reporter assays and Western blot analysis of human cell lines, neural progenitor cells and mouse primary corital neurons that over-expressed miRNAs, miRNA inhibitors and/or reporter constructs was used to assess miRNA mediated regulation of APP expression. Human subjects were recruited following IRB approved protocol, DNA was isolated from blood and sequencing based genotyping was utilized. **Results:** We demonstrate that six human, brain expressed miRNAs (miR-17-5p, 106a, 106b, 153, 324-5p, and 495) repress APP expression and used in situ hybridization of post-mortem human brain tissue to confirm brain expression and localization of these six miRNAs. We identified a SNP, rs45455403, that is located just outside of the miR-495 target site seed sequence. We tested the functional consequences of this SNP's minor allele using luciferase reporter assays. Introduction of the minor allele into the 3'UTR results in elimination of miR-495 repression of APP expression observed in the wild-type 3'UTR. rs45455403 is present in 6% of the African American (AA) community and therefore we are recruiting AA patients and controls to determine if this SNP increases the risk of developing AD. **Conclusions:** Our data demonstrates that the minor allele of rs45455403 eliminates miR-495 mediated repression of APP expression. Given the functional consequences of the minor allele of rs45455403 it is possible that this allele may alter risk of developing AD. We are in the process of testing this hypothesis.

FEATURED RESEARCH SESSIONS: F3-01 DISCLOSING RISK INFORMATION TO INDIVIDUALS AT IMMINENT RISK OF ALZHEIMER'S DISEASE

F3-01-01 DISCLOSURE OF APOE GENOTYPE TO PERSONS WITH MILD COGNITIVE IMPAIRMENT (MCI)

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Methods: We generated risk estimates using data obtained from a clinical trial involving 769 aMCI patients, which provided three-year conversion data stratified by APOE genotype (Petersen et al. 2005). We used an evidence-based approach in risk communication to develop graphics and language to communicate APOE genotype and a numerical risk estimate. Patients with aMCI are being recruited at four university medical centers (Harvard, Univ Michigan, Univ Penn and Howard) and randomized in a 2:1 ratio to either disclosure or non-disclosure arms. Scales of participant and caregiver distress, health behavior change and insurance/lifestyle change are measured at 6 weeks and 6 months. **Results:** Three-year risks for each age-group were: 8.4% for APOE-ε4 negative and 42.0% for APOE-ε4 positive individuals (ages 55-70), 20.5% for APOE-ε4 negative and 47.4% for APOE-ε4 positive (ages 71-77), and 30.7% for APOE-ε4 negative and 57.1% for APOE-ε4 positive (age 78 or older). Estimates based on MCI diagnosis and age alone (excluding genotype information) were 25.2% (ages 55-70), 34.0% (ages 71-77) and 43.9% (ages 78 or older). Educational materials were created to describe the possible APOE genotypes, an individual's APOE genotype result and three-year AD conversion risk. **Conclusions:** An evidence based procedure for risk estimation and an experimental trial of APOE genotype disclosure in aMCI patients has been designed and implemented. Preliminary results will be presented and discussed.

F3-01-02 DEVELOPMENT OF A STANDARDIZED APPROACH TO DISCLOSING AMYLOID IMAGING RESULTS IN MCI

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Background: Amyloid imaging is increasingly recognized as a powerful tool for predicting clinical outcomes in mild cognitive impairment (MCI). As this technology moves from the research setting into clinical practice, an emerging concern is that patients with MCI may have difficulty comprehending their test results. Given the lack of research on disclosing non-genetic biomarker information to cognitively impaired patients, the purpose of this two-phase study is to develop a standardized procedure for effectively communicating amyloid imaging results in the context of MCI. **Methods:** For phase 1, we convened a panel of experts in neuroimaging, neuropsychology, risk communication, regulatory affairs, and bioethics to determine the content and process for disclosing positive, negative, and inconclusive PiB-PET scan results to persons affected by MCI. The panel critically reviewed a series of outlines and scripted text for results disclosure in an iterative fashion. Visual aids were subjected to the same process of critique. Phase 2 remains in progress and aims to evaluate MCI patients' and family members' satisfaction with and comprehension of the materials developed in phase 1. Two out of a proposed sample of ten MCI dyads, including both amnestic and nonamnestic subtypes, have undergone mock (hypothetical) amyloid imaging results disclosure sessions and completed post-disclosure interviews. **Results:** Disclosure scripts for positive, negative, and inconclusive results, with accompanying visual aids, were developed. Each script was sequenced to review the purpose of amyloid imaging, disclose a hypothetical result, and interpret that result in terms of dementia risk and recommendations for clinical follow up. Scripts ranged from 245 to 300 words long with Flesch-Kincaid reading levels of 8th to 9th grade. All four participants agreed or strongly agreed with statements indicating that the session was "easy to follow," "included just about the right level of detail," and was "just about right" in length. All four rated the information as "clearly presented," and adequately restated, in their own words, the results that were disclosed. **Conclusions:** These preliminary findings support the feasibility of presenting amyloid imaging results in a manner that is satisfying to, comprehended by, patients with MCI and their families.

F3-01-03 DISCLOSURE OF AMYLOID STATUS IN SECONDARY PREVENTION TRIALS FOR ALZHEIMER'S DISEASE

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Background: As the field moves towards early intervention, there is increased reliance on biomarker evidence of preclinical Alzheimer's disease (AD) for inclusion into studies. There are a number of secondary prevention trial initiatives in the planning stages that will be conducted in asymptomatic individuals at-risk for AD on the basis of genetic and/or biomarker positivity. The disclosure of biomarker results with uncertain clinical implications in clinically normal older individuals raises important ethical issues. **Methods:** PET amyloid imaging and/or cerebrospinal fluid markers of Aß accumulation will be used to select eligible participants for the Anti-Amyloid treatment of Asymptomatic Alzheimer's disease (A4) trial being proposed by the Alzheimer's Disease Cooperative Study. This placebo-controlled trial will treat clinically normal amyloid-positive older subjects with a biologically active immunotherapeutic agent for 3 years to test the hypothesis that decreasing "upstream" amyloid accumulation will slow "downstream" neurodegeneration and rate of cognitive decline. Participants will be informed of their amyloid status, as only amyloid-positive individuals will be randomized to receive treatment or placebo, but a group of amyloid-negative individuals will participate in a natural history arm.