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Neuroimaging / New imaging methods

Optimization of early-phase florbetapir as a surrogate of FDG-PET in ageing and Alzheimer's clinical syndrome

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Abstract

Background: FDG-PET is a validated and widely used sensitive biomarker for neurodegeneration (N) in ageing and Alzheimer's clinical syndrome as highlighted in the β-amyloid (A)/tau (T)/N scheme (Jack *et al.*, 2016, 2018). Early-phase Florbetapir (eAV-45) appears as a promising proxy for FDG-PET but needs further validation. Optimization of the time window and preprocessing methods of eAV-45 are scarce, and no previous study assessed the sensitivity and the reproducibility of this measure in individual cases.

Method: We included 191 participants including young to elderly volunteers and Alzheimer's clinical syndrome patients, all of whom had both FDG-PET and dual-phase Florbetapir acquired on the same scanner, along with structural MRI and neuropsychological examinations. The time window was first optimized at the vertex level by correlation maximization between eAV-45 and FDG-PET, and correlation minimization between eAV-45 and late AV-45 (lAV-45). Then, the six reference regions used for PET intensity scaling were compared by computing metrics of: (i) vertex-wise pattern overlap between eAV-45 and FDG-PET (derived from patients versus controls comparisons and correlation with cognitive scores), and (ii) machine learning classification performance reflecting the discriminative power of both eAV-45 and FDG-PET at the individual level.

Result: The time interval from 0 to 4 minutes gave optimal vertex-wise within- and inter-subject correlations of both eAV-45 versus FDG-PET (maximal) and eAV-45 versus lAV-45 (minimal) (Figure 1). Balanced accuracy of pattern overlap was globally maximal with pons scaling (Figure 2), whereas classification performance between patients' subgroups and controls were similar across scaling regions for both eAV-45 and FDG-PET (Figure 3A). Finally, classification performance was significantly superior for combined early plus late AV-45 compared to FDG-PET alone (Figure 3B).

Conclusion: Results show that eAV-45 from 0 to 4 minutes with pons scaling is an optimal surrogate of FDG-PET in ageing and Alzheimer's clinical syndrome. This study highlights the strong potential of optimized dual-phase AV-45, allowing to outperform

FDG-PET discriminative power when combining both early plus late AV-45 information obtained from a single PET-tracer injection. Interestingly, the use of dual-phase AV-45 instead of FDG-PET plus lAV-45 will reduce the radiation dose, total time, number of visits and costs.

