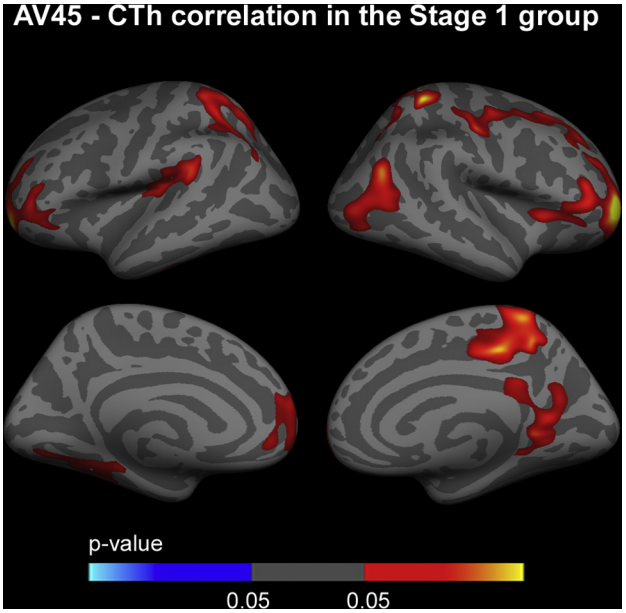
correlation between AV45 retention and increased cortical thickness in Stage 1 subjects (FIG1). The results were similar when correlating the mean SUVR with cortical thickness. The Stage 2 group also presented a cluster of increased cortical thickness in the AV45-CTh correlation analyses. **Conclusions:** Brain structure in preclinical AD follows a biphasic trajectory of changes. This study also shows that different brain areas could be at different stages in an individual. These results have implications in clinical trials in preclinical AD, both when selecting patients and when using MRI as a surrogate marker of efficacy.



O1-06-03 EFFECTS OF TAU DEPOSITION ON CEREBRAL GLUCOSE METABOLISM IN NORMAL OLDER ADULTS VARY BY AMYLOID LEVEL

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Background: Relationships between brain β-amyloid and glucose metabolism in cognitively normal older adults (OA) have been weak and inconsistent. We examined associations between tau and glucose metabolism and whether relationships varied with global Aβ burden. **Methods:** 47 OA (Table) received 18F-AV-1451 (tau, 80-100 min SUVR), 11C-PiB (Aβ, 35-90 min DVR), and 18F-FDG (30-60 min SUVR) PET, which were coregistered to T1-weighted MRI. We processed native-space T1 (FreeSurfer v5.3) to delineate cerebellar gray matter (PiB and AV-1451 reference region) and brainstem (edited to derive FDG pons reference). For each subject we calculated a weighted cortical PiB average to characterize Aβ-positivity. We warped OA MRI to MNI space (ANTS) and applied transformations to AV-1451 and FDG images. A cortical testing mask was created by intersecting AAL ROIs with high-probability gray matter (GM) voxels (SPM12 probability map). MNI-space FDG and AV-1451 PET images were masked and smoothed (4mm). We used SPM12 VBM (10mm FWHM smoothing) on T1 images to generate voxelwise MNI-space GM concentration images, which were also masked. We used a newly-developed Spatially Varying Coefficient Model to examine associations between increased tau accumulation and reduced glucose metabolism (within Aβ status group, controlling for local GM). This method incorporates false discovery control, accounts for continuity among adjacent voxels, and has higher detection power than voxel-wise analysis. Reported clusters are significant at $p<.0001$ (>=20 voxels). **Results:** Among Aβ- OA, increased AV-1451 uptake was significantly associated with reduced FDG metabolism (Figure) in clusters located in bilateral medial temporal lobes (MTL), with additional smaller clusters in inferior frontal cortex and temporo-occipital fusiform gyrus. Among Aβ+ OA, significant inverse AV-1451—FDG associations were located in right inferolateral temporal, and bilateral medial parietal and inferior medial frontal cortex. **Conclusions:** In cognitively normal Aβ- OA, tau deposition is associated primarily with reduced metabolism in MTL. In Aβ+ OA, increased tau deposition is associated with metabolic deficits in medial frontal and parietal cortex, typical of brain regions with Aβ accumulation. Although the mechanisms by which late-life tau and amyloid accumulation influence glucose metabolism are not well understood, these results suggest early tau accumulation interacts with Aβ to produce cortical hypometabolism.

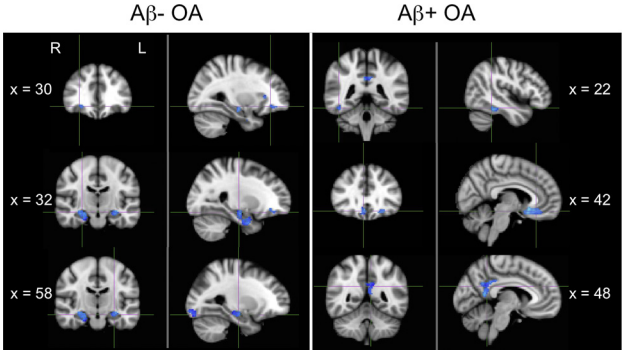

Figure. AV-1451—FDG associations by Aβ status. Clusters indicate significant negative associations between AV-1451 and FDG in Aβ- (left) and Aβ+ (right) older adults.

Table
Participant demographics

	Aβ-	Aβ+
N	26	21
Age, y	78.7 (6.9)	79.1 (3.6)
Sex (M/F)	9/17	7/14
Education, y	17.0 (1.9)	16.0 (2.1)
Global PiB DVR	1.01 (0.024)	1.37 (0.24)
MMSE	29.1 (0.98)	28.3 (1.4)

O1-06-04 CSF P-TAU IS CORRELATED WITH TAU PET, WHILE Aβ PET CORRELATES WITH Aβ1-42 AND THE T-TAU/Aβ1-42 RATIO

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