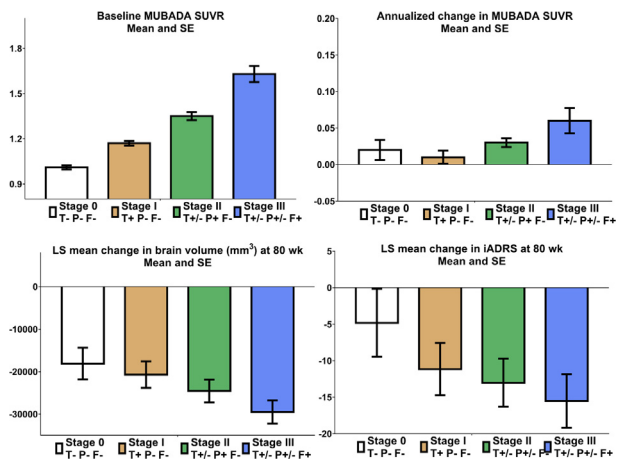
Stage	Lobar profile(s)	Tau level in temporal lobe	Tau level in parietal lobe	Tau level in frontal lobe
0	T-P-F-	Not elevated	Not elevated	Not elevated
I	T+P-F-	**Elevated**	Not elevated	Not elevated
II	T+/-P+F-	**Any level**	**Elevated**	Not elevated
III	T+/-P+/-F+	**Any level**	**Any level**	**Elevated**

2017). The aim of this study was to develop a simple, quantitative tau PET-based patient classification algorithm based on sequential lobar accumulation of flortaucipir signal. **Methods:** The EXPEDITION3 trial enrolled amyloid-positive patients with mild AD (MMSE 20-26). Flortaucipir images were acquired for a subset of participants at baseline, week 40 and week 80. We quantified tau burden in baseline scans from the placebo arm (N=97), using average SUVR values in atlas-based lateral temporal, parietal and frontal lobes with respect to a white matter-based reference region (PERSI). Elevated tau burden in the temporal (T+), parietal (P+) and frontal (F+) lobes bilaterally was determined using a single positivity threshold. All possible lobar profiles were grouped into four stages 0-III (T-P-F-, T+P-F-, T+/-P+F- and T+/-P+/-F+), reflecting the stereotypical patterns of tau spread inferred from neuropathological studies. A mixed effects repeated measures method was used to characterize changes in global weighted SUVR (MUBADA), cognition and structural MRI. **Results:** Lobar stages were strongly concordant with a global tau burden measured by MUBADA SUVR. On average, individuals belonging to more advanced lobar stages at baseline demonstrated numerically more rapid cognitive (MMSE, ADAS-Cog$_{14}$ and iADRS) and neurodegenerative (whole brain and whole temporal lobe volumes) decline over 80 weeks follow-up. In these analyses, approximately 25-30% of the cases were classified to each of stages I-III, with a slightly lower proportion assigned to stage 0. If scans were staged using a more rigorous sequential classification (T-P-F-, T+P-F-, T+P+F- and T+P+F+), <5% scans remained unclassified. **Conclusions:** We propose a simple quantitative algorithm based on suprathreshold lobar flortaucipir SUVR values for AD staging *in vivo*. Specifically, a symptomatic, amyloid-positive AD population may potentially be further segmented into four flortaucipir-measured pathological stages characterized by an escalating risk of cognitive decline. Further validation of these findings using independent datasets is warranted.



