GDS-slope, amyloid, GDS-slope X amyloid, and the covariates above. **Results:** In the model with baseline GDS, sex (p=0.0005; females with higher scores), higher age (p<0.0001), lower education (p<0.0001), and amyloid X time (p=0.0088; greater amyloid associated with greater PACC decline) were significant, but baseline GDS did not predict PACC decline. In the model with GDS-slope, higher age (p<0.0001), lower education (p=0.03) and GDS-slope X amyloid (p=0.0002) significantly predicted PACC decline, such that increasing GDS scores with baseline amyloid were associated with greater PACC decline. In secondary analyses holding time and all other predictors constant, longitudinally increasing GDS predicted decreasing PACC in those with amyloid levels above 1.10. **Conclusions:** Results suggest that worsening depressive symptoms in the setting of elevated amyloid are associated with cognitive decline. While future work is needed to determine causality, findings support the potential prognostic utility of depressive symptoms in identifying older adults at risk for cognitive decline and AD.

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TAU ACCUMULATION AND MEMORY DECLINE ARE MORE CLOSELY RELATED TO STRIATAL THAN CORTICAL AMYLOIDOSIS IN INDIVIDUALS WITH EARLY-ONSET AUTOSOMAL DOMINANT ALZHEIMER'S DISEASE

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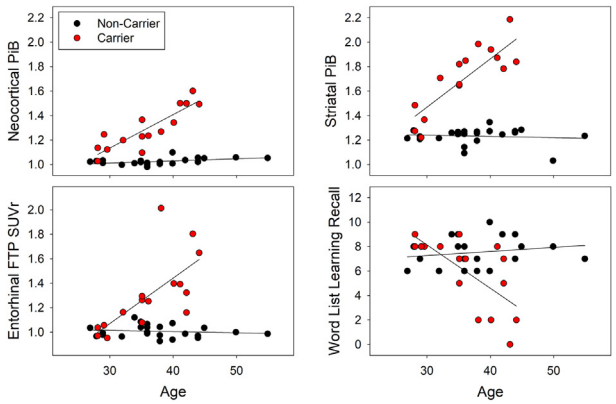

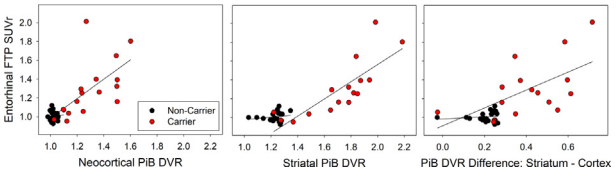

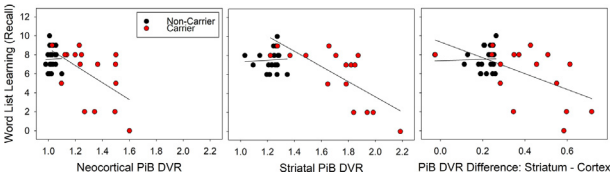

Background: To determine whether striatal amyloidosis can help predict disease progression in individuals at genetic risk for AD, we sought to examine the tau accumulation relationship with cortical and striatal amyloid, and with memory performance in non-demented individuals with autosomal dominant Alzheimer's disease (ADAD). **Methods:** Thirty-nine (16 carriers aged 28-44, 23 age-matched non-carriers) non-demented individuals from the Colombian kindred (PSEN1 E280A mutation) were evaluated using PiB-PET, Flortaucipir-PET (FTP; tau), and memory testing (CERAD Word List Learning). PiB was measured in Freesurfer-defined cortical and striatal (caudate/putamen) aggregates. FTP was measured in entorhinal and inferior temporal cortices. **Results:** Compared to non-carriers, mutation carriers had an age-related increase in cortical (Fig.1: 0.026±0.003DVR/year, p<0.0001) and striatal (0.041±0.006DVR/year, p<0.0001) PiB binding. The annual rate of PiB accumulation was significantly greater in striatum than cortex (0.015±0.007DVR/year, p=0.04). FTP binding increased with age (entorhinal: 0.039±0.009SUVr/year, p=0.0007; inferior temporal: 0.014±0.007SUVr/year, p=0.04) and memory scores decreased with age (-0.38±0.09items/year, p=0.0003). In mutation carriers, PiB was associated with FTP binding in entorhinal (Fig.2: cortex: 1.0±0.4SUVr/DVR, p=0.01; striatum: 0.9±0.2SUVr/DVR, p=0.0001) and inferior temporal (cortex: 0.6±0.2SUVr/DVR, p=0.03; striatum: 0.4±0.1SUVr/DVR, p=0.01), and with worse memory (Fig.3: cortex: -9.0±3.8items/DVR, p=0.03; striatum: -8.0±0.09items/DVR, p=0.001). Remarkably, striatal PiB binding predicted entorhinal FTP (0.9±0.3SUVr/DVR, p=0.02) and memory (-6.1±3.2items/DVR, p=0.07) after adjusting for age, indicating that striatal PiB can inform about tauopathy and memory for carriers having identical estimated years of dementia onset. In contrast, cortical PiB binding was not predictive after adjusting for age (p>0.9). The difference between striatal and cortical PiB was associated with FTP binding in entorhinal (Fig.2-right: 1.0±0.3SUVr/DVR, p=0.02) and with worse memory (Fig.3-right: -8.3±3.6items/year, p=0.03). Striatal PiB was significant when both PiB regions competed to predict entorhinal FTP (cortex: +0.1±0.4SUVr/DVR, p=0.9; striatum: +0.9±0.3SUVr/DVR, p=0.006) or memory performance (cortex: -0.6±4.6items/DVR, p=0.9; striatum: -7.7±3.0items/DVR, p=0.02). **Conclusions:** These findings suggest that striatal amyloid in preclinical ADAD may be more predictive of progression to dementia than cortical amyloid. This study provides insight into the role of striatal amyloid in the progression of AD, and informs the pre-symptomatic treatment trials targeting amyloid in this population.