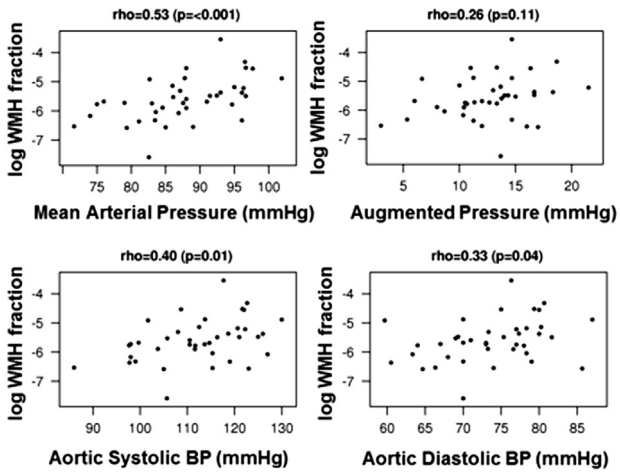

SATURDAY, JULY 12, 2014
ALZHEIMER'S IMAGING CONSORTIUM (IC)
IC-02
PRECLINICAL ALZHEIMER'S DISEASE AND BIOMARKERS

IC-02-01 GREATER SUBJECTIVE COGNITIVE CONCERNS CORRESPOND WITH ADVANCING STAGES OF PRECLINICAL AD

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Background: Emerging evidence suggests that subjective cognitive concerns (SCC) may herald initial cognitive decline at the preclinical stage of Alzheimer's disease (AD). While previous studies have investigated the relationship between SCC and amyloid (A b) burden and neurodegeneration (ND) separately, it remains unclear if increased SCC correlates with successive stages of preclinical AD. **Methods:** We studied 186 CN individuals from the Harvard Aging Brain Study (Clinical Dementia Rating Scale = 0, Geriatric Depression Scale <11). A b status was determined with PIB-PET imaging and ND was measured using two a priori imaging markers: hippocampus volume and glucose metabolism extracted from AD-vulnerable regions. A subjective cognitive concerns composite was calculated using subscales from three questionnaires. Linear regression models with A b and ND status as simultaneous predictors were used to predict SCC, controlling for age, education, and gender. A secondary analysis included APOE ε4 carrier status as a predictor. SCC were also examined across groups based on joint A b and ND status (Stage 0: A b -/ND-; Stage 1: A b +/ND-, Stage 2: A b +/ND+, and SNAP: A b -/ND+). **Results:** SCC was not related to age, gender or education. Both A b (p=0.002) and ND (p=0.036) were independently associated with greater SCC. APOE ε4 carrier status was not related to SCC and did not impact results from the initial model. Examination across groups revealed that SCC was greater in stage 2 compared to stage 0 (p<0.001), stage 1 (p=0.20) and SNAP (p=0.03). Furthermore, Stage 0 had lower SCC than both SNAP (p = 0.07) and stage 1 (p=0.03). There was no difference between Stage 1 and SNAP (p=0.45). **Conclusions:** We demonstrate independent and additive contribution of A b and ND status in predicting SCC, unaffected by APOE ε4 carrier status, such that individuals who are positive on both biomarkers show the greatest SCC, while individuals positive for a single biomarker show intermediate levels of SCC. This pattern is consistent with the hypothesis that the combination of A b and ND markers increases likelihood of cognitive decline.

IC-02-02 THE USE OF NEUROIMAGING BIOMARKERS IN PRECLINICAL ALZHEIMER'S DISEASE

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Background: Alzheimer's disease (AD) is a major public health issue. Atrophy assessed with structural MRI, hypometabolism and amyloid load have been recently proposed as neuroimaging biomarkers for the preclinical diagnosis of the disease, consistently with the amyloid cascade hypothesis. However the meaning and the relevance of each neuroimaging biomarker remain not completely understood. Our objective was to characterize populations defined according to each neuroimaging biomarker (i.e. positive vs negative cases) to further our understanding of their use in the preclinical diagnosis of AD. **Methods:** We prospectively included 54 healthy controls (HC) over 50 years old who all performed structural MRI, FDG-PET and Florbetapir-PET in the same neuroimaging center. All HC were then dichotomized into positive or negative independently for each of the three biomarkers considering the regions of greatest changes in AD. Then, demographic, neuropsychological and neuroimaging data were compared between positive and negative cases classified from MRI, FDG-PET or Florbetapir PET data. **Results:** Amongst the 54 HC, 12 (22%), 12 (22%) and 8 (15%) individuals were positive for atrophy, hypometabolism and amyloid deposition, respectively. Demographic and neuropsychological data were not statistically different between the positive and the negative subgroups, except for age that was higher in the amyloid positive versus negative subgroup. Interestingly, the atrophy positive subgroup showed both hippocampal and frontal atrophy, and posterior cingulate, temporoparietal and frontal hypometabolism compared to the atrophy negative subgroup. There was no difference in amyloid load between atrophy or hypometabolism positive versus negative subgroups and the amyloid positive group didn't differ from the amyloid negative in terms of grey matter atrophy or hypometabolism. However, when considering individuals with atrophy and/or hypometabolism together, there seems to be an inverse relationships between amyloid and neurodegenerative biomarkers such that those with more neurodegeneration tend to show lower amyloid deposition and reversely. **Conclusions:** The atrophy biomarker is associated with a mixed pattern of AD-like and frontal. The three biomarkers provide independent rather than redundant information. Our findings show that individuals tend to have either neurodegeneration or amyloid load but not both, suggesting additive rather than sequential/causative links between the current neuroimaging biomarkers in the pathological process of AD.

IC-02-03 EXISTING THRESHOLDS FOR PIB POSITIVITY ARE TOO HIGH

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Background: There is no consensus among researchers about the thresholds that define amyloid positivity and there is little known about the earliest phases of amyloid accumulation in older adults. The present study had two goals: first, to derive a cutoff that captures early accumulation using both DVR and SUVR data from our subjects and, secondly, to examine their pattern of amyloid accumulation. **Methods:** Amyloid accumulation was investigated in 152 cognitively