

Pittsburgh ADRC. Adjacent tissue sections were processed for A $\beta$  immunohistochemistry, and adjacent frozen tissue for A $\beta$ 1-40 and A $\beta$ 1-42 ELISA. **Results:** In every AD case, 6-CN staining labeled A $\beta$  plaques, but not other amyloid pathology (e.g. NFT, DN, NT). Pretreatment of tissue with formic acid completely abolished 6-CN staining. 6-CN was most readily detected in compact plaques containing A $\beta$ 1-40, but also detected A $\beta$ 1-42 plaques. Diffuse A $\beta$  plaques were lightly labeled with 6-CN. 6-CN-labeled plaque load did not correlate with A $\beta$ 1-40 or A $\beta$ 1-42 ELISA levels assessed separately. However, there was a significant positive correlation of 6-CN plaque load with total insoluble A $\beta$  ELISA levels ( $r=0.85$ ,  $p<0.05$ ) and a trend for a positive correlation with total A $\beta$  plaque load determined by quantitative immunohistochemistry. **Conclusions:** These data suggest that the extent of 6-CN labeling of plaques in AD brains reflects levels of total insoluble A $\beta$ , rather than either A $\beta$ 1-40 or A $\beta$ 1-42 peptides preferentially. Thus, 6-CN labeling (and by inference, PIB retention *in vivo*) should reflect the extent of abnormal folding of all A $\beta$  peptides into insoluble aggregates, and can prove useful for evaluation of anti-A $\beta$  therapies and facilitation of AD diagnosis.

**P2-370 AN INTEGRATED FRAMEWORK FOR COMPUTATIONAL NEUROANATOMY: COMPARING CORTICAL THICKNESS AGAINST MANUAL TRACING OF THE HIPPOCAMPUS**

Alex P. Zijdenbos<sup>1</sup>, Jason P. Lerch<sup>1</sup>, Alan C. Evans<sup>2,1</sup>, Norbert Schuff<sup>3</sup>, Michael W. Weiner<sup>3</sup>, <sup>1</sup>Neuralyse Inc., LaSalle, PQ, Canada; <sup>2</sup>McGill University, Montreal, PQ, Canada; <sup>3</sup>University of California at San Francisco, San Francisco, CA, USA. Contact e-mail: alex@neuralyse.com

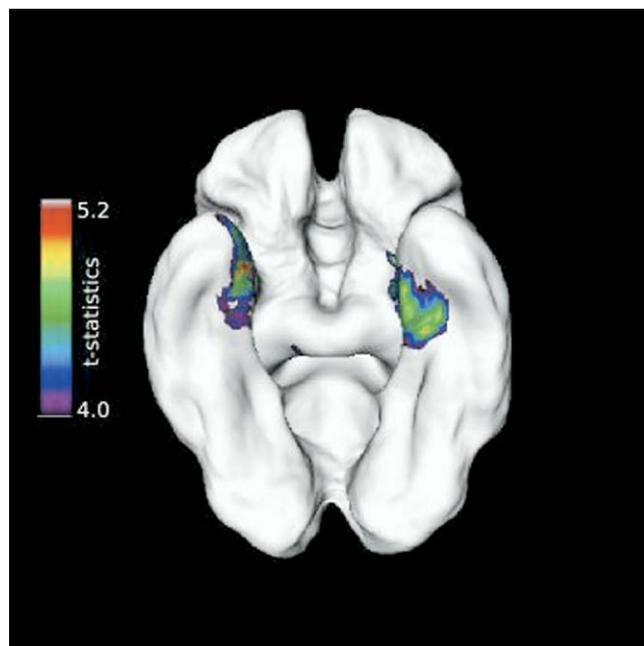
**Background:** Quantitative analysis of imaging data is rapidly gaining popularity as a surrogate marker of disease progression. Previous techniques for measuring longitudinal atrophy in healthy aging have measured hippocampal and entorhinal cortex volumes as well as whole brain atrophy and ventricular enlargement using the boundary shift integral method. Recently, a fully automated, integrated framework has been developed [1] for the quantitative analysis of neuroimaging data, which includes the assessment of cortical thickness (CT) throughout the brain [2]. **Objective(s):** In this work, we sought to demonstrate that CT is able to reproduce known patterns of AD progression. **Methods:** CT was measured in 3D T1-weighted MRI (MPRAGE) of 19 AD patients (10 follow-up scans) and 18 healthy controls (HC; 18 follow-up scans) and the rate of change of CT was compared with that of hippocampal volume as measured by manual tracing [3]. **Results:** The figure shows the correlation t-statistic between changes in hippocampal volume and in cortical thickness. Maximal correlation was observed bilaterally in the entorhinal cortex where the t-statistic exceeded 4.0. The rate of change of hippocampal volume was -6.7%/yr for AD and -1.5%/yr for HC, whereas CT analysis demonstrated -6.8%/yr (AD) and -2.8%/yr (HC) for entorhinal cortex (all  $p<0.05$ ). **Conclusions:** Cortical thickness analysis shows excellent agreement with established patterns of AD progression. Major advantages of automated CT measurement over traditional ROI delineation are the lack of intra- and inter-rater variability and the ability to measure change throughout the cortex [4]. Moreover, it provides a direct quantitative metric (thickness), unlike other automated strategies such as voxel-based morphometry. We believe that CT analysis will prove invaluable in the study of degenerative brain disorders and their treatment by its ability to detect subtle change as well as reduce costs.

[1] Zijdenbos et al., IEEE TMI, 21(2), 2002.

[2] Lerch et al., Neuroimage 24, 2005.

[3] Ezekiel et al., Alz Dis Assoc Disord 18(4), 2004.

[4] Lerch et al., Cerebral Cortex 15(7), 2005.



**P2-371 NICOTINIC RECEPTOR UPREGULATION AND THE COGNITIVE EFFECTS OF GALANTAMINE IN ALZHEIMER'S DISEASE: A HUMAN IN VIVO STUDY USING [<sup>18</sup>F]F-A-85380 PET**

Julia R. Ellis<sup>1</sup>, Victor L. Villemagne<sup>2</sup>, Pradeep J. Nathan<sup>1</sup>, Rachel S. Mulligan<sup>2</sup>, Sylvia J. Gong<sup>2</sup>, Clare L. Smith<sup>2</sup>, Henri Tochon-Danguy<sup>2</sup>, Greg R. Savage<sup>1</sup>, Christopher C. Rowe<sup>2</sup>, <sup>1</sup>Monash University, Victoria, Australia; <sup>2</sup>Austin Hospital, Victoria, Australia. Contact e-mail: Julia.Ellis@med.monash.edu.au

**Background:** The nicotinic cholinergic receptor system (nAChR) mediates particular aspects of cognition and is severely affected in Alzheimer's disease (AD). The relationship between the cognitive enhancing effect of galantamine and the up-regulation of nAChR has yet to be fully established. **Objective(s):** The current study aimed to quantify nAChR up-regulation in patients with mild AD following chronic galantamine treatment using [<sup>18</sup>F]F-A-85380 PET and examine the relationship between nAChR up-regulation and galantamine-induced changes in cognitive function. **Methods:** Ten drug naïve, non-smoking, AD patients (78 ± 12 years) underwent cognitive assessment and a static 20-min PET scan 100min after injection of 200MBq 2-[<sup>18</sup>F]F-A-85380 on two separate occasions (before and after 8-weeks, 16mg/d galantamine treatment). Brain regional binding was assessed through a simplified estimation of Distribution Volume (DVS), defined as the region to metabolite corrected venous plasma ratio at apparent steady state (100-120min post-injection). Correlational analysis was conducted to investigate the possible relationship between changes in DVS and cognition following galantamine treatment. **Results:** Treatment was well tolerated and only two patients experienced minor side effects at the 16mg/d galantamine dose. AD patients showed enhanced performance on global measures of cognition after galantamine treatment, reflected in an improvement in MMSE and AD Assessment Scale (ADAS-Cog) performance (10% and 35%, respectively). This improvement was also reflected in tasks measuring verbal fluency, verbal recall, and psychomotor function. On the repeat 2-[<sup>18</sup>F]F-A-85380 PET scans a small increase (6.3%) was observed in DVS, probably reflecting an increase in nAChRs binding sites. A trend level relationship was observed between changes in DVS and cognitive performance. **Conclusions:** [<sup>18</sup>F]F-A-85380 PET allows the evaluation of drug effects at the specific site of pharmacological action. There is some evidence to suggest that the observed improvements on specific measures of cognition might be related to the up-regulation of