Recently spectroscopic analysis of single transgenic APP[1], and double transgenic PS2APP[2] and APP-PS1[3] mice brains showed neurochemical profiles which deviate from that seen in wild-type mice as the transgenic mice age. **Objectives:** The purpose of this study was to compare the levels of the metabolites in question, mIns and taurine, in different mouse models of Alzheimer's disease: APP, PS1, APP-PS1 and wild-type. **Methods:** *In vivo* [1]H MR spectra from three 624-day-old APP, four 655-day-old PS1, seven 605-day-old APP-PS1, and four 610-day-old wild-type mice were obtained using a LASER sequence at 9.4 T (31-cm horizontal bore magnet equipped with Varian INOVA console) from an 18 μL voxel placed in the cortex and the hippocampus. The obtained spectra were analyzed using LCModel, and the quantification was obtained using tCr resonance as an internal standard. **Conclusions:** Levels of mIns are higher for APP-PS1, compared to wild-type, APP and PS1 mice but do not differ between wild-type, APP and PS1 mice. The taurine levels are higher for APP than for APP-PS1, PS1 and wild-type mice but do not differ between wild-type, APP-PS1 and PS1 mice. The elevation in taurine in only the APP mice would indicate that the neurochemical alteration in these mice is not a function of amyloid plaque burden; because, at a similar age of roughly 600 days the plaque load is greater in APP-PS1 mice which do not exhibit elevated levels of taurine. The fact that APP mice do exhibit an increase in taurine while APP-PS1 mice do not indicates that the taurine increase cannot simply be due to the presence of the APP mutation alone in the mouse genome.

1. Dedeoglu, A. *et al.*, *Brain Research* **1012**, 60-65 (2004).

2. von Kienlin, M. *et al.*, *Neurobiol. Dis.* **18**, 32-39 (2005).

3. Marjanska, M. *et al.*, *Proc. Natl. Acad. Sci. USA* **102**, 11906-11910 (2005).


P2-280 **DISRUPTION OF DEFAULT MODE CORRELATIONS IN AGING AND ALZHEIMER'S DISEASE**

Jessica R. Andrews[1], Abraham Z. Snyder[2,3], Justin L. Vincent[2], Cindy Lustig[4], Michael D. Fox[1], Marcus E. Raichle[2], John C. Morris[5], Randy L. Buckner[6,7], [1]*Division of Biology and Biomedical Sciences, Washington University, St. Louis, MO, USA;* [2]*Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, MO, USA;* [3]*Department of Neurology, Washington University School of Medicine, St. Louis, MO, USA;* [4]*Department of Psychology, University of Michigan, Ann Arbor, MI, USA;* [5]*Alzheimer's Disease Research Center, Department of Neurology, Washington University School of Medicine, St. Louis, MO, USA;* [6]*Department of Psychology and Center for Brain Sciences, Harvard University, Cambridge, MA, USA;* [7]*Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Boston, MA, USA. Contact e-mail: jandrews@wustl.edu*

Background: Growing interest has emerged in how activity patterns engaged in default cognitive modes differ in aging and AD (Lustig et al., 2003 PNAS; Greicius et al., 2004 PNAS). Some data have even suggested default activity patterns may be causal to disease-associated processes (Buckner et al., 2005 JN). **Objective(s):** To further investigate these observations, the present study characterized default mode activity using analysis of low frequency functional correlations between brain regions (Biswal et al., 1995 MRM; Fox et al., 2005 PNAS). BOLD-contrast fMRI imaging was used and the correlation coefficient between regions was the dependent measure. **Methods:** Functional correlations were explored in a large sample of 38 young adults (age 22.4 y; 18 M), 55 nondemented older adults (76.5 y; 18 M) and 17 older adults (76.9 y; 12 M) with a clinical diagnosis of AD in accordance with validated criteria using standard assessment protocols for both clinical and neuropsychological measures. Data were from Lustig et al. (2003 PNAS). To minimize anatomical biases, seed regions used for correlation analyses were defined in a separate data set of an equal number of young, nondemented older, and AD participants

