

into head, body and tail. From the segmented areas the volumes were calculated. All volume measurements were normalized for variations of intracranial volume. **Conclusions:** Of the 20 controls, one progressed to CI classification, as determined by standard clinical procedures. During this same time period (one year), eleven of the 22 CI subjects converted to AD. Using a clinical threshold of 10% change in volume, the subsegmentation method (12%) was more sensitive to change in volume as compared to the traditional total volumetric method (7%). Given these differences, the subsegmentation method should be further validated as a simple, non-invasive tool for the early detection of clinically significant changes in the hippocampus.

P-090

PATTERNS OF GRAY AND WHITE MATTER ATROPHY IN THE FRONTAL AND TEMPORAL LOBES IN FTD, SD, AND AD PATIENTS.

Linda L. Chao^{1,2}, Norbert Schuff^{1,2}, Colin Studholme^{1,2}, Howard J. Rosen¹, Maria L. Gorno-Tempini¹, Joel H. Kramer¹, Katherine P. Rankin¹, Bruce L. Miller¹, Michael W. Weiner^{1,2}; ¹UCSF, San Francisco, CA, USA; ²Magnetic Resonance Unit, San Francisco VAMC, San Francisco, CA, USA

Background: In neurodegenerative diseases with heterogenous histopathology like frontotemporal dementia (FTD) and semantic dementia (SD), the pattern of atrophy in different brain regions could be more informative in the differential diagnostic process than the amount of atrophy in a single brain region (i.e., hippocampal atrophy in Alzheimer's disease (AD)). Previous studies have used morphometric MRI analysis techniques to compare the patterns of atrophy in different neurodegenerative diseases; however, most have focused solely on gray matter (GM) atrophy. **Objective(s):** The aim of this study is to compare patterns of both gray and white matter (WM) atrophy in brain regions known to be preferentially involved in FTD, SD, and AD. **Methods:** Seventeen FTD patients, 12 SD patients, and 19 AD patients were studied with structural MRI. High-resolution, T1-weighted images were segmented into GM and WM and the volumetric data were analyzed with MANCOVAs. **Conclusions:** Relative to AD patients, FTD patients had less frontal GM and WM in both hemispheres ($p < 0.001$ for left frontal GM and WM; $p < 0.0001$ for right frontal GM and WM) while SD patients had less frontal GM in the left hemisphere ($p < 0.05$). The volume of the temporal lobe was reduced in both hemispheres in SD relative to AD patients ($p < 0.0001$ for left temporal GM and WM; $p < 0.05$ for right temporal GM; $p < 0.001$ for right temporal WM) while only the right temporal lobe volume differed between FTD and AD patients ($p < 0.05$ for right temporal GM and WM). Compared to each other, FTD patients had less right frontal lobe volume ($p = 0.01$ for GM and WM) while SD patients had less left temporal lobe volume ($p < 0.0001$ for GM and WM). Unlike the frontal and temporal lobes, there were no hippocampal volume differences between FTD, SD, and AD patients. Although FTD and SD have traditionally been associated with GM alterations, these results imply that a similar pattern of atrophy exists in the WM as in GM in these diseases. Further studies are needed to determine whether the WM atrophy observed in this study is indicative of general neuritic dystrophy involving both neuronal cell bodies and axons or Wallerian degeneration.

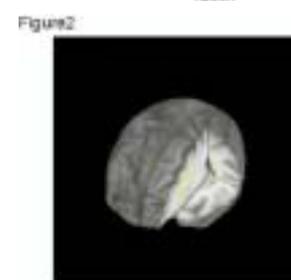
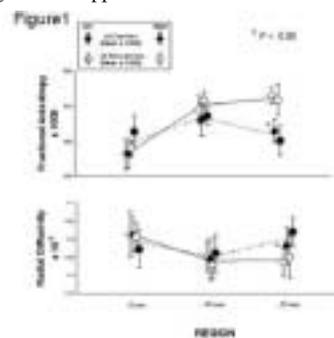
P-091

