negatives can be a problem in amyloid imaging. The question of “false positives” in amyloid imaging is subtle; for example, cognitively normal individuals may have brain Aβ, and the presence of a positive amyloid scan does not mean that other important pathology is absent (i.e., multiple pathological causes of dementia). With regard to tau imaging, still in its infancy, it seems that the distribution of the radiotracer is more informative than is the distribution of an amyloid PET tracer. From both pre-existing clinical-pathological data and the limited PET studies available, medial temporal lobe tau accumulation may not necessarily reflect the presence of AD. It seems that cognitive dysfunction and signs of brain degeneration may be more detectable as tau deposition is found in neocortex. Thus, both the sensitivity and specificity of tau as a biomarker of AD (in clinical or preclinical stages) is dependent on its location. Sensitivity and specificity, in this situation, may be more complex than a single scalar threshold. Finally, tau PET data may be complicated by binding of ligands to unusual sites such as the choroid plexus, brainstem, and basal ganglia. Conclusions: Although the availability of amyloid- and tau-PET have greatly improved the characterization of the continuum of AD, a number of situations may arise in which PET data interpretation may be complex or ambiguous.

**F1-03-04** HOW AD-SPECIFIC ARE AD-LIKE MRI BIOMARKERS?

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Background: Alzheimer’s disease is currently defined in molecular terms as the association of cortical amyloid and hyper-phosphorilated tau deposition. MRI biomarkers for AD capture neurodegenerative phenomena related to tissue loss, axonal damage, and synaptic loss but are blind to the underlying molecular pathology. On the other hand, neurodegenerative phenomena but not molecular pathology are closely related to clinical symptoms. Methods: Survey of the literature on structural MRI, diffusion MRI, and functional networks at rest including personal and international studies. Results: Non topographic structural MRI markers are sensitive to AD even at the pre-dementia MCI stage, while diffusion and functional network markers at the asymptomatic stage. Topographic information enhance specificity, but is complicated by the heterogeneity of the topography of molecular pathology in AD (e.g. early onset AD being more often neocortical and late onset limbic). The association of MRI with molecular biomarkers also enhances specificity to very high figures at the MCI stage (>90%). Conclusions: The specificity of MRI AD-like biomarkers lies in their topography. Enhancement of specificity can be achieved through the association with either molecular markers or different MRI markers.

**F1-04-01** LONGITUDINAL PERFORMANCE ON THE PRECLINICAL ALZHEIMER’S COGNITIVE COMPOSITE (PACC) IN SUBJECTS WITH BIOMARKER-DEFINED PRECLINICAL AD

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Background: The Preclinical Alzheimer Cognitive Composite (PACC) (Donohue, JAMA Neurol 2014) is the primary outcome measure in the Anti-Amyloid Treatment in Asymptomatic Alzheimer’s Disease (A4) prevention trial. The PACC was designed to track subtle cognitive decline in clinically normal older adults by combining tests of episodic memory, timed executive function and global cognition. Knowledge of how the PACC performs over time in a preclinical population is limited. The purpose of this study was to examine longitudinal performance on the PACC in subjects from the Harvard Aging Brain Study (HABS) who have biomarker-defined preclinical AD. Methods: Two hundred seventy-seven clinically normal older adults (mean MMSE=29±1.06; CDR=0) were classified as Aβ+(n=71) or Aβ−(n=206) at baseline and followed for a mean of 3.3±1.1 years. The effect of Aβ status and change on the PACC and its individual subtests, (i.e., MMSE, Digit Symbol, FCSRT and Logical Memory) were examined using linear mixed models (LMM) and non-linear mixed models of repeated measures (MMRM). Results: There were no baseline differences between Aβ groups on PACC performance. There was a significant decline in Aβ+ compared with Aβ− on the total PACC composite (Aβ X Time β=-0.08, p=0.001) and a similar pattern in each of the PACC components (MMSE β=-0.09, p=0.04, Digit Symbol β=-0.06, p=0.003; FCSRT β=-0.11, p=0.09 and Logical Memory β=-0.09, p=0.02). Additional examination of the FCSRT Free Recall (without cuing) also revealed a significant decline in Aβ+ compared with Aβ− groups (β=-0.13, p=0.0005). Free Recall in Aβ+ subjects preceded decline in Cued Recall at 2-years post-baseline, compared with four years post-baseline for Cued Recall. Conclusions: The PACC is sensitive to Aβ related cognitive decline at the preclinical stage of disease. Furthermore, earlier decline on the FCSRT Free Recall compared to Cued Recall suggests that inclusion of this measure in the PACC composite may improve sensitivity to detect the earliest memory changes in preclinical AD. These findings support the PACC as a promising cognitive outcome measure in AD prevention trials.

**F1-04-02** GLOBAL DETERIORATION SCALE (GDS) STAGE 2: PERSONS WITH SUBJECTIVE COGNITIVE IMPAIRMENT (SCI) ONLY SHOW SIGNIFICANT DECLINES IN GDS STAGING SYSTEM MEASURES OVER A 2-YEAR INTERVAL

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Background: In 1982 we published the Global Deterioration Scale (GDS) which describes 7 stages from normality to severe Alzheimer’s disease (AD). The GDS describes 3 pre-dementia stages including GDS stage 2, in which there is “subjective decline in cognitive functioning” only (SCI) and GDS stage 3 for which we