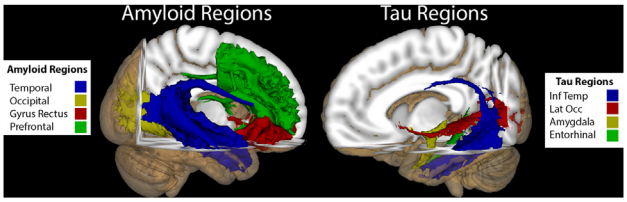
Table 2

Tau Regions	Mean Diffusivity	Axial Diffusivity	Radial Diffusivity	Fractional Anisotropy
Amygdala	0.6497	0.5991	0.6681	-0.6476
(R-value)	0.0026**	0.0067**	0.0018**	0.0027**
(P-Value)				
Entorhinal	0.5345	0.5101	0.5456	-0.6747
	0.0184*	0.0256*	0.0157*	0.0054**
Inferior	0.7878	0.7806	0.7716	-0.5229
Temporal	0.0004**	0.0004**	0.0004**	0.0288*
Lateral	0.660	0.5995	0.6583	-0.3163
Occipital	0.0019**	0.0067**	0.0022**	0.1871

* $p<0.05$

** $p<0.01$

The association for the tau regions between regional tau and DTI metrics in the β-amyloid positive subjects.



Deposition of tau in gray matter (GM) is associated with atrophy and cognitive impairment. However, the relationship between tau accumulation and white matter integrity has not been well characterized. We sought to correlate β-amyloid and tau deposition in predefined regions of interest (ROIs) with corresponding white matter (WM) projections from these ROIs. **Methods:** Sixty-nine participants underwent DTI, β-amyloid (florbetapir) and tau ([18F]AV-1451 (T807, flortaucipir)) positron emission tomography imaging. Twenty-one were β-amyloid positive, including 8 persons who were CDR>0. DTI metrics were processed in FMRIB software library, and GM regions were obtained with Freesurfer 5.3. Two sets of four AD-defined regions were evaluated based on either β-amyloid (Table 1) or tau (Table 2) accumulation. Probabilistic tractography projections were created for these predefined ROIs using ten cognitively normal individuals from the Human Connectome Project (Figure 1). The projections were applied to each participant's diffusion maps and average values calculated. Values were adjusted by age for partial correlations with either regional tau or β-amyloid. Correction for multiple comparisons was performed with false discovery rate correction (FDR). **Results:** Within β-amyloid defied regions, no association was seen between β-amyloid and diffusion metrics after FDR correction. With tau defined ROIs, Diffusion values within the occipital and temporal projections were associated with tau in β-amyloid positive individuals (Table 1). For the tau defined regions, β-amyloid did not associate with any diffusion metric. Significant associations were seen in all tau-defined regions for tau and absolute diffusion metrics in β-amyloid positive individuals (Table 2). No relationship was present between tau and diffusion metrics in the β-amyloid negative subjects. **Conclusions:** Tau and not β-amyloid accumulation was associated with changes in WM integrity. Observed changes were primarily seen in occipital and temporal projections. These results suggest that tau mediated changes primarily occur within posterior or temporal regions of the brain and are mediated by the presence of β-amyloid.

IC-01-03 RELATIONSHIP AMONG TAU, AMYLOID BURDEN AND BRAIN ATROPHY IN EARLY-ONSET ALZHEIMER'S DISEASE AND LATE-ONSET ALZHEIMER'S DISEASE