PARAHIPPOCAMPAL WHITE MATTER ABNORMALITIES IN APOE E4 CARRIERS WITHOUT VENTRICULAR ENLARGEMENT

Jay Nierenberg^{1,2}, Nunzio Pomara^{1,2}, Matthew J. Hoptman^{1,2}, Babak A. Ardekani^{1,2}, John Sidtis^{1,2}, Kelvin O. Lim³; ¹Nathan S. Kline Institute for Psychiatric Research, Orangeburg, NY, USA; ²New York University School of Medicine, New York, NY, USA; ³University of Minnesota School of Medicine, Minneapolis, MN, USA

Background: APOE $\epsilon 4$ is an important risk factor for late-onset sporadic Alzheimer's disease (AD). No neuroimaging markers are available for the preclinical diagnosis of AD. Disrupted white matter (WM) organization in AD has been supported by Diffusion Tensor Imaging (DTI) studies. **Objective(s):** To detect preclinical WM pathology in healthy elderly APOE $\epsilon 4$ carriers using

DTI. **Methods:** All participants (aged 60-77) were medically healthy with CDR=0 and MMSE scores ≥ 28 . 14 $\epsilon 4+$ and 15 $\epsilon 4-$ participants were group-matched for age and education. Imaging was conducted at 1.5 T. T₁-weighted, dual-echo and DTI images were collected using published sequences. Blind to genotype, graphical ROIs were applied to maps of fractional anisotropy (FA), trace, axial and radial diffusivity (DRa) in the right and left WM of the parahippocampal gyrus, in slices 5mm, 10mm and 15mm below the AC-PC plane. We also normalized DTI images to those of a representative participant in standard space to perform voxelwise group comparisons and voxelwise Spearman correlations with digit span scores (which differentiated groups). Volumes of the lateral ventricles and temporal horns were measured in T₁-weighted images in a standardized orientation. **Conclusions:** ANOVA showed significant Genotype-by-Region interactions for FA and DRa. T-tests localized the FA effects to ROIs at AC-PC -15mm (FA: $P < .02$, left; $P = .07$, right; Figure2). DRa showed similar significant effects on the left and trend on the right (Figure2). Voxelwise group analysis confirmed the left-sided group difference in FA in this region. No group differences were observed for any ventricular volume, nor did DTI measures correlate with any ventricular volumes. Cognitive deficits in $\epsilon 4$ carriers were confined to reduced digit span reverse scores (DSRS). In $\epsilon 4$ carriers, voxelwise analysis showed significant positive correlations between DSRS and WM FA of the left parahippocampal, left perisylvian and left frontal language regions (Figure1). Targeting medial temporal lobe WM, where the earliest neurofibrillary pathology is thought to occur, we found WM abnormalities in APOE $\epsilon 4$ carriers without ventricular enlargement. Increased DRa may relate to early axon-sparing myelin changes in AD. DSRS correlations with WM integrity in regions relating to semantic memory processing further support the functional relevance of these results.

**P-092**

NEUROPROTECTIVE EFFECTS OF HORMONE REPLACEMENT THERAPY IN HEALTHY POSTMENOPAUSAL WOMEN: A VBM STUDY

Marina Boccardi¹, Francesca Sabatelli¹, Cristina Testa^{1,2}, Roberta Ghidoni³, Lara Gigola³, Luisa Benussi³, Giuliano Binetti³, Giovanni B. Frisoni^{1,4}; ¹LENITEM, IRCCS San Giovanni di Dio-FBF, Brescia, Italy; ²Machine Vision Laboratory, Department of Mathematics and Computer Science, University of Udine, Udine, Italy; ³Laboratory of Neurobiology, IRCCS San Giovanni di Dio-FBF, Brescia, Italy; ⁴AFaR, Rome, Italy

Background: Estrogens are known to have protective effects on cognitive function in human, and on neurodegeneration in animal models. Data about