

groups. **Conclusions:** The patterns of atrophy on MRI in typical AD and PCA differ. The right hemisphere dominance, prominent involvement of the primary visual and visual association cortex, and sparing of the left hippocampus in PCA, suggest that it should be considered a distinct entity from typical AD.

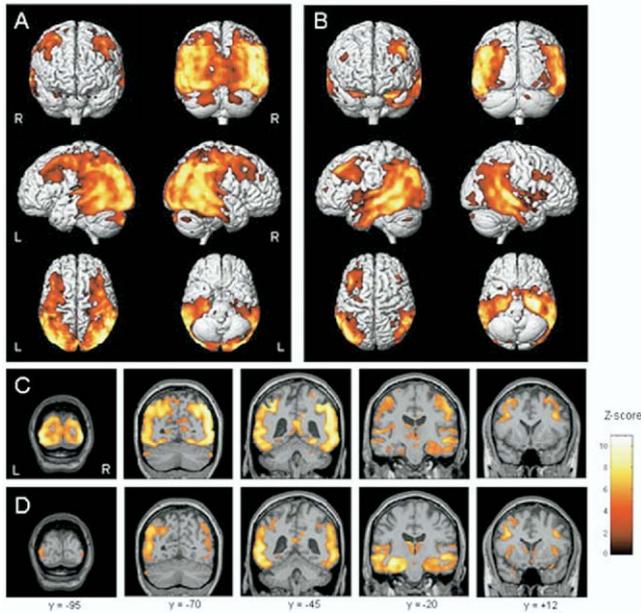


Figure: Grey matter atrophy in PCA (A and C) and AD (B and D), compared to healthy controls (corrected for multiple comparisons,  $p < 0.05$ ). Results have been overlaid both on a 3D surface render (A and B) and on representative coronal MRI slices (C and D) from a healthy control. Warmer colors indicate statistically greater differences between groups.

P2-349

#### ANALYSIS OF METABOLITE LEVELS AND RATIOS IN AGE MATCHED CONTROLS, MILD COGNITIVE IMPAIRMENT, AND ALZHEIMER'S DISEASE CONVERTERS USING $^1\text{H}$ MAGNETIC RESONANCE SPECTROSCOPY

Claudius Mueller, Brenda L. Bartnik, Sanjay Patra, Waheed Baqai, Floyd Petersen, Barbara A. Holshouser, Wolff M. Kirsch, Loma Linda University, Loma Linda, CA, USA. Contact e-mail: [cmueller@llu.edu](mailto:cmueller@llu.edu)

**Background:** Recent advances in clinical therapies require early identification of biomarkers distinguishing those patients with an increased risk of developing Alzheimer's disease (AD).  $^1\text{H}$  magnetic resonance spectroscopy (MRS) enables non-invasive measurement of metabolites. Previous studies have shown differences in metabolite ratios between control patients and those with mild cognitive impairment (MCI). **Objective:** The objective of this study was to compare the baseline metabolite levels and ratios in control and MCI subjects as part of a larger, ongoing sequential MRS study that documents possible relationships between cerebral metabolites and neuropsychological status. **Methods:** To date 28 control and 76 MCI subject participants have enrolled in this study. Of the 76 MCI participants, 14 have progressed cognitive impairment. Single voxel  $^1\text{H}$  MRS of the posterior cingulate gyrus was performed at 1.5T using a stimulated echo acquisition time (STEAM, TE = 20ms) sequence. Concentrations of NAA, choline (Cho), Cr, inositol (Ins) and glutamate-glutamine (Glx) were measured using a linear combination model (LCModel) routine, corrected for cerebrospinal fluid (CSF) contamination using tissue segmentation analysis and metabolite ratios calculated. Statistical significance ( $p < 0.05$ ) was determined using ANOVA with post-hoc Bonferroni statistical analysis. **Results:** The concentration of NAA was significantly reduced in the posterior cingulate gyrus of both the MCI subject ( $p = 0.001$ ) and progressive MCI subject ( $p = 0.04$ ) groups compared to controls. The Ins/NAA metabolite ratio was increased in the combined MCI subject ( $p = 0.004$ ) and progressive MCI subject ( $p = 0.008$ ) group

