SATURDAY, JULY 14, 2012
ALZHEIMER'S IMAGING CONSORTIUM (IC)
IC PLENARY: PL-01

IC-PL-01 | **PRESYMPTOMATIC ALZHEIMER'S DISEASE IN THE DOMINANTLY INHERITED ALZHEIMER'S NETWORK (DIAN)**

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Background: Alzheimer's disease has been hypothesized to begin years before the first clinical symptoms manifest and longitudinal studies of Alzheimer's disease biomarkers take years to demonstrate the full pathological cascade of events which lead to clinical dementia. Thus, the temporal order and magnitude of Alzheimer's disease pathologic processes are not well understood. Therefore, well-validated biomarkers and indicators of presymptomatic AD are needed to improve the design of clinical trials, develop more effective therapeutics and offer the opportunity for prevention trials. **Methods:** Biomarker studies of presymptomatic AD will be presented and compared with the Dominantly Inherited Alzheimer Network (DIAN), an international network of leading research centers to investigate autosomal dominant AD. Autosomal dominant AD has a predictable age at onset, and provides an opportunity to determine the sequence and magnitude of pathologic changes which culminate in symptomatic disease. Measurements to track disease progression using established clinical, cognitive, MRI, FDG-PET, PIB-PET, CSF and blood tests will be presented. **Results:** Autosomal dominant AD pathogenic mutations cause a series of changes beginning with increased soluble Aβ42, followed by amyloidosis, increased CSF tau, decreased brain glucose metabolism, decreased brain volume, and subtle cognitive impairment before frank dementia is manifest. Other cross-sectional studies support the similarities of autosomal dominant AD and later onset 'sporadic' AD. **Conclusions:** The sequence of events in AD pathophysiology offers opportunities for predictive testing and a time window of treatment for secondary prevention trials. Because the clinical and pathological phenotypes of dominantly inherited Alzheimer's disease are similar in many respects to those of the far more common late-onset Alzheimer's disease, the nature and sequence of brain changes in autosomal dominant Alzheimer's disease is likely be relevant for late-onset Alzheimer's disease.

IC ORAL SESSIONS: IC-O1
PRESYMPTOMATIC ALZHEIMER'S

IC-O1-01 | **EFFECT OF THE APOE-ε4 ALLELE ON LONGITUDINAL CHANGES IN CORTICAL THICKNESS IN NORMAL AGING**

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Background: Adults with at least one APOE E 4 allele are at increased risk of earlier onset of memory decline and Alzheimer's Disease (AD). Neuroimaging cortical thickness biomarkers have been identified that are predictive of progression to AD. Most evidence for the APOE e4 allele modulation of cortical development is from cross-sectional data. This study examined the longitudinal effect of the APOE e4 allele on cortical thickness in normal aging. **Methods:** Data were obtained from participants in the Seattle Longitudinal Study (SLS), a cohort-sequential longitudinal study of the relationship between aging, health, cognition and lifestyle (Schaie, 2005). The sample included 111 participants, Mage = 67 (age range 52 - 84), imaged on 3 occasions over 4 years. In our sample, there were 32 APOE e4 carriers and 79 APOE e4 non-carriers. Magnetization prepared rapid gradient echo (MPRAGE) imaging was performed on a Philips 3.0 T Achieva scanner. Cortical reconstruction and volumetric segmentation was performed with the longitudinal pipeline of the FreeSurfer image analysis suite version 5.1.0 (http://surfer.nmr.mgh.harvard.edu/). Cortical thickness values for each of the 68 parcels defined by the Desikan parcellation (Desikan et al., 2006) were extracted by subject and timepoint. We fit a linear mixed effects model for each parcel that included fixed effects of intercept, age, and APOE e4 carrier status, and the interaction of age and APOE e4 carrier status to predict slope in cortical thickness of each parcel. **Results:** The mean estimated cortical thickness at age 60 (intercept) was thinner for APOE e4 carriers than APOE e4 non-carriers in the left inferior parietal parcel and left and right frontal pole. Slope differences (age X e4 carrier status interaction) were found in: left temporal pole and superior frontal regions, and right transverse temporal and caudal anterior cingulate (Figure 1). In all regions except the right transverse temporal, APOE e4 carriers had a steeper rate of decline than noncarriers. **Conclusions:** The APOE 4 allele modulates mean thickness and rates of change both in areas associated with normal aging and in areas associated with progression to AD.
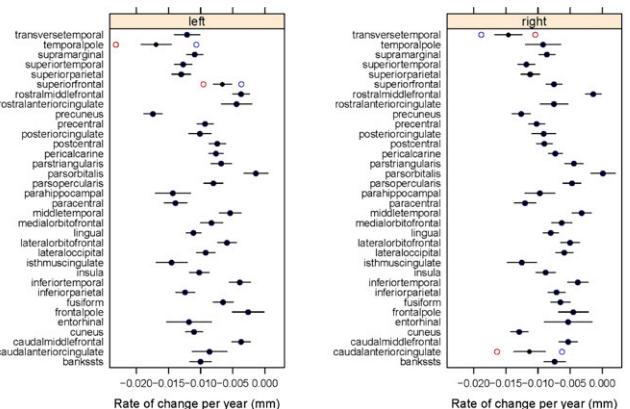
IC-O1-02 | **DIFFERENTIAL CORRELATION OF AMYLOID BINDING WITH HIPPOCAMPAL SUBFIELD VOLUME LOSS IN COGNITIVELY NORMAL PARTICIPANTS**

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Background: Pathological examination has suggested early involvement of CA1 and CA2 in hippocampal cell loss and manual tracing in amnestic MCI