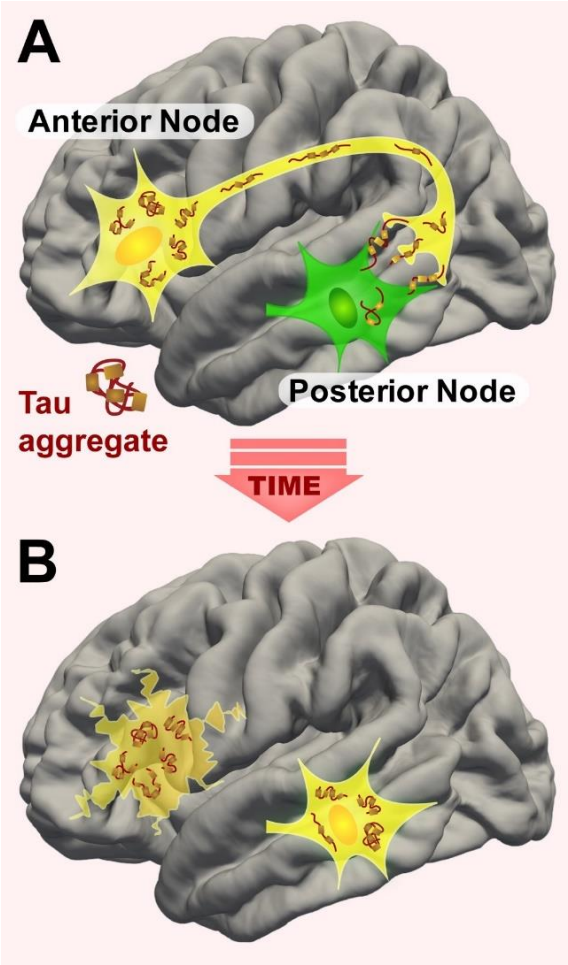
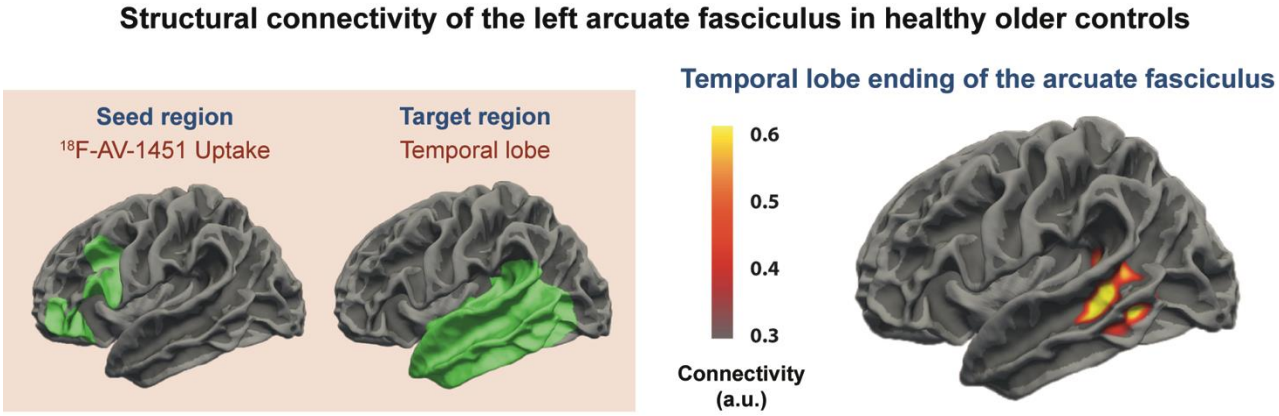
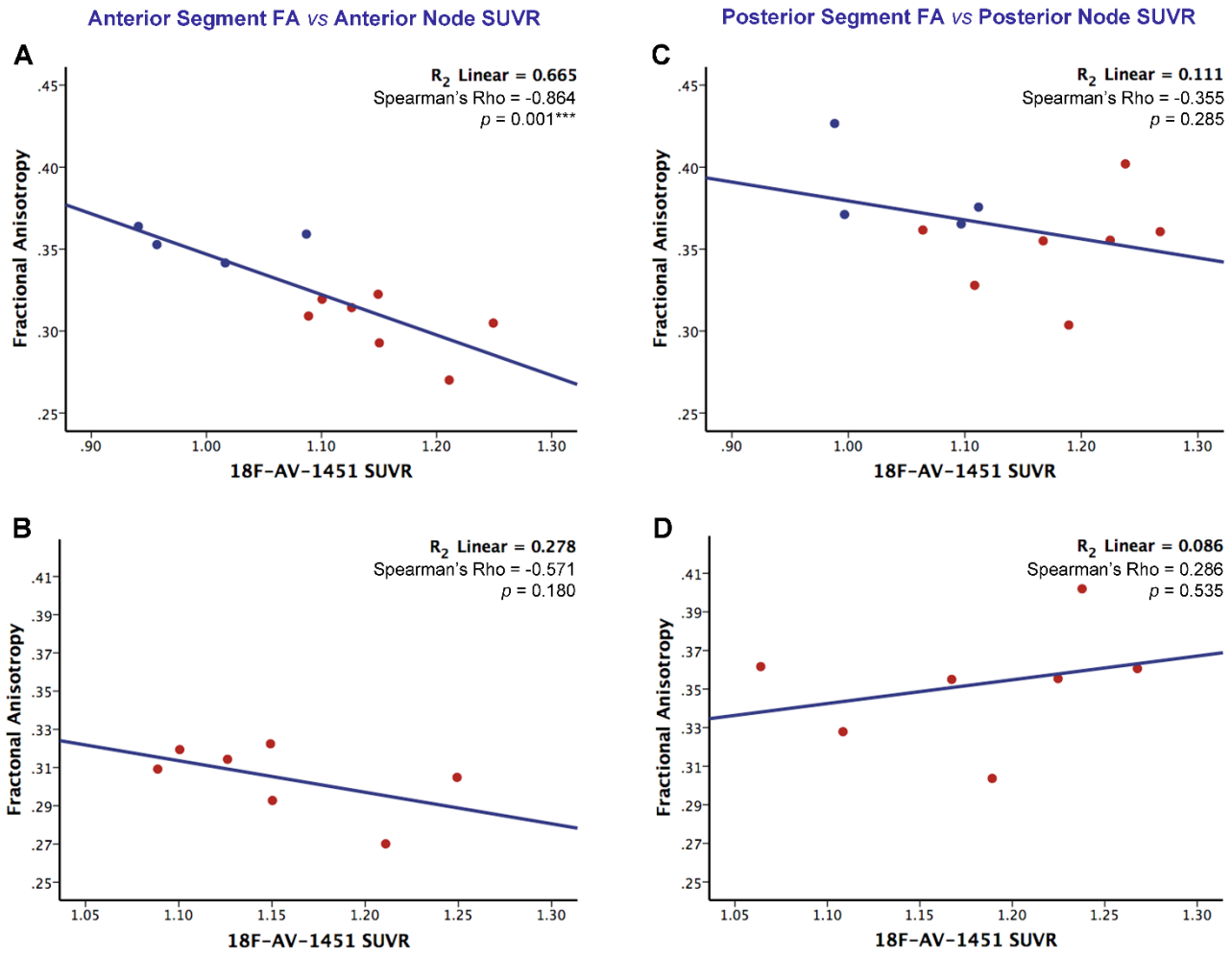