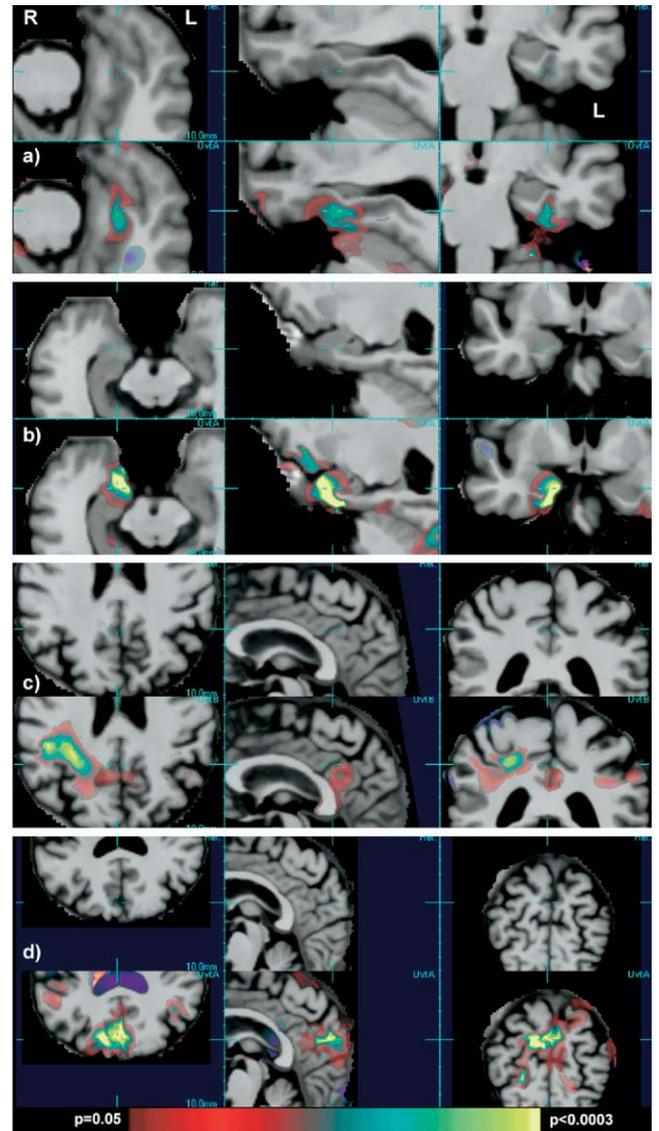
compared to controls. A significant increase ( $p = 0.03$ ) in the Cho/Cr metabolite ratio was observed in the progressive MCI group alone. **Conclusions:** Changes in the metabolite ratios are consistent with known cellular changes, specifically neuronal loss or dysfunction, the activation of glial cell populations and the turnover of cellular membranes. We are currently reviewing associations between magnetic resonance imaging and psychometric examination data for relationships that have not been previously documented.