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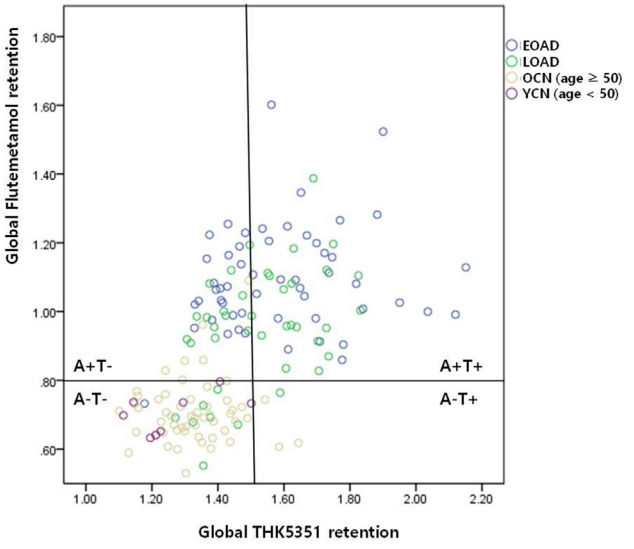
Background: We investigated the relationship among 18F-THK 5351 PET tau retention, amyloid burden and brain atrophy in early-onset Alzheimer's disease (EOAD) and late-onset Alzheimer's disease (LOAD). **Methods:** We included 158 participants including 54 patients with EOAD (onset age < 65), 41 patients with LOAD (onset age ≥ 65), 8 young participants (age < 50) and 55 elderly participants (age ≥ 50) with normal cognition, who completed 18F-THK5351 PET scans, 18F-flutemetamol (FMM) PET scans and 3T MRI. Brain atrophy was evaluated with cortical thickness and hippocampal volume. To investigate the distinct features of inter-regional correlation of THK and FMM retention, connectivity matrices were calculated in EOAD and LOAD, respectively. **Results:** Ninety-eight percent (53/54) of patients with EOAD were positive for FMM retention, whereas 82.9 % (34/41) of patients with LOAD were found as FMM positive. LOAD showed significant positive correlation between global FMM retention and global THK retention, cortical THK retention, and THK retention in the lateral temporal cortex. Meanwhile, EOAD did not show any significant correlation between global FMM retention and THK retention. On the contrary, only EOAD patients had significant negative correlation between mean cortical thickness or hippocampal volume and global THK retention, cortical THK retention, or THK retention in the lateral temporal cortex. THK retention in the mesial temporal areas did not have significant correlation with mean cortical thickness or hippocampal volume in any groups. There was no significant



correlation between global FMM retention and brain atrophy in any groups. There were positive correlations between THK retention in the frontal, parietal, occipital cortices or precuneus and FMM retention in the frontal, parietal cortices or precuneus. EOAD had weak positive correlation between THK and FMM retention only in the occipital cortex. **Conclusions:** LOAD showed gradual increase in both tau and amyloid and those two pathologies have association to each other. Whereas, in EOAD, tau and amyloid may develop more abruptly and independently. Brain atrophy was associated with tau burden in EOAD, however, was not correlated with amyloid burden in EOAD or LOAD. These findings suggest LOAD and EOAD may have different courses of pathomechanism.

