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, noninvasive 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.

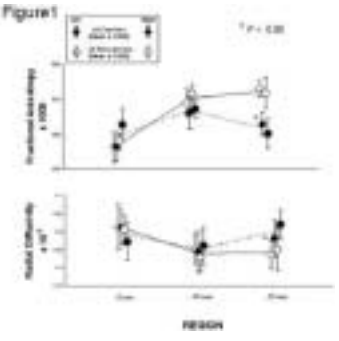
Linda L. Chao[1,2], Norbert Schuff[1,2], Colin Studholme[1,2], Howard J. Rosen[1], Maria L. Gorno-Tempini[1], Joel H. Kramer[1], Katherine P. Rankin[1], Bruce L. Miller[1], Michael W. Weiner[1,2]; *[1]UCSF, San Francisco, CA, USA; [2]Magnetic Resonance Unit, San Francisco VAMC, San Francisco, CA, USA*

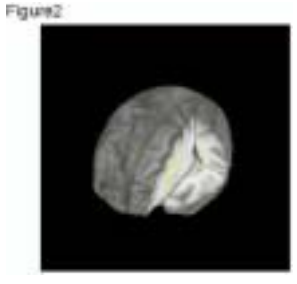
Background: In neurodegenerative diseases with heterogenous histopathology like frontotemporal dementia (FTD) and semantic dementia (SD), the pattern of atrophy in different brain regions could be more informative in the differential diagnostic process than the amount of atrophy in a single brain region (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 know 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-weighed 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. Lim[3]; *[1]Nathan S. Kline Institute for Psychiatric Research, Orangeburg, NY, USA; [2]New York University School of Medicine, New York, NY, USA; [3]University of Minnesota School of Medicine, Minneapolis, MN, USA*

Background: APOE ϵ4 is a 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 ϵ4 carriers using DTI. **Methods:** All participants (aged 60-77) were medically healthy with CDR=0 and MMSE scores≥28. 14 ϵ4+ and 15 ϵ4- participants were group-matched for age and education. Imaging was conducted at 1.5 T. T_1-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 T_1-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 ϵ4 carriers were confined to reduced digit span reverse scores (DSRS). In ϵ4 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 ϵ4 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 Boccardi[1], Francesca Sabattoli[1], Cristina Testa[1,2], Roberta Ghidoni[3], Lara Gigola[3], Luisa Benussi[3], Giuliano Binetti[3], Giovanni B. Frisoni[1,4]; *[1]LENITEM, IRCCS San Giovanni di Dio-FBF, Brescia, Italy; [2]Machine Vision Laboratory, Department of Mathematics and Computer Science, University of Udine, Udine, Italy; [3]Laboratory of Neurobiology, IRCCS San Giovanni di Dio-FBF, Brescia, Italy; [4]AFaR, Rome, Italy*

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

neuroprotection on human age associated changes in vivo are lacking. **Objective(s):** To evaluate the potential effects of estrogen replacement therapy (ERT) on brain morphology in a sample of healthy postmenopausal women. **Methods:** Forty women underwent 3D high resolution MRI: 17 never treated (age 60.8±6.6), 16 with current ERT (age: 57.4±4.3), 7 with past ERT of the same duration (age 63±3.5). Voxel-based morphometry with SPM99 was used to compare women under past and current ERT to those never treated, with $p<0.001$ uncorrected. **Conclusions:** Non treated versus women with past treatment (fig 1) showed atrophy of the leftcerebellum [z, cluster size (peak coordinates): 3.74, 437 (-38, -72, -26)], of bilateral temporal [right: 3.83, 142 (58, -44, 4), left: 3.58, 27 (-54, -8, 28)] and right orbitofrontal cortex [3.68, 123 (38, 42, 14)]. Non treated versus women with current treatment (fig 2) showed a similar pattern, but mainly limited to the right hemisphere: right orbitofrontal cortex [4.06, 178 (32, 38, -14)], right lingual gyrus and cerebellum [4.02, 209 (44, -34, -20); (32, -34, -30)], and extended to the occipital cortex [3.83, 159 (10, -98, 0)]. The use of ERT was associated with less regional brain atrophy, and the effect seems to be stronger in women with past treatment. The data support the view that ERT can protect against age-related neurodegeneration and cognitive decline.

Figure 1. Non treated versus women with past ERT.

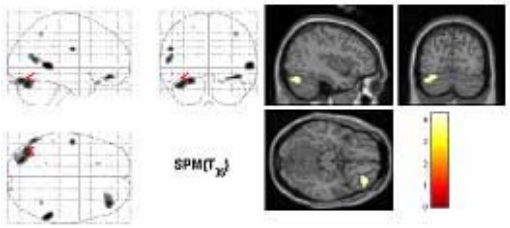
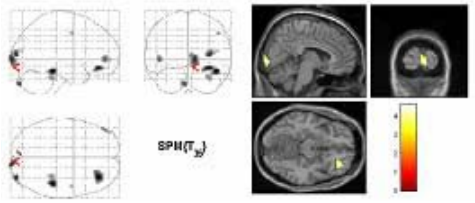


Figure 2. Non treated versus women with current ERT.

