ent hippocampal subfields. The aims of this study were: 1. To determine patterns of subfield atrophy in AD and MCI. 2. To determine if subfield measurements provide advantages over total hippocampal volume for differentiation between groups. 3. To study the influence of ApoE4 on subfields in elderly controls and AD. **Methods:** 75 subjects (47 cognitively healthy elderly controls (mean age: 68.4±8.0), 14 MCI (mean age 75.3±6.5 and 14 AD (mean age70.4±8.2) were studied with a high resolution T2 weighted imaging sequence aimed at the hippocampus. Apo e4 carrier state was known in 11 AD (ApoE3/ApoE4: 3/8) and 38 controls (ApoE3/ApoE4: 29/14). Entorhinal cortex (ERC), subiculum, CA1, CA1-CA2 transition zone (CA1-2 transition), CA3-4& dentate gyrus (CA3&DG) and total hippocampal volume were manually marked. Statistical analysis was done with multiple regression and stepwise discriminant analysis. **Results:** Compared to controls, AD had significantly smaller volumes of ERC (-28.4%), subiculum (-23.0%), CA1 (-20.2%), CA1-2 transition (-31.4%) and total hippocampal volumes (-19.1%). MCI had smaller CA1 (-14%) and CA1-2 transition (-26.1%) volumes. CA1-2 transition discriminated best between controls and MCI (Wilks' Lambda 0.68, p<0.0001) and CA1-2 transition and ERC (Wilks' Lambda 0.63, p<0.0001) between AD and control. ApoE4 exerted a negative effect on CA3&DG volumes in healthy controls (p = 0.036) and in a mixed group of AD and controls (p = 0.0003). In the latter group we also found a significant interaction between AD and ApoE4 (p = 0.029). **Conclusions:** The patterns of subfield atrophy in AD and MCI were consistent with patterns of neuronal cell loss/ reduced synaptic density described in histopathologcal studies. ApoE4 effects were restricted to CA3&DG, i.e., the subfield capable of neurogenesis throughout adult life. These preliminary findings suggest that hippocampal subfield volumetry might be a better measure for diagnosis of early AD and for detection of other disease effects than measurement of total hippocampal volume.

O1-02-05 AUTOMATED LONGITUDINAL 3D MAPPING OF HIPPOCAMPAL ADAS-COG DELAYED RECALL EFFECTS IN 293 NORMAL ELDERLY, MCI AND ALZHEIMER'S DISEASE SUBJECTS

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Background: The Alzheimer's Disease Assessment Scale Cognitive Subscale (ADAScog) is a primary outcome measure in Alzheimer's disease (AD) and mild cognitive impairment (MCI) clinical trials. Hippocampal atrophy has recently been proposed as a sensitive biomarker in AD and MCI. **Methods:** We applied a previously validated automated machine learning algorithm based on adaptive boosting (Morra et al., 2008) to segment the hippocampi in baseline and 12-month follow-up 3D T1-weighted brain MRIs of 109 cognitively normal elderly (NC), 133 MCI and 51 AD subjects from the ADNI study. We then applied the radial distance atrophy mapping approach to examine in 3D the structural hippocampal correlates of ADAScog delayed recall (ADAScog-DR). 3D statistical maps were corrected for multiple comparisons using permutation testing thresholded at p<0.01. **Results:** The groups were well balanced with regard to age, race and education. The MCI group had significantly more men (71%) relative to the NC (52%) and the AD group (51%). The MCI and AD groups showed a significant decline in ADAScog-DR over 12 months (MCI Δ=0.42, p=0.012; AD Δ=0.49, p=0.005). At baseline ADAScog-DR showed significant correlations with atrophy of CA1 and subicular hippocampal subregions in MCI (r=0.2-0.3, left pcorrected=0.03; right pcorrected=0.04) and the right mid/posterior CA1, CA2-3 and subiculum in AD (r=0.35-0.55, pcorrected=0.0004). At follow-up, ADAScog-DR correlated with atrophy of the left more then right CA1