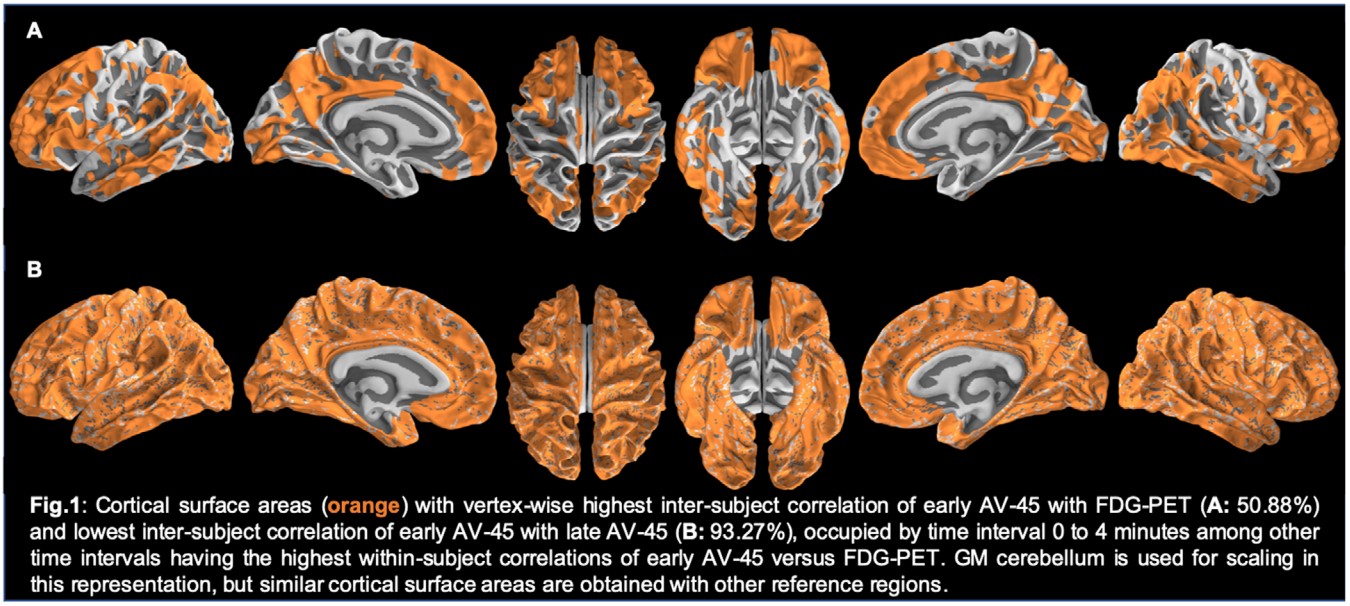

Fig.1: Cortical surface areas (**orange**) with vertex-wise highest inter-subject correlation of early AV-45 with FDG-PET (**A:** 50.88%) and lowest inter-subject correlation of early AV-45 with late AV-45 (**B:** 93.27%), occupied by time interval 0 to 4 minutes among other time intervals having the highest within-subject correlations of early AV-45 versus FDG-PET. GM cerebellum is used for scaling in this representation, but similar cortical surface areas are obtained with other reference regions.