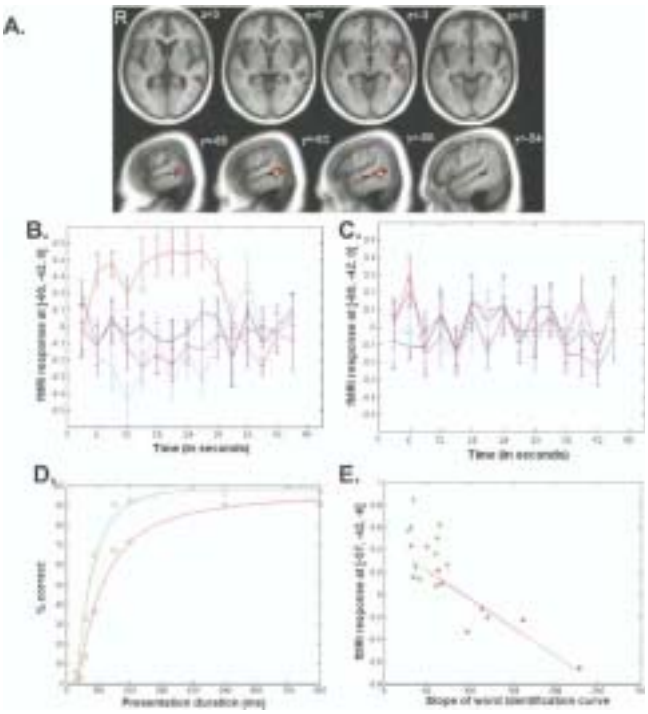


P-093

FMRI OF LANGUAGE AND SEMANTIC MEMORY IN AMNESTIC MILD COGNITIVE IMPAIRMENT

Rik vandenberghe[1], Mathieu Vandenbulcke[2], Ronald Peeters[3], Paul Vanhecke[3]; *[1]UZ Gasthuisberg, Leuven, Belgium; [2]Cognitive Neurology Laboratory KU Leuven, Leuven, Belgium; [3]Radiology Department, UZ Gasthuisberg, Leuven, Belgium*

Background: Language and semantic memory are impaired early in the disease course of AD. **Objective(s):** To determine whether sub-clinical changes of the system for language and semantic memory occur in amnestic MCI. **Methods:** 14 patients who fulfilled the Petersen et al. criteria for amnestic MCI and 14 matched healthy controls participated in this epoch-based fMRI experiment. Experimental factors were input-modality (printed words or pictures) and task (associative-semantic or visuoperceptual judgments) (Nature, 383, 254-256, 1996). In a separate psychophysical experiment we determined time-accuracy curves for word reading and picture naming in 10 of the MCI patients and 10 of the controls, with stimulus durations varying between 30 and 800 ms. Onset (a), steepness of slope (b) and asymptote (c) of the time-accuracy curves were determined mathematically. Using SPM02 and random effects analysis, we analysed the fMRI data for interaction effects between group and task and for correlations between the psychophysical parameters (a,b,c) of the time-accuracy curves and fMRI response amplitude. The left posterior middle temporal gyrus (Fig. A) showed a significant group by task interaction (-60,-42,0, ext. 18, Z=4.25, corrected $P<0.05$): In controls, it was activated during the associative-semantic compared to the visuoperceptual condition with words (Fig. B red vs magenta) but not with pictures (Fig. B blue vs cyan). As a group, MCI patients failed to activate this region during the associative-semantic compared to the visuoperceptual conditions (Fig. C red vs magenta). Sensitivity and specificity of this differential activation was high (Area Under the Curve (AUC) 0.84). The slope of the time-accuracy curve during word reading (psychophysical parameter b) was significantly steeper in controls (Fig. D, green) than in MCI (Fig. D, red). Steepness of the word-reading curve in MCI correlated with the amplitude of the posterior middle temporal fMRI response (-57,-42,-6, Z=3.57; r=0.90) (Fig. E). **Conclusions:** This converging evidence points to a lexical-semantic retrieval deficit due to left posterior middle temporal dysfunction as the earliest impairment within the language and semantic memory domain in incipient Alzheimer's disease. Acknowledgments: Medical Foundation Queen Elisabeth, FWO grant G.0277.05 and by KU Leuven Research Grant 0T/04/41.



P-094

ABNORMALITIES OF REGIONAL CEREBRAL BLOOD FLOW IN SUBCLASSIFICATIONS OF MILD COGNITIVE IMPAIRMENT

Fumio Yamashita[1], Kiyotaka Nemoto[1], Toru Kinoshita[2], Shin Hidata[1], Megumi Sasaki[1], Takashi Ohnishi[3], Hiroshi Matsuda[4], Takashi Asada[1]; *[1]University of Tsukuba, Tsukuba, Japan; [2]Kodama Clinic, Shinagawa, Japan; [3]National Center Hospital of Mental, Nervous and Muscular Disorders, National Center of Neurology and Psychiatry, Kodaira, Japan; [4]Saitama Medical School Hospital, Iruma, Japan*

Background: Mild cognitive impairment (MCI) is considered to confer an increased risk of progressing to dementia and most often Alzheimer's disease (AD). Recently published results of the Current Concepts in MCI Conference suggested subclassifications for MCI (MCI-amnestic, MCI-multiple domains slightly impaired, MCI-single nonmemory domain) based on the recognized heterogeneity in the use of the term. A number of neuroimaging approaches have been applied to MCI, however, such subclassifications have not been investigated to date. **Objective:** To investi-