(n= 24 total). Many participants also underwent diffusion tensor imaging (DTI) at nearby times to assess white matter integrity. **Conclusions:** Results revealed that functional correlations were dramatically reduced between anterior and posterior regions comprising the default mode in nondemented older adults compared to the young. Considerably more modest reductions in correlations were noted between the nondemented and AD older adult groups. We also examined relationships between functional correlation measures, performance on neuropsychological tests, and DTI in the same group of individuals, as they are useful to understand the interaction between potentially related changes in aging. Our results are consistent with the hypothesis that aging is associated with disconnection of distributed brain networks that show coordinated activity in young adults. Future analyses will explore whether our observed functional disconnection in aging is related to findings of white-matter degradation (e.g., O'Sullivan et al., 2000 Neurology; Head et al., 2004 CC) and also whether functional disconnection is prominent in nondemented aging in the absence of AD.
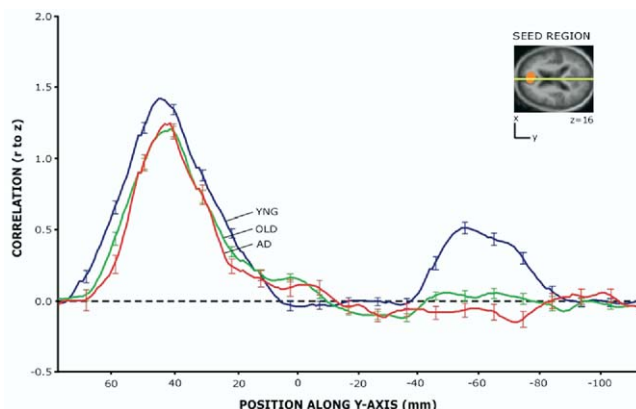
P2-281 **FLUID REGISTRATION DERIVED HIPPOCAMPAL ATROPHY RATES: RELIABILITY AND COMPARISON WITH MANUAL MEASURES, A METHODOLOGICAL APPROACH**

Laura A. van de Pol[1], Josephine Barnes[2], Rachael I. Scahill[2], Chris Frost[3], Emma B. Lewis[4], Richard G. Boyes[2], Ronald A. van Schijndel[1], Philip Scheltens[1], Nick C. Fox[2], Frederik Barkhof[1], [1]*VU Medical Centre, Amsterdam, The Netherlands;* [2]*Dementia Research Centre, Institute of Neurology, University College, London, United Kingdom;* [3]*London School for Hygiene and Tropical Medicine, London, United Kingdom;* [4]*Centre for Vision Speech and Signal Processing, University of Surrey, Guildford, United Kingdom. Contact e-mail: l.vandepol@vumc.nl*

Background: Manual segmentation is considered to be the gold standard in measurement of hippocampal volumes and, by extension, hippocampal atrophy rates on MRI. However, this technique is time consuming, requires skilled operators and is subject to errors in delineation. Regional non-linear (fluid) registration has been shown to track longitudinal changes in brain structures, using serial MRI to model change in a predefined region, such as the hippocampus. **Objective:** To validate regional non-linear (fluid) registration measurement of hippocampal atrophy rates against manual delineation in subjects with mild cognitive impairment (MCI). **Methods:** Hippocampi of 18 subjects with MCI were manually outlined twice on MRI scan-pairs (mean interval: 2.01 ± 0.11 years); volumes were subtracted to calculate change over time. Following global affine and local rigid registration, regional fluid registration was performed from which hippocampal atrophy rates were derived from the Jacobian determinants over the hippocampal region. Reliability for both methods and agreement between methods was assessed. **Results:** Mean hippocampal atrophy rates (%/yr) derived by manual delineation were: left: 2.13 ± 1.62; right: 2.36 ± 1.78 and for the regional fluid registration: forward: left: 2.39 ± 1.68; right: