Time-activity curves (TACs) for the full dataset (15 HC, 15 AD) were then generated from the VOIs using a MATLAB code. Parametric images of amyloid retention were generated by averaging the images (approximately 50-70 min post- injection) from a subset of subjects and normalizing that to the cerebellum grey to get a standardized uptake value ratio (SUVR). Data across the subset of subjects was compared using the statistical methods of SPM. **Results:** The VOI analysis showed increased uptake of 18F-tracers in cortical grey matter areas expected to contain β-amyloid plaques associated with Alzheimer's disease (AD) for all three tracers. The statistical analysis on the voxel specific parametric images showed significant uptake ($p<0.05$) in orbito-frontal and lateral temporal cortices as well as precuneus and posterior cingulate. Thus SPM statistical analysis supports the semiautomated VOIs quantification methods. These results are consistent with reported findings of amyloid pathology in AD in postmortem tissue. SPM analysis for the full set of data is underway and will be presented. **Conclusions:** Semiautomated approach provides a precise method for quantifying the uptake of 18F-labelled imaging agents for imaging β-amyloid plaque in multicenter trials.

P2-026 **INTERRELATION BETWEEN CORTICAL NICOTINIC RECEPTORS AND ACETYLCHOLINESTERASE ACTIVITY IN MILD ALZHEIMER'S PATIENTS AS ASSESSED BY PET**

Ahmadul Kadir[1], Ove Almkvist[2], Anders Wall[3], Bengt Långström[3], Agneta Nordberg[1], *[1]Division of Alzheimer Neurobiology, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Stockholm, Sweden; [2]Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Stockholm, Sweden; [3]Uppsala Imanet AB, Imanet, GE Healthcare, Uppsala, Sweden. Contact e-mail: Ahmadul.Kadir@ki.se*

Background: Patients suffering from Alzheimer's disease (AD) experience a marked reduction in cortical nicotinic acetylcholine receptors (nAChRs) and the cortical acetylcholinesterase (AChE) activity. Studies have correlated the cognitive impairment observed in AD patients with a deficit in central cholinergic neurotransmission. One of the most valuable tools for evaluating cholinergic neurotransmission in AD patients is positron emission tomography (PET). The aim of this study is to investigate the relationship between the cortical nicotinic receptors and AChE activity in mild AD patients as assessed by PET. Furthermore, to investigate the association between measures of cognitive function and AChE activity. **Methods:** Eighteen patients with mild AD (mean age: 69 ± 2; mean MMSE score: 26 ± 1, mean ± SE) were recruited in this study. A dual tracer model with administration of ^{15}O-water for regional cerebral blood flow and (S)(-)^{11}C-nicotine was used to assess nicotine binding sites (k_2*) in the brain by PET. In this model low k_2* value indicates higher ^{11}C-nicotine binding in the brain. ^{11}C-PMP-PET was used to assess the brain AChE activity (k_3). Cognitive function was assessed using neuropsychological tests of global cognition, episodic memory, attention, and visuospatial ability. **Results:** Significant positive correlations were observed between the values of cortical ^{11}C-nicitine binding (k_2*) and AChE activity (k_3) in the following brain regions: the right frontal ($r = -0.54$; $p<0.02$), right parietal ($r = -0.49$; $p<0.04$) and left parietal ($r = -0.47$; $p<0.05$) cortices, all other cortical regions showed positive but not significant correlation. In the present study, mean cortical AChE (k3) activity significantly correlated with the results of attention test [Digit Symbol test ($r= 0.45$; $p<0.04$, *one-tail*) and Trail Making Test A ($r= -0.47$; $p<0.05$)]. No significant correlation was observed between AChE activity and the results of tests of episodic memory or visuospatial ability. **Conclusions:** Cortical ^{11}C-nicotine binding positively correlated with the AChE activity in mild AD patients. This finding indicates that AD patients with low AChE activity had a lower number of cortical nicotinic receptors. Furthermore, we observed that mean cortical AChE activity in AD patients significantly correlated with the results of tests of attention.

P2-026 **ANATOMICAL CORRELATES OF BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS: AN SPM ANALYSIS OF 207 DEMENTIA PATIENTS**

Sue J. Kang[1], Sang Won Seo[1], Sang Soo Cho[2], Hansol Kim[3], Yong Jeong[3], Juhee Chin[1], Duk L. Na[1], *[1]Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [2]Seoul National University Shool of Medicine, Seoul, Republic of Korea; [3]Korea Advanced Institute of Science and Technology, Seoul, Republic of Korea. Contact e-mail: susue73@hotmail.com*

Background: More than 50% of patients with dementia experience behavioral and psychological symptoms of dementia (BPSD). The aim of the study was to identify neural correlates of BPSD in a large series of dementia patients using [(18)F]fluoro-2-deoxy[illegible]lucose (FDG)-PET. **Methods:** Participants were 207 patient[illegible]mentia who consisted of 167 with probable Alzheimer di[illegible]l 46 with frontotemporal lobar degeneration (FTLD)[illegible]lemen-tia, 16 semantic dementia, and 9 progr[illegible]). The subjects comprised 141 women (66.2[illegible] the mean age was 65.3±9.8 years (range:[illegible] MMSE was 17.9±6.3 (range: 0-29), and the[illegible]e: 0.5-3). Of all symptoms, the most frequen[illegible] least frequent was hallucination (11.3%). T[illegible]-PET under the same scanning conditions. [illegible]ng the Neuropsychiatric Inventory (NPI). V[illegible]rametric mapping (SPM99) was used for st[illegible]s: Of 10 behaviors examined, after controll[illegible]nd FTLD), age, sex, and MMSE, 5 behavio[illegible] with the hypometabolism of brain: delusio[illegible], apathy, and aberrant motor behavior. Delu[illegible]n hypometabolism in the posterior part of right i[illegible], inferior frontal gyrus (mainly the right pars orbitalis),[illegible]uperior frontal gyrus anterior to supplemental motor area,[illegible]right insular. Hallucination: the right lingual gyrus, the right supramarginal gyrus, and the right superior frontal gyrus. Anxiety: the right precuneus and the right posterior cingulate gyrus, and the right supramarginal gyrus. Apathy: the right superior, middle, and inferior frontal gyri, the right lateral orbitofrontal cortex, the right medial frontal and cingulated gyri, and the right cerebellum tonsil. Aberrant motor behavior:the right superior, middle, and inferior frontal gyri, the right motor cortex, the right orbitofrontal gyrus, middle and inferior temporal cortex, the left middle frontal gyrus, and the left orbitofrontal gyrus. **Conclusions:** These findings indicate that some BPSDs are associated with decreased metabolism of specific parts of the brain.

P2-027 **ASSOCIATION OF COGNITIVE DEFICITS WITH SYNCHRONOUS NEURAL INTERACTIONS AS REVEALED BY MAGNETOENCEPHALOGRAPHY: A CANONICAL CORRELATION ANALYSIS**

Elissaios Karageorgiou[1,2], **Scott M. Lewis**[1,2], J. Riley McCarten[1,3], Arthur C. Leuthold[1,2], Laura S. Hemmy[1,3], Susan E. McPherson[1,3], Susan J. Rottunda[1,3], Apostolos P. Georgopoulos[1,2], *[1]University of Minnesota, Minneapolis, MN, USA; [2]Brain Sciences Center, Veterans Affairs Medical Center, Minneapolis, MN, USA; [3]GRECC, Veterans Affairs Medical Center, Minneapolis, MN, USA. Contact e-mail: ?*

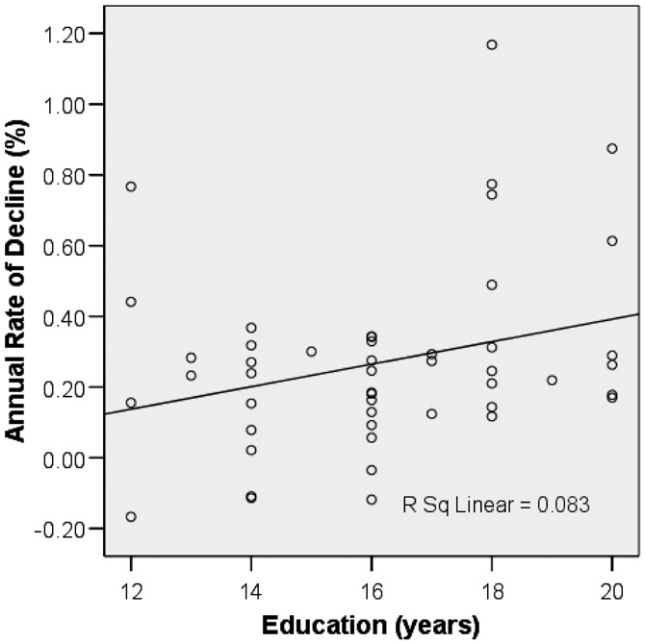
Background: In a recent study we showed that synchronous neural interactions (SNI) assessed by magnetoencephalography (MEG) in a simple fixation test can be used as a functional biomarker for brain disorders (Georgopoulos et al., J. Neural Engineer. 4:349-355, 2007). The SNI variables consist of partial zero-lag cross-correlations estimated between pairs of 248 axial gradiometer sensors after prewhitening of the MEG time series. In this study we evaluated the relations between cognitive deficits and SNI. **Methods:** We studied 8 healthy volunteers, 18 patients with mild cognitive impairment and 16 patients with Alzheimer's disease (mean age: 75.9 ± 0.9) who performed a

battery of neuropsychological (NP) tests and of which SNI measurements were obtained. An ANCOVA was performed for each of the NP tests and SNI variables, using group membership as fixed factors, and age, sex and years of education as covariates. Only variables with a significant group effect in the ANCOVA (13 NP tests and 33 SNI variables) were used. A canonical correlation analysis was then performed between those NP and SNI variables. **Results:** We found that the first five of the canonical-variate-pairs (CVP) were statistically significant. The contribution of each of the NP and SNI variables to the canonical correlation depended on the canonical-dimension of each CVP, as follows. The first CVP related to language and attention with bilateral involvement of SNI; the second CVP had a stronger relation to language with elements of memory and attention, and involved mostly left hemispheric SNI; the third CVP related to more global deficits and bilateral SNI contribution; the fourth CVP related mostly to memory with bilateral SNI involvement; finally, the fifth CVP related mostly to attention with left hemispheric SNI involvement. **Conclusions:** These results reveal how information in the SNI relates to specific aspects of cognitive deficit.

P2-028 RATE OF WHOLE BRAIN VOLUME DECLINE IN A COHORT OF COGNITIVELY NORMAL PARTICIPANTS WITH FAMILY HISTORY OF ALZHEIMER'S DISEASE: A LONGITUDINAL STUDY

Erik K. Kastman[1,2], Barbara B. Bendlin[1,2], Guofan Xu[1,2], Michele L. Ries[1,2], Donald G. McLaren[1,2], Michele E. Fitzgerald[1,2], Britta M. Jabbar[1,2], Kristopher J. Kosmatka[1,2], Sterling C. Johnson[1,2], [1]*William S. Middleton Memorial Veterans Hospital, Madison, WI, USA;* [2]*University of Wisconsin, Madison, WI, USA. Contact e-mail: ekk@medicine.wisc.edu*

Background: Previous functional MRI studies have shown that parental family history (FH+) of Alzheimer's disease (AD) is associated with preclinical brain differences compared to controls (FH-). In this study, we examine the rate of Whole Brain Volume (WBV) decline in FH+ participants and examine the impact of modifying factors. Over 240 subjects have received baseline scans at time of this submission; 49 have returned for a four-year follow-up. **Methods:** All subjects were imaged with 3T T1W MRI scans and received a comprehensive neuropsychological battery. Two gender and APOEe4 balanced cohorts were scanned: a middle-aged FH+ cohort (N: 35, mean age: 56) and an older preclinical dementia Mild Cognitive Impairment (MCI) and control cohort (N: 6,8; mean age: 73, 71 respectively). Percent change in WBV was calculated using SIENA (FMRIB), and Pearson correlations and independent samples T-tests were performed using SPSS. **Results:** WBV in cognitively normal FH+ participants declined at an annual rate of .23% (not dependent on genetic status). There was no change in cognition from baseline to follow-up, nor was there a relationship between cognition and brain volume decline. In contrast, level of education was positively correlated with WBV decline ($p<.05$). Rate of decline was significantly faster in participants with greater levels of education. WBV in MCI subjects declined at an annual rate of .85%, while age-matched controls declined at .50%. This trends towards significance but more participants are needed. **Conclusions:** Within our returning cohort, the rate of annual brain volume decline was not affected by APOE4 status, but was correlated with education. Our finding supports a similar positive relationship reported by Fotenos et al. (2008) between SES and annual brain volume decline, which has been hypothesized to be a measure of cognitive reserve delaying disease expression. The annual brain volume decline of the FH+ sample (.23%) is similar to published rates for this age range (.2%-.3%), which might suggest that FH has no effect on the rate of decline, but to completely address this a FH- sample is needed.



P2-029 MEDIAL TEMPORAL LOBE ATROPHY AND RATE OF LOSS PREDICTS FUTURE COGNITIVE DECLINE IN PATIENTS WITH MEMORY COMPLAINTS WITH OR WITHOUT MEMORY DEFICITS: A COMPARISON OF METHODS

Jonathan Kennedy[1], Barnes Josephine[1], Archer Hilary[1], Tracey Pepple[1], Jasper D. Sluimer[2], Wouter J. P. Henneman[2], Martin N. Rossor[1], Nick C. Fox[1], [1]*Institue of Neurology, University College London, London, United Kingdom;* [2]*VU University Medical Centre, Amsterdam, Netherlands. Contact e-mail: kennedy@dementia.ion.ucl.ac.uk*

Background: To evaluate three measures of medial temporal lobe atrophy in individuals with symptoms of memory loss but no objective memory impairment (SNCI) and mild cognitive impairment (MCI) and their ability to predict future cognitive decline. **Methods:** Thirty-two subjects with SNCI, 18 with MCI and 24 healthy age matched controls underwent T1-weighted volumetric magnetic resonance imaging (MRI) at baseline and a year later. Baseline scans were evaluated using a validated visual assessment of medial temporal lobe atrophy (MTA) and secondly by using manual outlining with multiple views to provide a measure of hippocampal volume. Thirdly changes in adjusted total hippocampal volumes over the first year were calculated using the hippocampal boundary shift integral. For each measure left and right hippocampal data were used to calculate an average value. The outcome of the study was clinical diagnosis at 3 years based upon annual clinical and neuropsychological assessments. Subjects were classified as 'converters' if they progressed to a diagnosis of MCI or dementia, or 'non-converters' if they remained cognitively stable. **Results:** 7 of our SNCI group and 11 of our MCI group converted to a diagnosis of MCI or dementia. Baseline MTA score ($p<0.001$), baseline hippocampal volume ($p<0.001$) and annualised hippocampal atrophy rate ($p<0.001$) were all predictive of future cognitive decline at three years. Comparing cross sectional measures suggested that combination of hippocampal volume and MTA discriminated better than MTA alone ($p = 0.005$) but not volume alone ($p=0.06$), suggesting volume was a better discriminator. Combining volume and rate of atrophy provided better discrimination than either volume ($p=0.03$) or atrophy alone ($p=0.013$) suggesting that both independently contribute in discriminating converters from non-converters. When restricting analysis to the SNCI group we found that all three individual measures were predictive of conversion ($p<0.02$). **Conclusions:** Measures of medial temporal lobe atrophy are predictive of clinical progression in those reporting memory complaints. These results do not appear to depend on the MCI group who are known to be at greater risk of progressive cognitive