IC-01-04 A ROBUST, SIMPLIFIED BRAAK-TYPE CLASSIFICATION SCHEME FOR FLORTAUCIPIR F-18 TAU PET IMAGES

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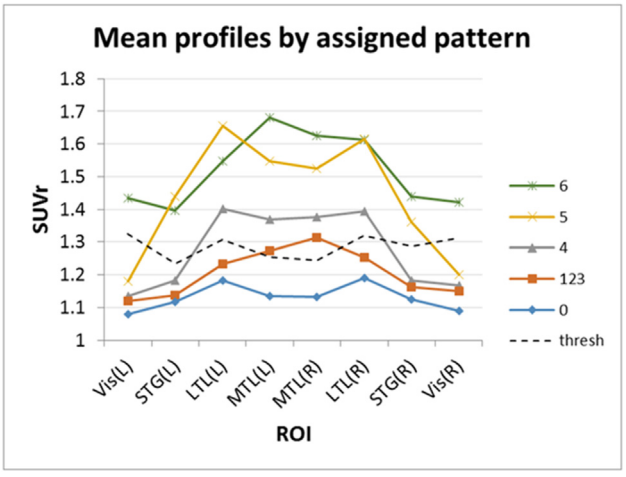
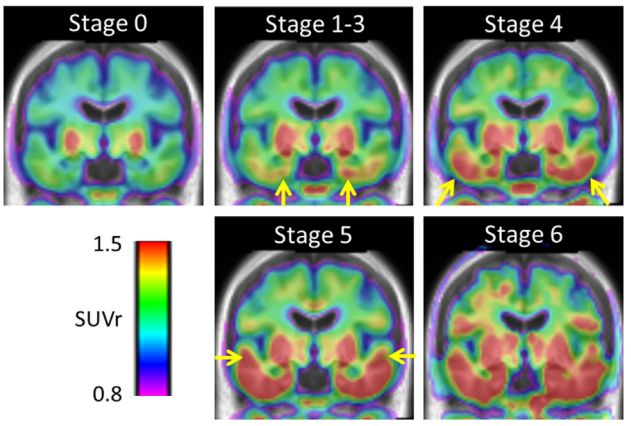
Background: Using ROIs based on the Braak staging scheme, patterns of [18F]-flortaucipir binding consistent with expectations from tau neuropathology can be observed in vivo [Schwarz et al., Brain 2016]. However, small regions of interest (ROIs) are potentially sensitive to variations in image preprocessing, atrophy and experimental noise. Medial temporal lobe (MTL) regions distinguishing stages 1-3 are prone to contamination from adjacent extraparenchymal signals and binding to the choroid plexus. Our aim was to identify a simplified and practical flortaucipir PET staging scheme for AD, robust to the above nuisance factors. **Methods:** Four ROIs were defined from standard Harvard-Oxford or Juelich (FSL) atlas structures: (1) an MTL ROI comprising the anterior hippocampus, the parahippocampal/entorhinal and fusiform gyri; (2) a lateral temporal lobe (LTL) ROI comprising the anterior inferior and middle temporal gyri; (3) anterior superior temporal gyrus; and (4) primary visual cortex. We compared larger and smaller variants on these ROIs, and evaluated the effect of grey-matter masking. Individual subject ROI profiles were binarized at 3SD above the mean signal in each ROI from 14 young controls and matched to predefined Braak-like patterns. Staging (0, 1-3, 4, 5 or 6) was performed on each hemisphere independently and the most advanced stage taken. Stages 1-3 were not differentiated. Performance was





evaluated in terms of maximizing test-retest consistency (N=21) and minimizing the number of unassigned profiles (N=21+236). The algorithm was then prospectively applied to flortaucipir scans from ADNI-2 (N=101). **Results:** The larger ROIs and simplified staging scheme yielded higher test-retest consistency and reduced number of unassigned profiles than the published approach. The variant ROIs and grey matter masking did not improve performance. Applied to the ADNI data set, 91% of subjects were classified into a typical predefined estimated Braak stage pattern (Figure). Higher stage tau patterns were associated with more advanced disease severity and amyloid positivity. **Conclusions:** This simplified flortaucipir staging scheme provides a practical and robust means of classifying tau patterns in vivo in terms of involvement of the sentinel brain regions proposed by Braak. It is easily implemented using widely available atlases, and may complement other tau PET summary measures.

IC-01-05 FIRST-IN-HUMAN PET STUDIES WITH THE NEXT GENERATION TAU AGENT 18-F PI-2620 IN ALZHEIMER'S DISEASE, PROGRESSIVE SUPRANUCLEAR PALSY, AND CONTROLS

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Background: Intracellular tau deposition is a key pathologic feature of Alzheimer's disease (AD) and other neurodegenerative disorders. Recently, positron emission tomography tau probes have been developed for in vivo detection of brain tau load, although quantification is challenging due to high off-target binding and slow kinetics. Further, different tau radiotracers have different affinities for tau species. PI-2620 is a novel tracer with an IC50 of 1.8 nM for tau in AD brain homogenate competition-assays and binds specifically to tau deposits in AD brain sections (Braak I-VI), Pick's, and progressive supranuclear palsy (PSP) pathologies. This first-in-human study assesses 18-F-labelled PI-2620 in AD, PSP, and healthy volunteers. **Methods:** In an ongoing clinical imaging study, participants diagnosed with mild Alzheimer's (AD), non-AD tauopathies (e.g. PSP), and healthy volunteers (HV) undergo dynamic PET imaging for over 3 h following 370 MBq bolus