

tivity theory will be employed for their analysis. The long term objective is to determine whether an individual's capacity for compensatory atypical memory network activation is related to incidence of clinical dementia. **Methods:** This study forms one arm of the LAPSES study, a population-based longitudinal investigation of psychiatric, cognitive, neurological and neuroimaging characteristics of individuals with early memory complaints. Our paradigm is a 3T fMRI delayed match-to-sample task focused on episodic and spatial memory retrieval, in which the number of active visuospatial elements which define 'easy', 'moderate' and 'hard' task difficulty conditions are matched across subjects in pretesting by application of 90%, 70% and 50% performance criteria, respectively. While the active visuospatial elements vary across task difficulty, the overall number of elements is held constant by employing 'filler' stimuli, thus matching the perceptual load within subjects across the experiment. Connectivity tools employed to characterize functionally active memory-dependent networks will include Principal Component Analysis and wavelet analysis. **Results:** Preliminary functional connectivity data from 10 individuals with early memory complaints will be presented, with a focus on differential network activation when undergoing tasks of contrasting difficulty level. **Conclusions:** The significance of differential network activation with respect to task gradient will be discussed in relation to clinical neuroscience and prognosis of dementia.

P2-365 EFFECTS OF AGING ON WHOLE BRAIN GRAY AND WHITE MATTER VOLUMES AND HIPPOCAMPAL SUBFIELDS

Susanne G. Mueller, Lara Stables, Antao Du, Nathan M. Cashdollar, Norbert Schuff, Michael W. Weiner, *Center for Imaging of Neurodegenerative Diseases, San Francisco, CA, USA. Contact e-mail: smuller@itsa.ucsf.edu*

Background: Although memory is commonly affected in elderly healthy subjects, neuroimaging studies seeking for age related hippocampal volume loss have been controversial. One reason for this might be that the hippocampus is not homogenous but consists of histologically and functionally different subfields which might be differently affected by age. **Objectives:** 1. To test for global age related gray and white matter volume changes. 2. To test if hippocampal age effects are global or subfield specific. **Methods:** 45 cognitively normal controls (aged 21-85, mean 54.5 ± 17.4 , m/f: 27/18) were studied on a 4T magnet with the following sequences: 1. Volumetric T1-weighted gradient echo MRI (MPRage) resolution $1 \times 1 \times 1$ mm. 2. High resolution T2-weighted fast spin echo $0.4 \times 0.5 \times 2$ mm resolution, angulated perpendicular to the long axis of the hippocampus. The MPRage was segmented into gray (GM) and white maps (WM) which were used for optimized voxel-based-morphometry (VBM) in SPM2. The entorhinal cortex (ERC), subiculum, CA1, CA2 and CA3/4/dentate-compound were marked on the high resolution image on 5 consecutive slices using anatomical landmarks. The influence of age, gender and total intracranial volume on hippocampal subfields was tested using linear regression and regionally unbiased tests for age related GM/WM reductions were performed using SPM2. **Results:** VBM showed age related GM reductions bilaterally in hippocampus, putamen, thalamus, cerebellum, operculum, anterior and posterior cingulate and parieto-occipital and frontal cortex while WM reductions were found in corona radiata, corpus callosum, and periventricular, temporal and frontal WM. Significant negative age effects were found for ERC ($p > 0.005$) and CA1 ($p < 0.00001$) and significant age and gender effects ($p < 0.025$) for CA2 which was primarily driven by volume loss in men. Neither CA1 nor ERC volume loss were correlated with GM losses after correction for age effects. **Conclusion:** Healthy aging is associated with regionally restricted volume loss that involves cortical regions including ERC. In the hippocampus, age effects are restricted to specific subfields, notably CA1 while others, e.g. subiculum are less affected. This regionally distinct pattern of atrophic changes, particularly also in the hippocampus, may have diagnostic value for early detection of Alzheimer's disease.