and subiculum in MCI (r=0.2-0.3, pcorrected=0.003) and the right anterior CA1 and subiculum in AD (r=0.25-0.45; pcorrected=0.017). Correlations between baseline ADAScog-DR and posterior right hippocampal atrophy were observed at trend level in NC (r=0.2-0.4; pcorrected=0.07). Correlations with the global ADAScog ratings (ADAScog11 and ADAScog-modified) were generally less significant than those observed with ADAScog-DR. **Conclusions:** We demonstrated regionally specific correlations between ADAScog-DR and hippocampal atrophy in MCI and AD. The MCI 3D maps revealed correlations with hippocampal subregions known to be affected early in MCI. Our high throughput automated segmentation approach is a promising technique for analyzing large epidemiological and clinical trial datasets.
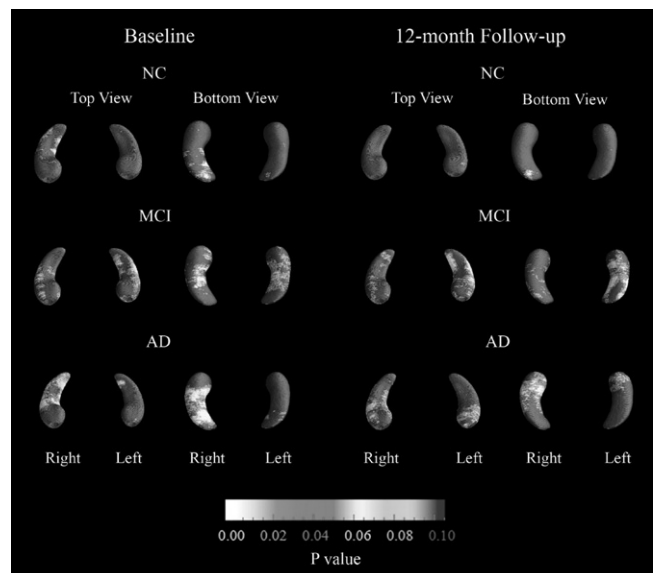
O1-02-06 TWELVE-MONTH CEREBRAL METABOLIC DECLINES IN PROBABLE ALZHEIMER'S DISEASE AND AMNESTIC MILD COGNITIVE IMPAIRMENT: PRELIMINARY FINDINGS FROM THE ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE (ADNI)

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Background: In a small positron emission tomography (PET) study, we previously characterized twelve-month cerebral metabolic rate for glucose (CMRgl) declines in moderate probable Alzheimer's disease (pAD) patients and estimated the number of patients needed to detect disease-modifying treatment effects in a single-center randomized clinical trial (RCT, Alexander et al, 2002). The objectives of this study are to characterize twelve-month CMRgl declines in mild pAD and amnestic mild cognitive impairment (aMCI) patients from the multi-center Alzheimer's Disease Neuroimaging Initiative (ADNI) and estimate the number of mild pAD patients and MCI patients needed to evaluate a putative disease-slowing treatment in twelve-month multi-center RCTs. **Methods:** SPM5 was used to characterize twelve-month declines in 17 mild pAD patients (baseline age 71±12, MMSE 24±2) and 46 aMCI

patients (baseline age 66±13, MMSE 27±2). Maximal CMRgl declines were used to estimate the number of mild pAD and aMCI patients needed per group to detect disease-modifying treatment effects in six- or twelve-month multi-center RCTs with 80% power and P≤0.001 uncorrected for multiple comparisons. **Results:** The pAD patients had twelve-month CMRgl declines in posterior cingulate, precuneus, parietal, temporal and frontal regions and the aMCI patients had twelve-month CMRgl declines in the posterior cingulate, precuneus, parietal and temporal regions. To detect a 20% treatment effect on posterior cingulate CMRgl declines, we estimate the need for 153 mild pAD patients per group and 728 aMCI patients per group in twelve-month RCTs. **Conclusions:** This study provides preliminary information about twelve-month CMRgl declines in mild pAD and aMCI patients and the number of patients needed to detect disease-modifying treatment effects in a twelve-month multi-center RCT. Future analyses will extend our findings to the entire ADNI cohort, provide power estimates for 6, 12, 18 and 24-month multi-center RCTs using specified search regions versus ROIs, and compare these power estimates to those using clinical ratings, other imaging modalities and other image-analysis techniques.

