mg of citalopram prior to the start of the central nervous system stable isotope labeling kinetics study of Abeta, as previously described. A lumbar catheter was placed and hourly sampling of blood and CSF was conducted during and after administration of a stable-isotope labeled amino acid (13C6-leucine). Metabolism of Abeta was measured using stable isotope labeling kinetics (SILK-Aβ®) assay (as in Bateman et al., 2006) with the addition of stable isotope spike absolute quantitation (SISAQ™) to allow for quantitation of Abeta concentrations (C2N Diagnostics). **Results:** Placebo (n = 9) and citalopram (n = 11) treated subjects did not differ on any demographic variables. Citalopram-treated subjects had significantly lower mean total Abeta concentrations (36.7 +/- 10.5) ng/mL than placebo-treated (54.6 +/- 15.5) ng/mL ($p = 0.007$) over the hours 5-36. During the same period there was a trend towards lower newly generated Abeta ($p = 0.06$) in the citalopram group (7.5 +/- 1.3) ng/mL vs placebo (9.3 +/- 1.4) ng/mL however the groups did not differ in their fractional synthesis or clearance rates. **Conclusions:** We corroborate our prior findings in a prospective human study showing that citalopram lowers Abeta concentrations compared with placebo. We had also expected to see a lower rate of Abeta production and a decrease in newly generated Abeta, thus we are currently replicating and extending our results. The ability to decrease Abeta concentrations is potentially important as a preventive strategy for AD.

P4-068 PRE-SYMPTOMATIC FUNCTIONAL BRAIN CHANGES IN PS1 E280A MUTATION CARRIERS COMPARED WITH OTHER BIOMARKERS: PILOT DATA FROM THE ALZHEIMER'S PREVENTION INITIATIVE BIOMARKER PROJECT

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Background: The Alzheimer's Prevention Initiative project has conducted pilot biomarker studies to characterize and compare age-related changes in preclinical autosomal dominant Alzheimer's disease in the PS1 E280A mutation kindred from Antioquia, Colombia. We previously presented evidence of changes in florbetapir positron emission tomography (PET) 17 years before, cerebrospinal fluid Aβ42 and Tau 14 years before, and hippocampal volume reductions 7 years prior to the median age of MCI onset. We have now completed FDG PET and functional MRI assessments for comparison. **Methods:** Fifty family members from Colombia received FDG PET measurements on a Siemens Biograph mCT 64 PET CT scanner with 30-min dynamic emission scan acquired 30-min after the IV administration of 5mCi of FDG. The cohort included 11 symptomatic carriers: 7 with MCI (46 years +/- 4.5), 4 with AD dementia (51 years +/- 1.9), 19 cognitively normal mutation carriers (33 years +/- 8.0) and 20 non-carriers (NC, 34 years +/- 8.5) between ages 20-56 years old. Regional-to-whole brain cerebral metabolic rates of glucose (CMRgl) were compared between PS1 E280A mutation carriers and NC, accounting for age effects. A nonlinear model was used to characterize CMRgl decline and to estimate the age at which its reductions in mutation carriers became apparent as compared to NC. Voxel-wise comparison of resting state fMRI default mode network (DMN) was performed between carriers and NC using a 10mm spherical posterior cingulate seed region. **Results:** Compared to non-carriers, symptomatic and pre-symptomatic mutation carriers had significantly lower CMRgl in posterior-cingulate, precuneus, parietal and temporal regions, which was associated with increasing age. Precuneous CMRgl reductions appear to begin approximately 18 years prior to the typical median age of MCI onset, roughly similar to the age at fibrillar amyloid accumulation and CSF Aβ and Tau changes. Compared to non-carriers, symptomatic and pre-symptomatic mutation carriers also had significantly reduced resting state functional connectivity in the DMN. **Conclusions:** Functional PET and MRI imaging identifies pre-symptomatic brain changes in PS1 E280A carriers. FDG PET reductions are seen near the time of fibrillar amyloid accumulation. These biomarkers provide additional tools for evaluating pre-symptomatic Alzheimer's disease.

P4-069 ASSOCIATION OF ANKLE BRACHIAL INDEX AMONG THE ELDERLY WITH NORMAL COGNITION, AMNESTIC MILD COGNITIVE IMPAIRMENT AND ALZHEIMER'S DISEASE

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Background: Vascular disorders have been implicated in the development of cognitive decline and dementia and atherosclerosis is believed to be involved in the development of the most common type of dementia, Alzheimer's disease. Although a low ankle-brachial index (ABI) reflects the presence of atherosclerosis of the arterial walls in the lower extremities and is a good indicator of generalized atherosclerosis, data on cognitive prognosis of patients with a low ABI are limited.This study aimed to investigate the association of the ABI to several grades of cognitive impairment including normal cognition (NC), amnestic mild cognitive impairment (MCI) and Alzheimer's disesase (AD) in the Korean elderly. **Methods:** Five hundred ninety five subjects (NC 100, amnestic MCI 291 and probable AD 204) aged 60 years old and over enrolled in the Dementia and Age-associated Cognitive Decline Clinic of an university hospital and in a service program for the early detection and management of dementia in the community. The ABI was measured as a generalized atherosclerosis. The subjects were divided into 3 groups according to the ABI tertiles and and a multivariate logistic regression analysis was applied to determine the association between the ABI and the grades of cognitive impairment. Measurement included height, weight, body mass index (BMI), blood pressure, serum total cholesterol, LDL cholesterol, triglyceride, hemostatic factors, and presence of cardiovascular diseases. **Results:** Subjects with NC were significantly younger than those with either of amnestic MCI or probable AD and well educated than those with probable AD. Subjects with NC also was higher in height and lower in body weight, systolic and diastolic blood pressure, serum total cholesterol, LDL cholesterol and various hemostatic factors. When the subjects were divided into 2 groups (NC versus aMCI and AD), after adjusting for confounding factors, the lowest ABI tertile was significantly associated with an increased risk of cognitive impairment such as aMCI and AD. (OR=2.65, 95%CI=1.43-4.95). **Conclusions:** This cross-sectional study suggests that the ABI may be an independent risk factor for cognitive impairment and useful in identifying older individuals at higher risk of AD and amnestic MCI, a prodromal stage of AD.