P2-366 AMYLOID DEPOSITION BEGINS IN THE STRIATUM OF PRESENILIN-1 MUTATION CARRIERS FROM TWO UNRELATED PEDIGREES

William E. Klunk¹, Daniel A. Pollen², Chester A. Mathis¹, Julie C. Price¹, Majaz Moonis², Carol F. Lippa³, Keith A. Johnson⁴, Alan J. Fischman⁴, Nicholas D. Tsopelas¹, Brian J. Lopresti¹, Scott K. Ziolko¹, Wenzhu Bi¹, Judith A. Saxton¹, Beth E. Snitz¹, Shelley A. Hulland¹, Joan M. Swearer², Howard J. Aizenstein¹, Steven T. DeKosky¹, ¹University of Pittsburgh, Pittsburgh, PA, USA; ²University of Massachusetts, Worcester, MA, USA; ³Drexel University, Philadelphia, PA, USA; ⁴Harvard Medical School, Boston, MA, USA. Contact e-mail: klunkwe@upmc.edu

Background: Postmortem pathological studies have provided a retrospective reconstruction of the natural history of amyloid deposition in Alzheimer's disease (AD). While these studies have been valuable, recently developed PET radiotracers such as Pittsburgh Compound-B (PIB) allow prospective natural history studies of amyloid deposition in living subjects. Although it is difficult to predict which cognitively normal elderly are destined for brain amyloid deposition, carriers of mutations in the presenilin-1 (PS1) gene are known with certainty to be destined for AD and the accompanying amyloid pathology. **Objective:** Determine the early stages of the natural history of amyloid deposition in carriers of PS-1 mutations causing autosomal dominant early-onset familial AD. **Methods:** Three asymptomatic (C410Y; 35, 37, 38 y/o) and three symptomatic (A426P; 43, 45, 49 y/o) carriers of PS1 mutations and unaffected siblings were evaluated at the University of Pittsburgh Alzheimer Disease Research Center. Two more asymptomatic carriers (C410Y; 42 & 45 y/o) were evaluated at MGH. PIB PET imaging (15mCi, 60-90min) was then performed (ECAT HR+). Logan graphical analysis was applied to estimate regional PIB retention (distribution volume, DV), normalized to a cerebellar reference region DV to yield DV ratios (DVRs). MRI was performed for co-registration and partial volume correction. **Results:** Siblings (without mutations) of PS-1 mutation carriers showed no abnormalities on PIB PET imaging. The three clinically symptomatic mutation carriers showed markedly disproportionate accumulation of PIB in the striatum, but several other cortical areas with high PIB retention in sporadic AD (particularly precuneus) showed moderately increased PIB retention. The asymptomatic PS1 mutation carriers <40 y/o showed PIB retention mainly limited to the caudate, putamen and some thalamic nuclei, but not globus pallidus. The older asymptomatic cases showed early deposition in precuneus and frontal cortex as well. **Conclusions:** Amyloid deposition driven by PS-1 mutations appears to begin in the striatum. This may be different from sporadic AD, in which deposition may begin in frontal and precuneus cortex, but this is currently not clear. After the initial asymptomatic striatal phase, amyloid deposition in PS-1 mutation carriers appears to progress in a more typical fashion just prior to emergence of clinical symptoms.

P2-367 PROGRESSIVE CORTICAL THICKNESS DECLINE IN ALZHEIMER'S DISEASE

Jason Lerch^{1,2}, Alex Zijdenbos², Andrew Janke¹, Alan Evans^{1,2}, Norbert Schuff³, Michael Weiner³, ¹McGill University, Montreal, PQ, Canada; ²Neuralyse Inc, Montreal, PQ, Canada; ³University of California at San Francisco, San Francisco, CA, USA. Contact e-mail: jason@bic.mni.mcgill.ca

Background: Thickness of the cerebral cortex is known to decline in AD. Moreover, as the disease progresses additional cortical structures become afflicted by the spread of neurofibrillary tangles. **Objective:** We hypothesized that disease progression could be quantified and patterns of longitudinal change between healthy aging and AD compared using automated cortical thickness analyses. **Methods:** T1-weighted MRIs obtained from 19 AD patients (10 follow-up scans), and 18 Healthy Controls (HC, 18