O1-02-07 | *IN VIVO* CHARACTERIZATION OF 18F-BAY94-9172: A NOVEL β-AMYLOID PET LIGAND FOR THE DIAGNOSIS OF ALZHEIMER'S DISEASE

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Background: Access to the Aβ tracer 11C-PiB is restricted by its short half-life. 18F-BAY94-9172 is a new Aβ tracer with a longer decay half-life better suited to widespread clinical use. We evaluated this tracer in humans and calculated the radiation dosimetry. **Methods:** Fifteen healthy elderly controls (HC), 15 AD, and 5 FTLD patients with mild to moderate dementia, underwent PET imaging after injection of 300 MBq of 18F-BAY94-9172. Scans were acquired 90-120 min. post injection and Standardized Uptake Value ratios (SUVR) were calculated using the cerebellum as reference region. Three of the HC underwent serial whole body scans for the determination of biodistribution and radiation dosimetry calculation using OLINDA. **Results:** Cortical 18F-BAY94-9172 binding was markedly elevated in all AD patients. There was no cortical binding in most FTLD or HC subjects. One FTLD and three HC showed mild cortical binding but less than in AD. Binding was greatest in the precuneus/posterior cingulate and frontal cortex, followed by lateral temporal and parietal cortex. 18F-BAY94-9172 binding did not correlate with dementia severity in AD. Higher SUVR in neocortical areas were observed in AD (2.02±0.28) when compared with HC (1.29±0.17) and FTLD (1.22±0.17). Visual interpretation was 100% sensitive and 90% specific for detection of AD. Whole body imaging and blood measurements showed rapid metabolism with predominantly hepatic clearance. The mean effective radiation dose was 14.67 ± 1.39 μSv/MBq resulting in radiation exposure of 4.4 mSv from a 300MBq (8 mCi) study. **Conclusions:** 18F-BAY94-9172 should assist in the early diagnosis of AD and the differential diagnosis of AD from FTLD. The radiation dose compares favourably to other radiological investigations and is slightly less than that of 18F-FDG. The robust visual findings, acceptable radiation exposure, and the longer radioactive half-life make 18F-BAY94-9172 attractive for clinical use.

O1-02-08 | THE INNOMED/ADDNEUROMED FRAMEWORK FOR MULTICENTER MRI ASSESSMENT OF LONGITUDINAL CHANGES IN ALZHEIMER'S DISEASE

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Background: The framework and first 24 months experience of the AddNeuroMed multi-center MRI study of longitudinal changes in Alzheimer's disease (AD) is described. AddNeuroMed is part of the European Union founded and EFPIA sponsored InnoMed programme and aims to develop and validate novel surrogate markers based upon in vitro and in vivo models in animals and humans, using AD as a test platform. The study duration is from September 2005 to January 2009. The imaging work package of AddNeuroMed aims to perform a multi center MRI study similar to a drug trial. This includes the installation of calibrated MRI pulse sequences, the acquisition of phantom scans, the establishment of routines for communication and data -flow, -collection, -storage, -backup, -quality control (QC), -quality assurance (QA), -evaluation and site feedback. Measurements from the MRI scans will be related to clinical and proteomics measures. **Methods:** MRI scans are collected at six different European MRI sites with a data collection and coordination center at Karolinska Institutet, Stockholm. Data management, workflow control and image QC are guided by the Loris database system (McGill Brain Imaging Centre, Montreal). The MRI acquisition protocol is the same as that employed by ADNI, with the addition of T1 and T2 relaxometry and MRS in a subset of patients. **Results:** A total of 360 healthy control subjects, MCI patients or Alzheimer's disease patients will be scanned at baseline and 3 and 12 months thereafter. As of October 2007, 341 and 196 subjects have been scanned at baseline or at 3 month, respectively. All images have been databased and the baseline MRI data processed to produce measures of gray and white matter, CSF and hippocampal volumes together with cortical thickness. 97 % of all of the T1 volumes passed QC which demonstrates the excellent performance of the participating scanning sites. **Conclusions:** Hence, AddNeuroMed is successfully collecting data in a European multi-site MRI study. A database has been implemented and QC and QA is being performed on a routine basis.

SUNDAY, JULY 27, 2008
ORAL
O1-03
DISEASE MECHANISMS: APP

O1-03-01 | REDUCED AMYLOID DEPOSITION IN MICE OVEREXPRESSING RTN3 IS ADVERSELY AFFECTED BY PREFORMED DYSTROPHIC NEURITES

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