FIGURE 1

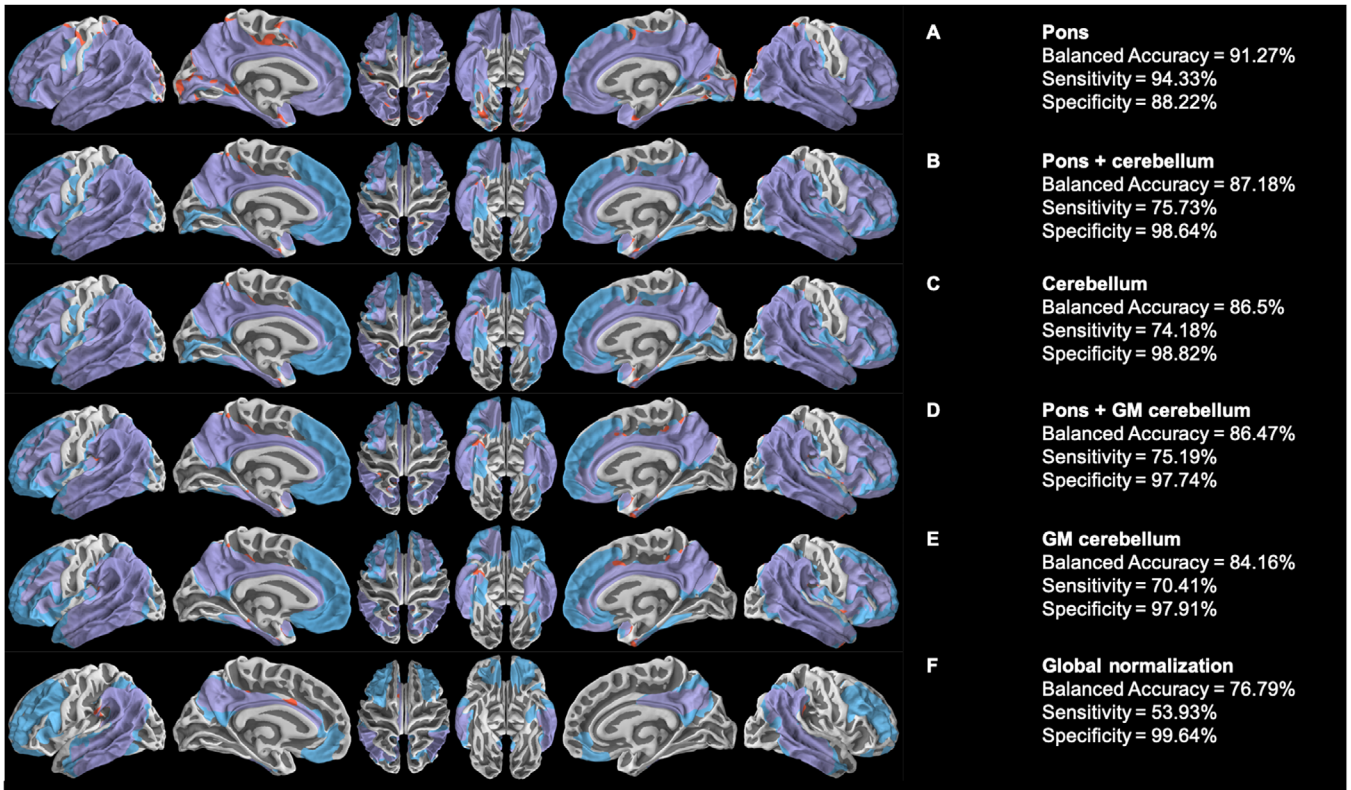

Fig.2: Computation of metrics of vertex-wise pattern overlap (purple) between early AV-45 (orange) and FDG-PET (blue) across reference regions used for PET scaling, derived from Aβ- controls (CN) vs. Aβ+ Alzheimer's disease (AD) patients comparisons

FIGURE 2

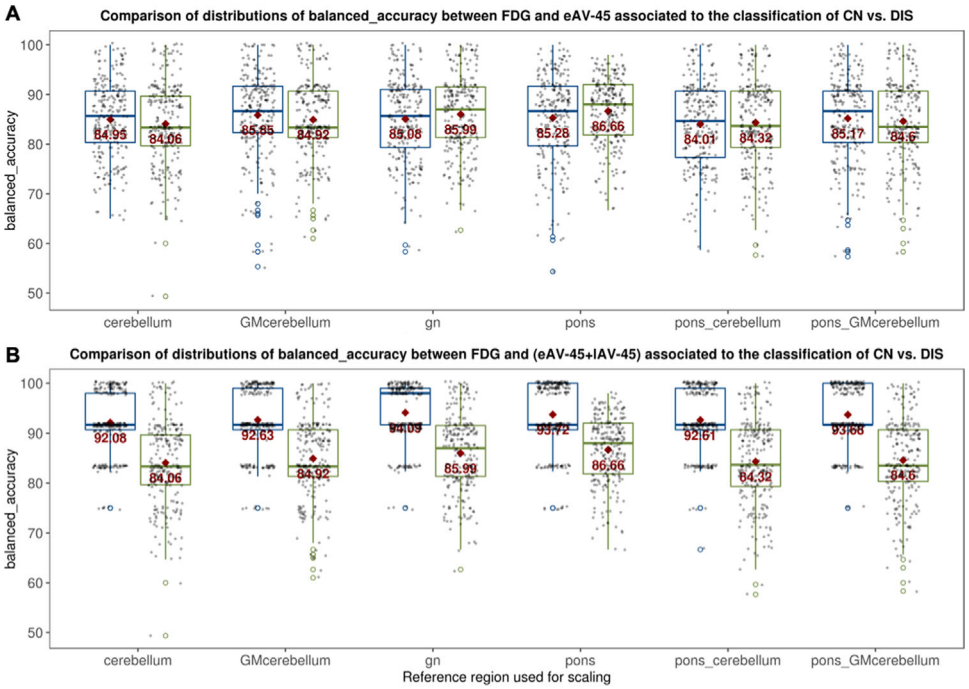

Fig.3: Comparison of distributions of balanced accuracy derived from linear SVM classification of Aβ- controls (CN) vs. Aβ+ patients (DIS), between FDG-PET and early AV-45 (A), and between FDG-PET and combined (early plus late) AV-45 (B) across reference regions used for PET scaling

FIGURE 3