Coordinating Center (NACC; N=869), Religious Orders Study (ROS; N=174), Rush Memory and Aging Project (MAP; N=149), clinical trial of the drug Tarenflurbil (N=2,524), AddNeuroMed study (N=303), and Adult Changes in Thought (ACT; N=746). First, we performed pre-statistical harmonization to identify tests in common across studies. Second, we used a two parameter graded-response item response theory model to estimate cognitive ability scores for each observation at all time points in all studies. **Results:** The cognitive composite was normally distributed and scaled to have mean=50 and standard deviation=10. The median follow-up time in the pooled sample was 3.1 years (range: 0-18 years). The cognitive composite had interval-level properties, was highly internally consistent (Cronbach's alpha=0.88), had minimal floor or ceiling effects, and demonstrated reliable measurement precision over a broad range of ability levels (See Figure.). **Conclusions:** Our methods can be used to calibrate neuropsychological test results across diverse settings and studies into a summary measure of global cognitive functioning. Psychometric properties of the measure holds substantial promise for advancing work to evaluate cognitive decline over time in persons with AD, making it an optimal phenotype for a GWAS of cognitive decline.

ORAL SESSIONS: O4-08: DIAGNOSIS AND PROGNOSIS: NON-AMYLOID

O4-08-01 ASSOCIATION BETWEEN THE ALZHEIMER'S DISEASE–RELATED HYPOMETABOLIC CONVERGENCE INDEX AND CLINICAL RATINGS IN COGNITIVELY NORMAL OLDER ADULTS WITH AND WITHOUT SIGNIFICANT FIBRILLAR AMYLOID BURDEN: FINDINGS FROM THE ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE

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Background: We previously developed a voxel-based hypometabolic convergence index (HCI) to characterize, in a single measurement, the extent to which the pattern and magnitude of hypometabolism in a person's flourodeoxyglucose positron emission tomography (FDG-PET) image corresponds to that in patients with the clinical diagnosis of Alzheimer's dementia (Chen and Ayutyanont et al., 2010). In this study, we characterized and compared HCIs and their relationship with poorer clinical ratings in cognitively normal "fibrillar beta-amyloid positive and negative" older adults from the Alzheimer's disease Neuroimaging Initiative (ADNI). **Methods:** Florbetapir PET scans from 225 cognitively normal subjects 76±6 years of age were used to characterize mean cortical-to-cerebellar standard uptake value ratios (SUVRs) and classify the images as fibrillar beta-amyloid positive and negative using an SUVR threshold previously found to be associated with moderate or frequent neuritic plaques (Fleisher et al., 2011). FDG-PET scans from 71 beta-amyloid positive and 154 beta-amyloid negative subjects were used to generate HCIs, compare this index, and relate them to lower MMSE and higher ADAS-Cog scores (i.e., measures of clinical severity) in the two subject groups. **Results:** beta-amyloid positive groups had significantly higher HCIs than the beta-amyloid negative groups (p=0.0024). HCIs were significantly associated with poorer MMSE and ADAS-Cog scores in the beta-amyloid positive group (r = -0.38, p=0.001 and r=0.36, p=0.002, respectively) but not in the beta-amyloid negative group (r=0.007, p=0.936 and r=0.06, p=0.458, respectively). **Conclusions:** Fibrillar beta-amyloid burden in cognitively normal older adults is associated with an AD-related index of cerebral hypometabolism, and this index is associated with poorer clinical ratings in those who are beta-amyloid positive.

O4-08-02 PIB-NEGATIVE AMNESTIC MILD COGNITIVE IMPAIRMENT RELATED WITH LOW PLASMA APOLIPOPROTEIN A1 LEVEL

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Background: Very little is known about the characteristics of amnestic mild cognitive impairment (aMCI) with no or very little cerebral amyloid beta protein (beta-amyloid) deposition, so called PIB-negative aMCI (aMCI-). We aimed to investigate the distinct clinical and neuroimaging characteristics, and plasma lipid-related components of aMCI- by comparing aMCI with high cerebral beta-amyloid deposition, so called PiB-positive aMCI (aMCI+), and cognitively normal (CN) old individuals. **Methods:** Twenty eight patients with aMCI (13 aMCI- and 15 aMCI+) and 35 CN elderly individuals were included. All participants received comprehensive clinical and neuropsychological assessment based on the CERAD protocol, PiB-PET, FDG-PET, volumetric MRI, and quantification for plasma lipid components with apolipoprotein A1 (APOA1) and B (APOB), and were followed up 1 year after. **Results:** Duration of illness was significantly longer in aMCI- than aMCI+ (4.6 ± 2.1 vs. 1.2 ± 1.4 years). After 1 year, no aMCI- subject converted to Alzheimer's disease (AD) dementia, while 26.7% of aMCI+ converted to AD dementia. Brain images of aMCI- individuals were quite different from those of aMCI+, which had typical early or prodromal AD patterns. aMCI- subjects showed decreased regional cerebral glucose metabolism in the right culmen and left fusiform gyrus, and decreased gray matter density in the right middle temporal gyrus, compared with aMCI+ subjects. They also showed decreased left temporal, right inferior frontal and precentral gray matter density compared with CN subjects. Plasma APOA1 level was significantly lower in aMCI- than in both aMCI+ and CN subjects. Plasma APOA1 also showed significant correlation with global cognition measured by MMSE and CDR-SOB, as well as regional brain metabolic changes and atrophy, even after controlling various potential confounders including demographic variables and global cortical PiB retention. **Conclusions:** Our findings suggest that in spite of the similarity in cross-sectional cognitive features, aMCI- has quite different clinical progression pattern compared to aMCI+. While aMCI+ can be regarded as aMCI due to AD process, the cognitive deficits of aMCI- appears to be related with the alteration of cholesterol transport mechanism medicated by APOA1, independent of AD process.

O4-08-03 NON-BETA-AMYLOID-RELATED STRUCTURAL, METABOLIC AND WHITE MATTER FIBER INTEGRITY CHANGES IN EARLY MCI

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Background: According to the amyloid cascade hypothesis, β-amyloid (beta-amyloid) pathology is an early event in Alzheimer's disease (AD), followed by structural, functional and finally cognitive changes. If beta-amyloid+ is essential for AD, beta-amyloid- cognitive decline is non-AD, which may involve changed structure and function compared to beta-amyloid- cognitively healthy persons (NL). However, the changes should be different from those seen in beta-amyloid+ cognitive decline. In this study, we tested the specific hypothesis that there are differences in brain structure, metabolism, and white matter (WM) connectivity between