elderly (n=45)	75.4 ± 6.1	2.32 ± 0.3	7.23 ± 0.9
MCI (n=5)	78.8 ± 4.4	2.17 ± 0.2	6.54 ± 0.6
AD (n=5)	73.6 ± 8.4	1.58 ± 0.3	6.00 ± 1.2

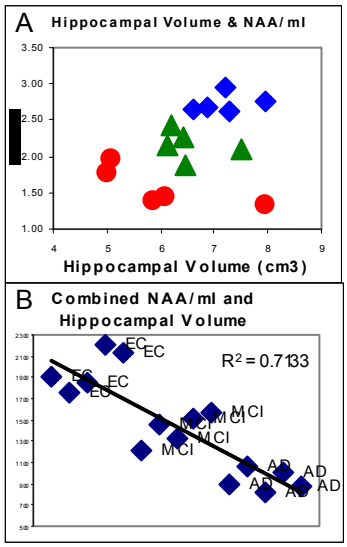
RESULTS: NAA/mI ratios were significantly different between AD (n=5) and MCI (n=5) ($p = 0.005$), MCI and EC (n=5) ($p = 0.001$) and AD compared to EC ($p < 0.001$) (Figure 1A and B). Hippocampal volumes alone were not significantly different (Figure 2A and B). When total hippocampal volume and NAA/mI are combined (Figure 3A and B), results showed significant linear correlations ($R^2 = 0.71$, $p<0.01$) and MCI subjects were easily distinguishable from EC and AD.



Figures 1A + B. Scatter (A) and statistical (B) plots of NAA/mI.



Figures 2A + B. Scatter (A) and statistical (B) plots hippocampal volumes.



Figures 3A + B. Combining the two measures easily distinguishes MCI from AD or elderly controls in scatter plot (A) and shows strong correlation (B).

CONCLUSION: Volumetric measurement of the hippocampus strongly correlates with 1H MRS markers, even when, for technical reasons, MRS is acquired in a different region: we infer that loss of neurons (decrease in NAA/Cr) contributes to atrophy and the shrinking of the hippocampus. Thus, as hypothesised (5), quantitative MRI and MRS, when combined provide improved biomarkers over either alone in clinical diagnosis of MCI. Longitudinal studies will likely predict disease progression, contributing to improvements in AD- drug discovery as cost-effective biomarkers significantly reduce 'group-sizes'.

REFERENCES: (1) Heister et al. Neurology 2011; 77: 1619-1628. (2) Kantarci. BJR 2007; 80:S146-S152. (3) Freesurfer software program. http://surfer.nmr.mgh.harvard.edu/. Martinos Center for Biomedical Imaging, Harvard University. (4) Tran ISMRM 2010 p.

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