

Figure Legends

Figure 1: PiB-PET voxelwise rate of change across the mean follow-up period of 20 months.

Top: Mean values of PiB-PET rate of change across the mean follow-up period of 20 months according to each clinical group and rendered onto a 3D surface using the Anatomist/BrainVISA software (www.brainvisa.info).

Bottom: SPM glass brain render of the statistical voxelwise comparisons by clinical group on the PiB-PET rate of change images (two sample t-tests) thresholded at $p < 0.001$ uncorrected ($k > 50$ voxels).

AD = Alzheimer's disease; MCI = Mild Cognitive Impairment; HC = Healthy Controls.

Figure 2: Voxelwise ANCOVA on the PiB-PET rate of change images using clinical status, clinical conversion and PiB status as categorical predictors.

Top: Mean values of PiB-PET rate of change across the mean follow-up period of 20 months according to each PiB status group (PiB+, PiB-) rendered onto a 3D surface using the Anatomist/BrainVISA software (www.brainvisa.info). Top left: SPM glass brain render of the regions showing a PiB-PET rate of change significantly positive (higher than zero) within the PiB- group using a voxelwise one sample t-test and thresholded at $p < 0.001$ uncorrected ($k > 50$ voxels).

Bottom: SPM glass brain render and slice renders of the main effect of the PiB status on PiB rate of change images thresholded at $p < 0.001$ uncorrected ($k > 50$ voxels). Note that the other main effects and interactions were not significant (see text for details).

PiB+= high global neocortical amyloid burden; PiB-= low global neocortical amyloid burden.

Figure 3: Histogram of the distribution of the global neocortical PiB-PET rate of change values amongst the healthy controls.

The vertical purple rectangle illustrates the PiB Accumulation status cut-offs ($+0.014 \text{ SUVR}_{\text{pons}}/\text{year}$ - $+0.022 \text{ SUVR}_{\text{pons}}/\text{year}$) used to determine two subgroups: Accumulators ($> +0.022 \text{ SUVR}_{\text{pons}}/\text{year}$) and Non-Accumulators ($< +0.014 \text{ SUVR}_{\text{pons}}/\text{year}$).

Figure 4: Plot of the global neocortical PiB-PET rate of change across the mean follow-up period of 20 months according to the baseline global neocortical PiB-PET values.

Vertical black bar indicates the PiB status cut-off ($0.71 \text{ SUVR}_{\text{pons}}$) used to determine the PiB status (PiB+ vs. PiB-).

The horizontal grey rectangle illustrates the PiB Accumulation status cut-offs ($+0.014 \text{ SUVR}_{\text{pons}}/\text{year}$ - $+0.022 \text{ SUVR}_{\text{pons}}/\text{year}$) used to determine the PiB Accumulation status (Accumulators vs. Non-Accumulators).

AD-AD = Alzheimer's disease diagnosis at baseline and at follow-up; MCI-AD = Mild Cognitive Impairment diagnosis at baseline-Alzheimer's disease diagnosis at follow-up (converters); MCI-MCI = Mild Cognitive Impairment diagnosis at baseline, still MCI at follow-up (non-converters); MCI-HC = Mild Cognitive Impairment diagnosis at baseline-Classified as "Healthy controls" at follow-up (non-converters); HC-AD = Healthy Controls at baseline-Alzheimer's disease diagnosis at follow-up (converters); HC-MCI = Healthy Controls at baseline- Mild Cognitive Impairment diagnosis at follow-up (converters); HC-HC = Healthy controls at baseline, still HC at follow-up (non-converters).

Figure 5: Voxelwise ANCOVA on the PiB-PET rate of change images in Accumulators using clinical status, clinical conversion and PiB status as categorical predictors.

Top: Mean values of PiB-PET rate of change in Accumulators across the mean follow-up period of 20 months according to each PiB status group (PiB+, PiB-) and rendered onto a 3D surface using the Anatomist/BrainVISA software (www.brainvisa.info).

Bottom: SPM glass brain render and slice renders of the main effect of the PiB status on PiB-PET rate of change images in Accumulators thresholded at $p < 0.001$ uncorrected ($k > 50$ voxels). Note that the other main effects and interactions were not significant.

PiB+= high amyloid burden; PiB-= low amyloid burden.

Figure 6: Estimated course of fibrillar amyloidosis: from no A β burden to mean A β burden in PiB+ Alzheimer's disease patients.

The dynamics of PiB accumulation are estimated using the median PiB rate of change observed in the PiB- Accumulators (+0.030 SUVR_{pons}/year: bold green line; Inter-Quartile Range: +0.024 - +0.042 SUVR_{pons}/year: green area) to reach the PiB+ status threshold (from a baseline +0.50 SUVR_{pons} to +0.71 SUVR_{pons}), and then the median PiB rate of change observed in the PiB+ Accumulators (+0.041 SUVR_{pons}/year: bold green line; Inter-Quartile Range: +0.028 - +0.059 SUVR_{pons}/year: green area) to reach the mean neocortical A β burden in AD (from a baseline +0.71 SUVR_{pons} to +1.02 SUVR_{pons}). As a whole, it would take about 7 years for a PiB- subject to reach the PiB+ status threshold and about 7.5 additional years for a PiB+ accumulator to reach the mean AD neocortical A β burden. Note that the range of global neocortical PiB retention values observed in this study for each clinical group shows a considerable overlap (vertical arrows on the left represent the 95% inter-centile ranges of global neocortical PiB-PET retention in each clinical group) which indicates that A β burden only poorly relates to the clinical stage. AD = Alzheimer's disease; MCI = Mild Cognitive Impairment; HC = Healthy Controls.