O3-13-03 THE RELATIONSHIP BETWEEN TAU PET AND OTHER AD BIOMARKERS IN AUTOSOMAL DOMINANT ALZHEIMER DISEASE

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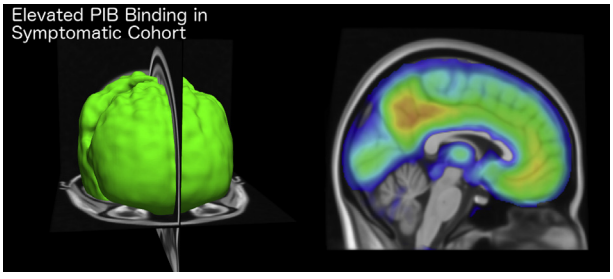
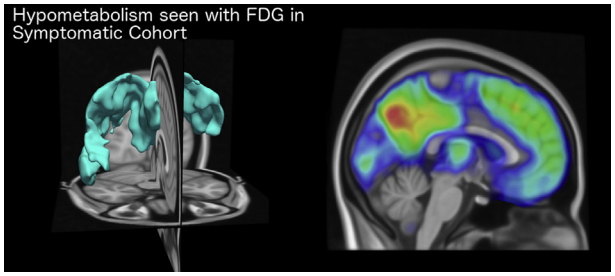
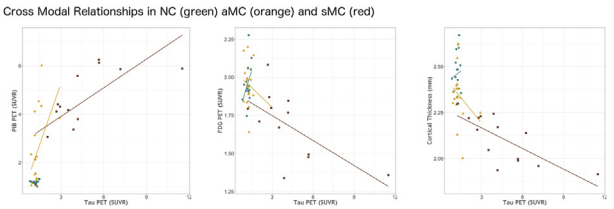
Background: In autosomal dominant Alzheimer disease (ADAD), there is a conservation of age of symptom onset within families. This consistency allows participants to be staged according to their estimated years to symptom onset (EYO). This provides an elegant model to study the emergence of AD biomarkers during the transition from preclinical to clinical stages of the disease. ADAD cohorts also provide robust populations of mutation carriers with preclinical and clinical AD as well as familial controls that are mutation non-carriers. **Methods:** ADAD participants were drawn from families known to have mutations in presenilin 1, presenilin 2, and amyloid precursor protein genes. The cohort consisted of 16 mutation non-carriers (NC), 20 asymptomatic carriers (aMC, CDR=0), and 15 symptomatic carriers (sMC: 13 CDR 0.5, 1 CDR=1, 1 CDR=3). Participants had tau (flortaucipir), beta-amyloid (PiB), and metabolic imaging (FDG) PET imaging as well as structural MRI. Voxel-wise PET data were nonlinearly aligned to the MNI152 atlas using a two-stage registration. Voxel-wise statistics were performed comparing groups using permutation testing. Data were additionally analyzed using regions of interest derived from Freesurfer. Primary comparisons were between NC, aMC, and sMC groups. **Results:** All four modalities showed significant group effects, with worse AD pathology in the sMC individuals relative to both the aMC and NC groups (Figures 1-4). There was a clear spatial overlap in what regions of the brain were affected by pathology, with a common focus in the precuneus and lateral parietal regions. There was a prominent cross-modal relationship

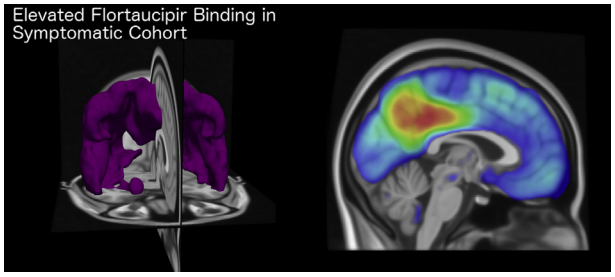


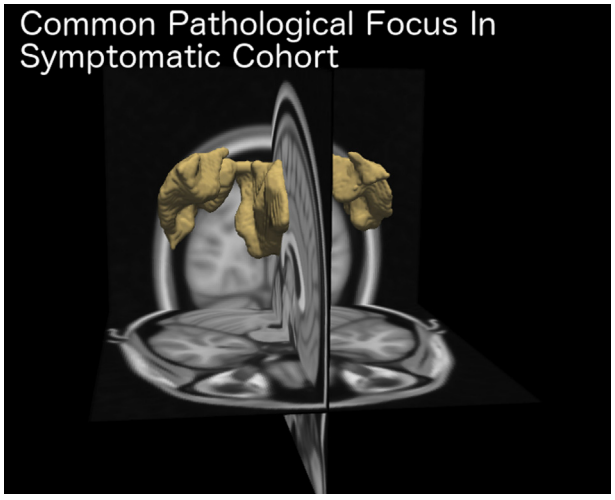




Cross Modal Relationships in NC (green) aMC (orange) and sMC (red)

between tau and the other three biomarkers. For the entire sample there was a significant correlation between precuneus tau and PiB (r=0.73, p=0.000000004), FDG (r=-0.63, p=0.002), and cortical thickness (r=-0.69, p=0.00000003). The strength of these relationships varied by group (Figure 5) but were particularly prominent in the sMCs. **Conclusions:** We found overlapping spatial patterns of biomarker change in ADAD, with pathological changes consistently located in the precuneus and lateral parietal regions across all four biomarkers. The degree of beta-amyloid, hypometabolism, and cortical thinning were all strongly correlated with tau pathology measured with flortaucipir.





O3-13-04 **[18F]-AV-1451 BINDING PROFILE IN EARLY AND LATE-ONSET ALZHEIMER'S DISEASE AND SUSPECTED NON-ALZHEIMER PATHOPHYSIOLOGY**

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