

borderline CSF A β_{42} can already be indicative of underlying AD pathology. Future research should focus on discordant cases to clarify the underlying possibly neuropathological causality.

IC-P-006 **EARLY AMYLOID ACCUMULATION AND ITS COGNITIVE CONSEQUENCES IN HEALTHY ADULTS**



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Background: The recent failures of anti-amyloid clinical trials has led to a shift towards trials aimed at earlier intervention, underscoring the need for information about the earliest stages of amyloid accumulation and its impact on cognition. Autopsy and amyloid PET imaging data have converged to suggest that the orbitofrontal cortex (OFC) may be one of the earliest sites of amyloid accumulation, whereas posteromedial regions exhibit accumulation later and are potentially more closely linked to dementia onset. In the present study, we examined whether the OFC and penumbral regions may provide a window into the earliest stages of amyloid accumulation by measuring change in amyloid over 4 years, particularly in middle-aged adults and those who were initially amyloid-negative. Additionally, we assessed whether this early accumulation was associated with subtle cognitive deficits. In comparison, we also examined whether posteromedial amyloid accumulation appears later and is associated with AD-related cognitive deficits. **Methods:** 83 participants (age 30-89) were included from the Dallas Lifespan Brain Study who completed florbetapir PET and a cognitive battery at baseline and 4-year follow-up. Regional amyloid accumulation was measured (Time 2-Time 1 SUVR) in the following Freesurfer-derived ROIs: OFC ROIs (medial OFC, lateral OFC, pars orbitalis); Posteromedial ROIs (precuneus, posterior cingulate, isthmus cingulate). **Results:** Consistent with the lateral OFC and pars orbitalis as early sites of amyloid accumulation, accumulation was detected in both middle-aged adults and adults who were amyloid negative at baseline (Figure 1a). The rate of accumulation in lateral OFC and pars orbitalis was associated with deficits in follow-up reasoning performance (but not episodic memory or processing speed), even after restricting to those who were amyloid negative at baseline (Figure 2). In comparison, high precuneus amyloid accumulation was predominately restricted to older, amyloid positive adults (Figure 1b) and was associated with AD-typical deficits in episodic memory. **Conclusions:** These findings support the use of the OFC and penum-

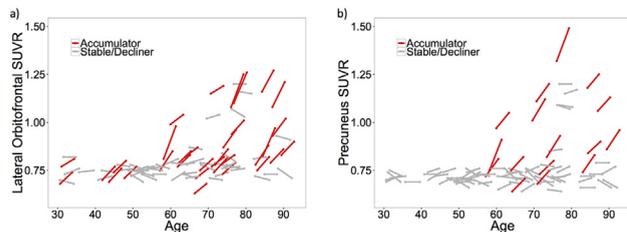


Figure 1. Regional Amyloid Accumulation over 4 Years across the Lifespan. Lines represent change in SUVR as a function of age for (a) lateral orbitofrontal cortex and (b) precuneus. Within each region, individuals were grouped into accumulators (red) and stable/decliners (gray) based on a cluster analysis. Consistent with the OFC as an earlier site of accumulation, chi-square tests revealed a higher proportion of accumulators in the lateral orbitofrontal cortex than the precuneus across the full sample, in middle-aged adults alone and in those who were amyloid negative at baseline.

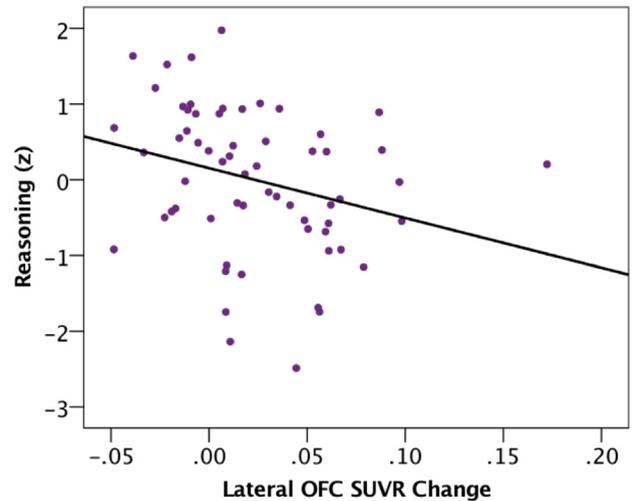


Figure 2. Cognitive Consequences of Early Amyloid Accumulation in OFC. In those who were amyloid negative at baseline, increasing regional amyloid accumulation in the lateral orbitofrontal was related to lower follow-up reasoning performance, suggesting accumulation in the OFC may have negative consequences for reasoning even at this early stage of disease progression.

bral regions as markers of the earliest stages of amyloid accumulation, and provide evidence that even at this early stage, negative consequences of amyloid accumulation may already be apparent.

IC-P-007 **HOW AMYLOID PET CHANGES COGNITIVE CARE: A BROADER VIEW**



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Background: Amyloid PET imaging is a reliable biomarker of Alzheimer's disease pathology and could prove valuable in clinical care. A standard formulation is that diagnostic testing should be performed only if it modifies drug or surgical treatment. There are, however, many additional reasons for knowing the cause of the cognitive impairment with greater certainty. Although some recommendations are relevant irrespective of diagnosis, others depend upon the specific cause of cognitive impairment identified. Provider confidence in the diagnosis also affects the willingness to discuss difficult, lifechanging recommendations. **Methods:** We identified 8 independent, non-drug care recommendations that would be altered depending upon the cause of cognitive impairment and used them as outcomes in a study of the clinical use of amyloid PET. Amyloid PET with 18F-flutemetamol was performed in 15 patients (9 men, 6 women, mean age 64.6, age range 51-85) whose diagnosis was uncertain after an otherwise complete dementia specialist evaluation. Scans were read visually, aided by quantitative analysis using Cortex ID software and classified as either positive indicating significant pathology or negative. We evaluated changes in physician diagnosis, diagnostic confidence and recommended care practices before and after amyloid PET imaging. **Results:** Significant binding in the cerebral cortex was present in 13 (87%) of the scans. In 14 patients (82%) recommended care practices changed after amyloid PET. These recommendations involved planning for likely stable or progressive disease course (33% change), monitoring for disease complications (13%), disease specific