Supplemental Figure 1. Tau propagation hypothesis. **(A)** In nfvPPA, involvement of the anterior node of the syntactic network causes motor language impairment. An affected neuron (in yellow) in the anterior node contains tau aggregates; through its axon it is connected to a neuron in the posterior node, still healthy (in green) but being invaded by tau through its synapse with the neuron in the anterior node. **(B)** The neuron in the anterior node eventually dies, losing its axon, which used to travel in the arcuate fasciculus. Tau, however, remains in the tissue of the anterior node and can be detected by tau PET, which also detects tau in the posterior node, where a still viable but impaired neuron now contains tau. Note that the axon of the posterior node neuron, which may also travel in the arcuate fasciculus, is not depicted for the sake of simplicity.



Supplemental Figure 2. Diffusion tensor imaging structural connectivity. Seed in the area of the frontal lobe with increased tau deposition in nfvPPA (Figure 2C) and group-averaged image of the ending of the arcuate fasciculus in the lateral temporal lobe displayed on the FreeSurfer fsaverage gray-white matter boundary surface. For each subject, the significance cluster was defined by the 90th percentile of arcuate fasciculus density at the gray-white matter boundary. The color bar indicates in arbitrary units (a.u.) for how many patients a given voxel was significant.



Supplemental Figure 3. Correlation between [^{18}F]AV-1451 tau PET and fractional anisotropy (FA) of the arcuate fasciculus. There was a negative correlation between fractional anisotropy of the anterior segment of the arcuate fasciculus (y > -24) and tau deposition in the anterior node, which was significant when healthy controls were included (A) and trended when only patients were considered (B). By contrast there was no correlation between fractional anisotropy in the posterior segment (y < -24) and tau in the posterior node (C, D). This findings suggest that axons of neurons in the anterior node were more affected in correlation with the amount of tau, namely that the process was older than in the posterior node, where there was a similarly elevated tau level, but axonal sparing. This finding is in complete agreement with the postulate diagramed in Supplemental Fig 1.

Supplemental Table 1. Progressive Aphasia Severity Scale (PASS) performance

	Patients with nfvPPA (Mean ± *SD*)
Single Word Comprehension	**0.2** ± *0.2*
Reading	**0.6** ± *0.5*
Auditory Comprehension	**1.3** ± *1.3*
Articulation	**1.6** ± *1.3*
Repetition	**1.8** ± *1.1*
Writing	**1.9** ± *1.0*
Functional Communication	**1.9** ± *1.2*
Word Retrieval and Expression	**2.0** ± *1.1*
Syntax and Grammar	**2.3** ± *0.8*
Fluency	**2.7** ± *0.5*

Ratings range from "normal" (0), to "questionable/very mild" (0.5), "mild" (1.0), "moderate" (2.0), or "severe" (3.0) impairment. nfvPPA: non-fluent variant of primary progressive aphasia; *SD*: Standard deviation.