APOE-e4 carriership (MCI 41%, dementia 48%) was more frequent than in subjects with both biomarkers normal (MCI 26%, dementia 34%) but less frequent than in subjects with both biomarkers abnormal (MCI 70%, dementia 57%). Both MCI and demented subjects with SNAP had lower MMSE scores than subjects with normal biomarker scores but higher scores than subjects with both biomarkers abnormal. **Conclusions:** SNAP is common in subjects with MCI and dementia and is associated with age and APOE genotype. The high frequency of SNAP in elderly subjects with a clinical diagnosis of AD suggests that at high age clinical criteria may often not be specific for AD.

F3-02-04 BEYOND PART: VASCULAR MECHANISMS OF NEURODEGENERATION TYPICALLY SEEN IN ALZHEIMER'S DISEASE

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Background: Some models of Alzheimer's disease (AD) posit β-amyloid (Aβ) deposition to be a precursor of neurodegeneration within regions most affected by AD. However, one quarter of cognitively normal (CN) older people show signs of neurodegeneration without detectable Aβ burden, so called SNAPs. Such findings suggest the involvement of non-Aβ pathological processes in AD-typical brain injury. One of these mechanisms might be vascular damage. The presentation will cover current research studies into vascular mechanisms of neurodegeneration and relationships with Aβ deposition as well as cognitive functions in non-demented older people. **Methods:** Cross-sectional studies will be summarized mainly investigating cognitively-normal and mildly-impaired older adults. Measurements include Aβ deposition (measured using PIB PET imaging), AD-typical brain injury (measured using cortical thickness, gray-matter volume, or glucose metabolism), white matter lesions (WML, measured using MRI), vascular risk factors (measured using the Framingham Coronary Risk Profile Index) and cognitive test performance. **Results:** In CN older adults, accumulation of abnormal neurodegeneration biomarkers (such as cortical thinning, hippocampal atrophy, or hypometabolism) was significantly related to larger WML volumes, but not to Aβ deposition. In fact, Aβ deposition was only associated with cortical thinning, when individuals with some level of cognitive impairment were included in the study. In this population, vascular risk factors also potentiated the impact of Aβ on the brain, as indicated by a significant interaction of the two processes on cortical thinning. Neurodegeneration emerging from non-Aβ pathways was associated with poor cognition at baseline and exacerbated cognitive decline, when occurring in combination with Aβ deposition in CN older people. **Conclusions:** Brain injury in AD-typical regions occurs regardless of detectable Aβ deposition in CN older people, as seen in the SNAP cases. Neurodegeneration measured using neuroimaging markers can be associated with WML, a surrogate of vascular disease. However, it is also possible that low (or subthreshold) Aβ levels might be sufficient to "cause" neurodegeneration in the presence of vascular risk. Finally, the co-occurrence of Aβ and non-Aβ pathways has synergistic effects on preclinical cognitive decline. These findings stress the importance to consider non-Aβ pathological processes in preclinical stages of AD.

TUESDAY, JULY 21, 2015
FEATURED RESEARCH SESSIONS
F3-03
RISK DISCLOSURE IN THE ERA OF ALZHEIMER'S PREVENTION RESEARCH: A BOLD NEW FRONTIER

F3-03-01 DISCLOSING APOE GENOTYPE STATUS TO INDIVIDUALS AT RISK FOR ALZHEIMER'S DISEASE: APPLYING LESSONS LEARNED FROM THE REVEAL STUDY TO PREVENTION TREATMENT TRIALS

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Background: Clinical researchers have begun to use genetic testing (e.g., *APOE* genotyping) to identify high-risk populations for participation in Alzheimer's disease (AD) prevention trials. Communication of *APOE* status to study participants (e.g, in Alzheimer's Prevention Initiative) should be informed by available evidence on the safety and efficacy of genetic risk disclosure. **Methods:** The Risk Evaluation and Education for Alzheimer's Disease (REVEAL) Study is a series of multi-site randomized clinical trials that has examined the psychological and behavioral impact of genetic susceptibility testing for AD. Lifetime disease risk estimates (range: 13-77%) based on APOE genotype, age, gender, race, and family AD history were developed based on published epidemiological studies; these were delivered within various genetic counseling and education protocols. Primary outcomes included validated measures of anxiety, depression, and test-specific distress, with secondary outcomes including measures of recall and comprehension of test results, as well as changes in health-related behaviors following genotype disclosure. **Results:** Across three completed trials, genetic risk information was provided to 648 cognitively normal adults (mean age = 57 years, 64% female, 79% Caucasian, 14% African American, 88% with an AD-affected first degree relative, 38% ε4-positive). Anxiety and depression scores were well below standard cutoffs for clinical concern at one year after genotype disclosure, with no differences by genetic risk status (BAI Δ=0.1, p=.86; CES-D Δ=0.5, p=.43). Prior to testing, only 3% of participants believed test results could predict with certainty whether or not a person would develop AD. Ultimately, 39% of ε4-positive and 71% of ε4-negative participants rated the overall impact of their genetic risk information as positive, compared to only 15% of ε4-positive participants and 2% of ε4-negative participants who rated it negative. ε4-positive participants were more likely than ε4-negatives to report behavioral responses to risk information, including changes in long-term care insurance and use of vitamins or nutritional supplements. **Conclusions:** Findings suggest that *APOE* genotype status can be safely and effectively disclosed to high-risk individuals. The proposed APOE4 trial presents an opportunity to examine how the impact of *APOE* disclosure might differ in the context of a prevention trial enrolling only ε4 homozygotes.

F3-03-02 APPLYING LESSONS LEARNED FROM REMOTE GENETIC COUNSELING IN BREAST CANCER TO ALZHEIMER'S DISEASE

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