

# Supplementary Material

## Suspecting Non-Alzheimer's Pathologies and Mixed Pathologies: A Comparative Study Between Brain Metabolism and Tau Images

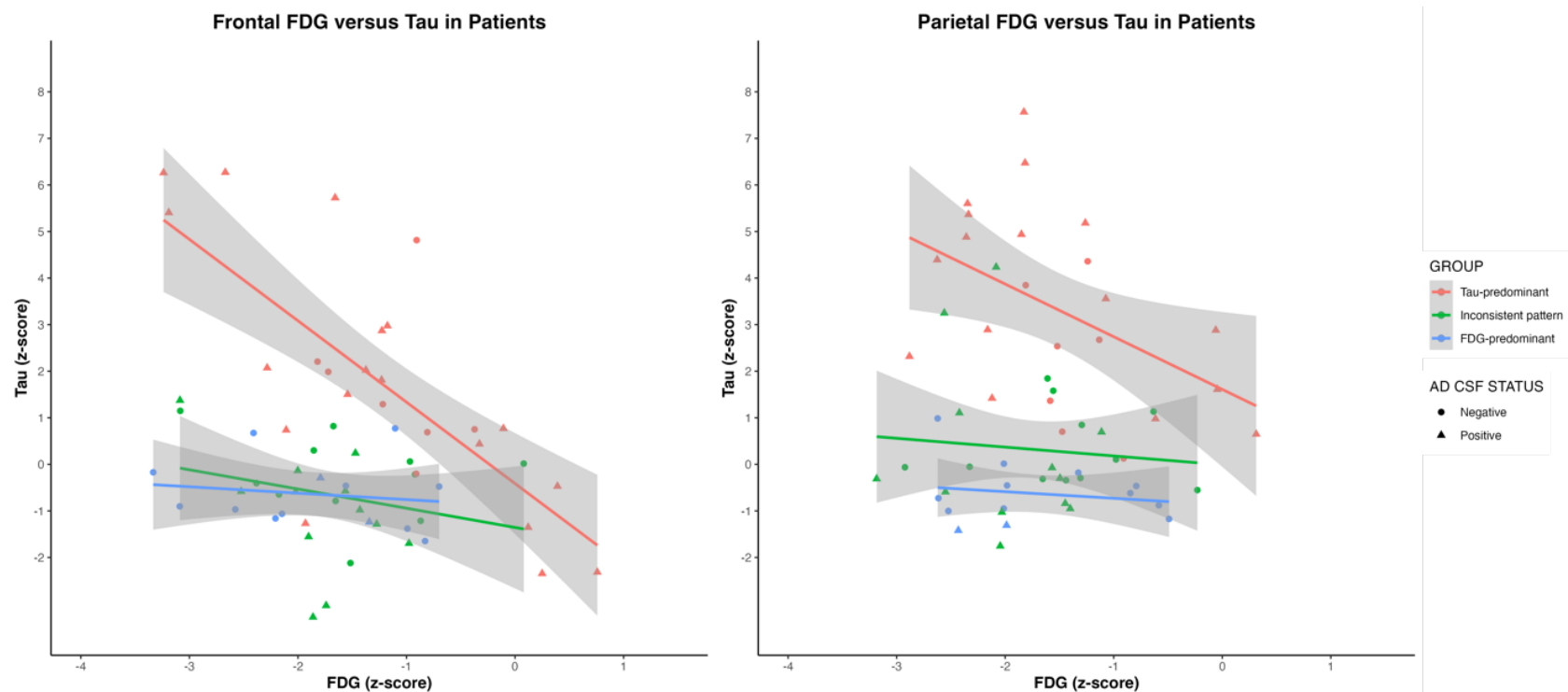
### **Supplementary Material 1.** Group classification using frontal and parietal lobes separately.

For all but six patients (90%), a frontal classification was identical to a frontoparietal classification. For all but nine patients (85%), a parietal classification was identical to a frontoparietal classification. Fifteen participants (25%) are classified differently by a parietal and a frontal classification. The number of participants with hypometabolism exceeding tauopathy increased from the temporal (n=13) to the parietal (n=31) to the frontal (n=38) lobe, as tau burden decreased from the temporal (mean  $z=2.81$ ) to the parietal (mean  $z=1.58$ ) to the frontal (mean  $z=0.31$ ) lobe. However, whereas all 13 participants with hypometabolism exceeding tauopathy in the temporal lobe were classified similarly when using the parietal, the frontal, or the frontoparietal classification; four of the 31 participants classified with predominant hypometabolism in the parietal lobe had greater tauopathy than hypometabolism in the frontal lobe. Similarly, eleven of the 38 participants classified with predominant hypometabolism in the frontal lobe had greater tauopathy in the parietal lobe.

### **Supplementary Material 2.** Tau-FDG associations in the frontal and parietal lobes.

When excluding the bilateral insula, splitting the frontoparietal region of interest into parietal and frontal regions of interest gave similar results. Although higher Tau PET signal is observed in the parietal compared to the frontal lobe (Supplementary Figure 1), the association between tau and FDG mean lobar z-scores is similar in both lobes ( $p=0.378$  using the Steiger's Z test). Pearson's correlation tends to be higher in the frontal ( $R=-0.29$ ,  $p=0.022$ ) than in the parietal lobe ( $R=-0.17$ ,  $p=0.187$ ) with an intermediate  $R=-0.22$ ,  $p=0.091$  in the frontoparietal. Mean Tau-FDG association across the 14 parietal regions in the whole sample gives an  $R=-0.02(\pm 0.44)$ , while we find an  $R=-0.16(\pm 0.35)$  across the 26 frontal regions.

## Supplementary Figure 1. Frontal and Parietal Tau versus FDG in Patients



CSF positivity is defined by a Total Tau/A $\beta_{42}$  ratio > 1.1 [1]. Group legend: Tau-predominant corresponds to Tau  $\geq$  FDG both in the temporal and in the frontoparietal. Inconsistent corresponds to Tau  $\geq$  FDG in the temporal and Tau < FDG in the frontoparietal. FDG-predominant corresponds to Tau < FDG both in the temporal and in the frontoparietal lobe.

[1] Bayart JL, Hanseeuw B, Ivanoiu A, van Pesch V (2019) Analytical and clinical performances of the automated Lumipulse cerebrospinal fluid A $\beta_{42}$  and T-Tau assays for Alzheimer's disease diagnosis. *J Neurol* **266**, 2304-2311.