P2-350

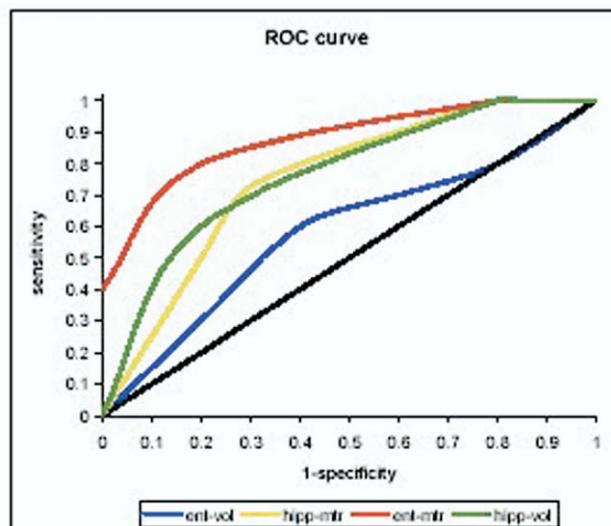
#### REGIONS OF BRAIN ATROPHY THAT PREDICT COGNITIVE DECLINE

Valerie A. Cardenas, Linda L. Chao, Colin Studholme, Shannon T. Buckley, Nathan M. Cashdollar, Norbert Schuff, Michael W. Weiner, San Francisco VA/University of California, San Francisco, CA, USA. Contact e-mail: [valerie@itsa.ucsf.edu](mailto:valerie@itsa.ucsf.edu)

**Background:** Previous studies have shown that brain atrophy predicts conversion to dementia, but investigated limited brain regions and measures of cognition. **Objective:** To determine the spatial pattern of brain atrophy at baseline associated with future cognitive decline. **Methods:** 3D T1-weighted MRI and neuropsychological testing were obtained from 38 subjects with mild cognitive impairment ( $78 \pm 6$  yrs of age, 16 women, MMSE  $28.3 \pm 1.5$ ) and 7 controls ( $71 \pm 4$  yrs, 3 women, MMSE  $29.6 \pm 0.9$ );



neuropsychological testing was repeated after 1 year. We applied deformation based morphometry [1] and investigated the relationship between brain structure at baseline and future cognitive decline. Baseline deformation maps were dependent variables in regression analyses, and independent variables included annualized cognitive change, cognitive score at baseline, head size, age, and group. Separate regressions were computed for change in MMSE, CDR, and for the following California Verbal Learning Test subtests: short and long delay cued recall (SDCR and LDCR), and immediate and short delay free recall (IDFR and SDFR). **Results:** The figure (right brain is image left) shows T-statistic maps overlaid on the group average spatially normalized MRI. A negative association between structure and cognitive change on SDCR is shown in (a), where reduced tissue volumes in the left ERC at baseline are associated with greater performance decline. Smaller tissue volumes in the hippocampus at baseline were also related to greater declines in SDCR, as shown in (b). Associations between structure and LCDR were similar. Panel (c) shows reduced tissue volume in the posterior cingulate cortex at baseline is associated with greater decline in SDFR; adjacent white matter and left ERC were also implicated. These regions were less significantly associated with decline on IDFR. Smaller volumes of frontal and parietal white matter at baseline were associated with MMSE decline. Future declines in CDR were related to smaller baseline volumes of frontal and parietal lobes, particularly in the precuneus region (d). **Conclusions:** Deformation morphometry reveals focal brain atrophy on MRI that predicts future cognitive decline, and may allow earlier and more precise separation of normal aging from early Alzheimer's disease. [1] C. Studholme et al, NeuroImage, Vol 21 (2004), pp 1387-1398.



	Area	Std. Error	Asymptotic Sig.
hipp-mtr	.720	.092	.045
ent-mtr	.812	.091	.004
hipp-vol	.752	.085	.021
ent-vol	.554	.113	.622

**P2-351**      **ROLE OF MAGNETIZATION TRANSFER IMAGING IN EARLY DIAGNOSIS OF ALZHEIMER'S DISEASE**

Noor Jehan Kabani<sup>1</sup>, Adrienne Dorr<sup>1</sup>, John G. Sled<sup>2</sup>, Howard Chertkow<sup>3</sup>, <sup>1</sup>Sunnybrook and Women's College Health Sciences Centre, Toronto, ON, Canada; <sup>2</sup>Hospital for Sick Children, Toronto, ON, Canada; <sup>3</sup>Lady Davis Institute, Montreal, PQ, Canada. Contact e-mail: nkabani@sten.sunnybrook.utoronto.ca

