[**F]AV1451 deposition pattern across the Alzheimer’s disease spectrum - Characterization at the individual level

### BACKGROUND AND OBJECTIVES
The extent to which older adults along the Alzheimer’s disease (AD) spectrum follow a similar tau-PET deposition pattern and have similar level of accumulation is not clear. We focused on inter-individual [**F]AV1451-PET binding across the typical Braak stages and using a more fine-grained parcellation of 34 brain regions in ADNI participants, ranging from cognitively normal older adults (CN), participants with early mild cognitive impairment (EMCI), late MCI (LMCI) and AD dementia. Our objective is to characterize deposition pattern across diagnostic groups, amyloid status, and to examine regional differences at the individual level by considering different regional thresholds.

### PARTICIPANTS
Participants along the Alzheimer’s disease spectrum (CN, EMCI, LMCI, AD) from ADNI who had a [**F]AV1451 scan. Amyloid positivity was taken from the ADNI database, i.e. [**F]AV45 global SUVR > 1.1

### REGIONS OF INTEREST
Standardized uptake value ratios (SUVR) were averaged in regions approximating the different Braak stages (I, III, IV, V, VI; see below). The hippocampus (Braak II) was not included due to non-specific binding of the tracer.

SUVR in 34 regions from the FreeSurfer Desikan atlas were also extracted, as a more fine-grained approach to examine binding across the AD spectrum and in young adults.

### RESULTS
Using composite regions approximating the different Braak stages, only 4% of amyloid-negative individuals, regardless of their clinical diagnosis, had elevated SUVR in Braak I or in further stages.

In the amyloid-positive group, 17% CN, 43% EMCI and 67% LMCI/AD had elevated SUVR in Braak I. Across all participants, few had elevated tau further than Braak stage IV, with either a liberal or conservative threshold.

Regions presenting the most often elevated SUVR were the entorhinal cortex, the parahippocampal gyrus, the amygdala, the inferior and middle temporal gyri, and the temporal pole.

Of note, the binding pattern of [**F]AV1451 seemed to differ between young adults and ADNI participants. In regions corresponding to early Braak stages (I-III), young adults generally presented low SUVR, while in many regions part corresponding to early Braak stages Freesurfer Desikan atlas regions

### CONCLUSIONS
We looked at the individual level, to assess whether there was a stereotypical pattern of elevated tau deposition across Braak stages and across the 34 brain regions (based on liberal and conservative thresholds; shown in figures above). SUVR matrices are shown on the left and thresholded matrices based on the thresholds are shown on the right.

In the amyloid-negative group (left), only 5 participants showed focal binding in one or more brain regions despite having low SUVR in the entorhinal cortex/Braak I. In amyloid-positive participants (right) with elevated tau in Braak I, 25% CN and only 50% LMCI/AD had elevated SUVR in Braak I. Across all participants, few had elevated tau further than Braak stage IV, with either a liberal or conservative threshold.

Using a parcellation of 34 brain regions, very few amyloid-negative individuals showed elevated tau signal in any region (using either liberal or more conservative thresholds), while amyloid-positive individuals tended to have elevated tau across all regions.

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### CONCLUSIONS
There was significant overlap in SUVR ranges across all individuals for the majority of regions, which yielded only small differences between using a liberal or conservative threshold.

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### CONCLUSIONS
We applied Gaussian mixture models with two components across all participants to derive a liberal threshold (50% probability to be in either distribution) and a conservative threshold (90% probability to be in the high distribution) for the Braak composite regions and the 34 brain regions. We compared SUVR values and tau "elevation" based on the thresholds across diagnostic groups, amyloid status, and compared to young adults.

### ANALYTICAL METHODS
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### SUMMARY
Using a parcellation of 34 brain regions, very few amyloid-negative individuals showed elevated tau signal in any region (using either liberal or more conservative thresholds), while amyloid-positive individuals tended to have elevated tau across all regions.

### REFERENCES

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