

Supplementary Figure Legend:

Procedure for data handling and transformation.

A) Coregistration. First, for each patient, all MRI and PET data were coregistered onto their corresponding baseline MRI (MRIt0) by coregistering the follow-up MRI (MRIt18) onto the baseline MRI (MRIt0), the follow-up PET (PETt18) onto the coregistered follow-up MRI (rMRIt18) and the baseline PET (PETt0) onto the baseline MRI (MRIt0).

B) PVE correction. Then, coregistered PET data (rPETt0 and rPETt18) were corrected for PVE due to both CSF and WM using their corresponding MRI data. We used a voxel-based approach classically applied in our laboratory, and implemented in the 'PVE-lab' software.

C) Scaling. Individual cerebellar-vermis ¹⁸FDG uptake mean values were automatically extracted from the corrected PET data during the PVE correction step. Then, each corrected PET data (rPET_{PVE}t0 and rPET_{PVE}t18) was scaled by this individual value.

D) Spatial normalization parameters. Optimal spatial normalization parameters were estimated from MRI data using the optimized Voxel-Based Morphometry procedure. First, customized template and priors (of the whole brain and the GM, WM, and CSF sets) were created from MRIt0 and rMRIt18 of the whole patient group (n=34 images). Second, a softmean-MRI was created for each patient so that common spatial normalization parameters can be obtained for each pair of PET data. This mean-MRI corresponded to the average of the baseline and the coregistered follow-up MRI. Third, the 17 softmean-MRI were segmented and the resulting GM data sets were used to determine the optimal normalization parameters using the customized GM prior as template.

E) Processing for analyses with baseline and follow-up PET data. The corrected and scaled PET data ($rPET_{PVE_div}t0$ and $rPET_{PVE_div}t18$) were then spatially normalized applying the optimal parameters calculated as described above, smoothed with a Gaussian kernel of 10mm, and entered in the following SPM2 analyses:

i) a *'Population main effect: 2 cond's, 1 scan/cond'* (paired t-test) with 2 conditions (baseline and follow-up) to assess the pattern of metabolic evolution in all aMCI patients,

ii) a *'Multi-group: conditions & covariates'* (repeated measures ANOVA) with 2 groups (converters and non-converters) and 2 conditions (baseline and follow-up) to assess the patterns of metabolic evolution in converters and in non-converters separately with a 1 -1 and a 0 0 1 -1 contrast respectively, and to highlight areas of greater metabolic decrease in converters as compared to non-converters through a 1 -1 -1 1 interaction contrast, onto the voxels exhibiting significant metabolic decreases in converters (using the inclusive masking procedure of SPM2), corresponding to Volumes of Interest (VOI).

F) Processing for analyses with PET-PAC maps. The corrected and scaled PET data ($rPET_{PVE_div}t0$ and $rPET_{PVE_div}t18$) were used to calculate PET-PAC maps. PET images resulting from the PVE correction procedure correspond to a thin band of GM with PET value different from 0 and all non-GM voxels set to zero. Since PVE correction of each pair of PET scan was performed from two different MRI, the thin band of GM could be slightly different between the two PET of a same individual. Thus, before estimating the PAC between both scans, the pairs of PET data were first slightly smoothed (FWHM=4mm) - so that segmentation differences not due to atrophy would be limited, and then masked to exclude voxels with null value either on

the baseline or in the follow-up PET scan - so that PET-PAC would only be estimated in common (non zero) voxels. Finally a PET-PAC map, corresponding to the metabolic percent annual changes from baseline to follow-up scan, was calculated for each patient with MATLAB 6.5. These 17 PET-PAC maps were then spatially normalized applying the optimal parameters calculated as described above, smoothed with a Gaussian kernel of 10mm, and entered in two independent 'Single subjects: covariates only' (correlation) SPM2 analyses using either the Mattis-PAC as covariate to assess the relationship between metabolism changes and global cognitive decline, or the mean PET-PAC value of each VOI to highlight the brain networks whose dysfunction or relative preservation may be related to that of each VOI. Note that the mean PET-PAC values of each VOI were extracted using the 'binary ROIs analysis' option of the 'fMRI-ROI analysis' SPM2 toolbox.