**Background:** Elderly individuals who suffer from significant memory impairment in the absence of decline in functional and intellectual ability are classified as having mild cognitive impairment (MCI). The cognitive condition of such individual may either remain stable (MCIs) or may decline further (MCI progressors or MCIP), leading to the diagnosis of Alzheimer's disease (AD). **Objective:** This research focuses on the use of magnetization transfer (MT) imaging for early diagnosis of dementia. **Methods:** In a longitudinal study where 35 MCI subjects were scanned and clinically followed for two years, we found that MT measurement was more reliable in differentiating MCIP from MCIs. In this study 10 out of 35 MCI developed AD over a two year interval. Time 1 volumetric and MTR was used to create receiver operating characteristic (ROC) curves of the hippocampus and entorhinal cortex. Compared to volume, the MTR was found to be a better parameter in discriminating between MCIP to MCIs. **Results:** Using an MTR of 31.4% as a cut-off for the entorhinal cortex, the accuracy of correct classification, sensitivity and specificity of the measure was 80% each. A positive likelihood ratio of 4 suggested that subjects with an MTR of 31.4% or lower were four times more likely to develop the disease, whereas the negative likelihood ratio was 0.25. In contrast, an 80% sensitivity of hippocampal volume resulted in 52% specificity and 60% accuracy in differentiating the two sub-groups of MCI. Additionally the positive likelihood ratio for hippocampal volume as a diagnostic factor was 1.67. **Conclusions:** Compared to volumetric measurement which is labor intensive, these findings show that MTR produces better results in differentiating MCIs from MCIP whether the MTR of the entire structure is measured or only 20 randomly selected voxels in the region of interest.

**P2-352**      **VOXEL-WISE ANALYSIS OF AMYLOID DEPOSITION IN EARLY-STAGE ALZHEIMER'S DISEASE AND RELATIONSHIP WITH COGNITIVE MANIFESTATIONS**

Natalie Nelissen, Patrick Dupont, Mathieu Vandenbulcke, Koen Van Laere, Guy Bormans, Alfons Verbruggen, Luc Mortelmans, Rik Vandenberghe, K.U. Leuven, Leuven, Belgium. Contact e-mail: Natalie.Nelissen@med.kuleuven.be

**Background:** Postmortem studies have shown a relatively poor correlation between global or regional measures of neuritic amyloid deposition and cognitive dysfunction ante mortem. **Objective:** We examined whether in vivo amyloid imaging in early-stage clinically probable Alzheimer's disease (AD) reveals a more robust relationship. **Methods:** 12 early-stage AD patients (MMSE > 21, mean 23, sd 2; age: mean 71, sd 5) and 11 matched elderly volunteers received a Pittsburgh Compound B PET scan. Quantification using a Logan analysis with cerebellar cortex as a reference region resulted in parametric maps of volume of distribution ratios (DVR). DVR-maps of patients and controls were compared using a two-sample t-test in SPM (voxel-level  $p_{uncorrected} < 0.001$ , cluster-level  $p_{corrected} < 0.05$ ). All participants completed a standard neuropsychological protocol. A factor analysis of the neuropsychological data yielded 3 factors. The first factor (eigenvalue 8.16) clustered Raven's color progressive matrices ( $r=0.87$ ), Trail Making test ( $r=-0.85$ ), Token test ( $r=-0.72$ ), and Boston Naming test scores ( $r=0.71$ ). Factor 2 (eigenvalue 1.44) clustered Auditory Verbal Learning test total learning ( $r=0.74$ ), long-term percentage recall ( $r=0.83$ ), delayed recall ( $r=0.78$ ) and recognition ( $r=0.88$ ) scores. Factor 3 (eigenvalue 1.03) consisted of the verbal associative-semantic task of the Psycholinguistic Assessment of Language Processing in Aphasia (PALPA) ( $r=0.87$ ). The factor scores were entered as regressors in a multiple linear regression analysis with local DVR-values or global amyloid load (sum of all DVR values in the brain) as outcome measure. **Results:** At a stringent statistical threshold, patients showed extensive amyloid deposition in bilateral anterior inferior temporal gyri compared to controls (58, 4, -46,  $Z=4.01$ ; 48, 34, -26,  $Z=3.69$ , extent 2761  $2x2x2$  mm<sup>3</sup> voxels,  $p=0.009$ ;