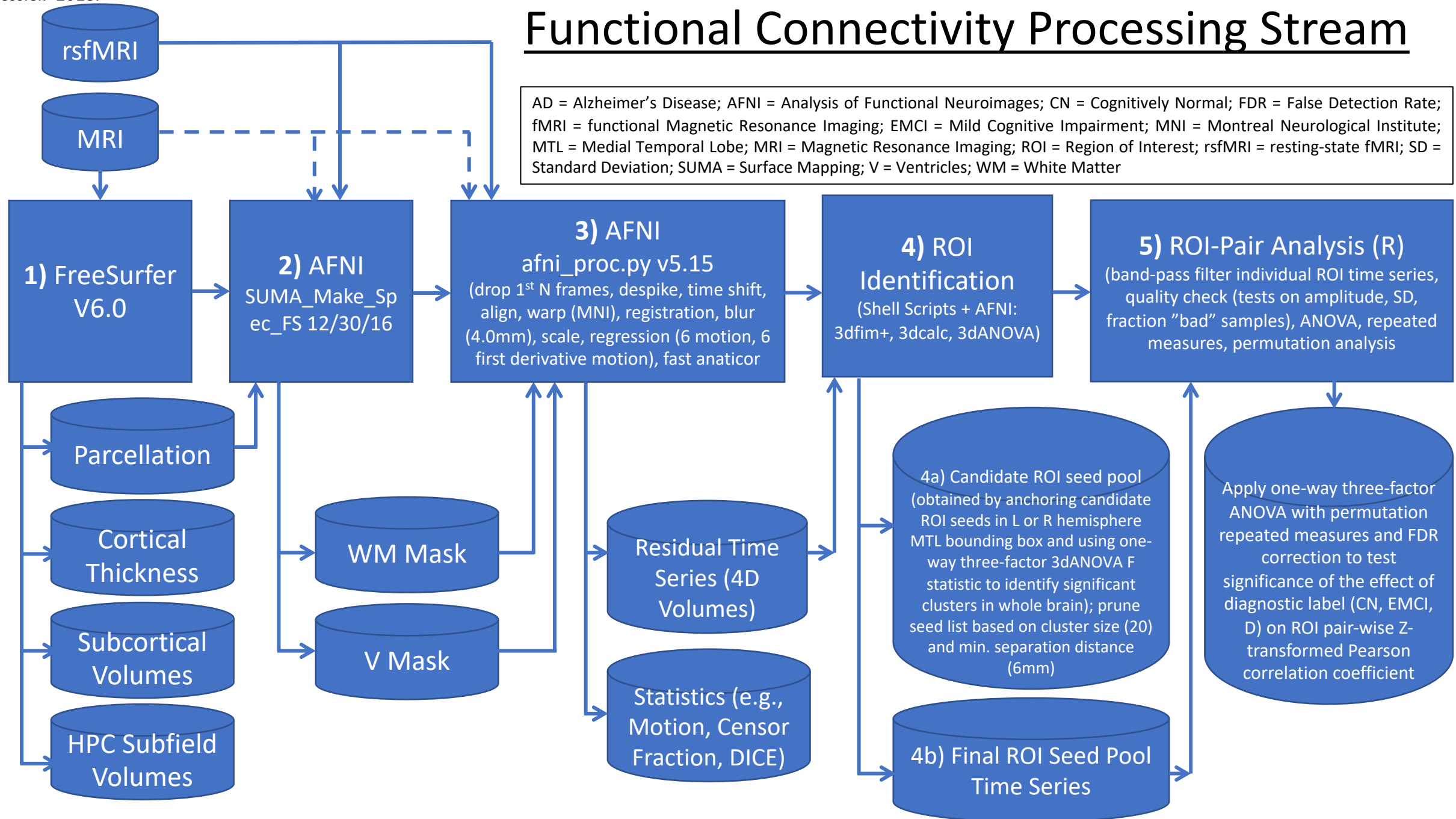
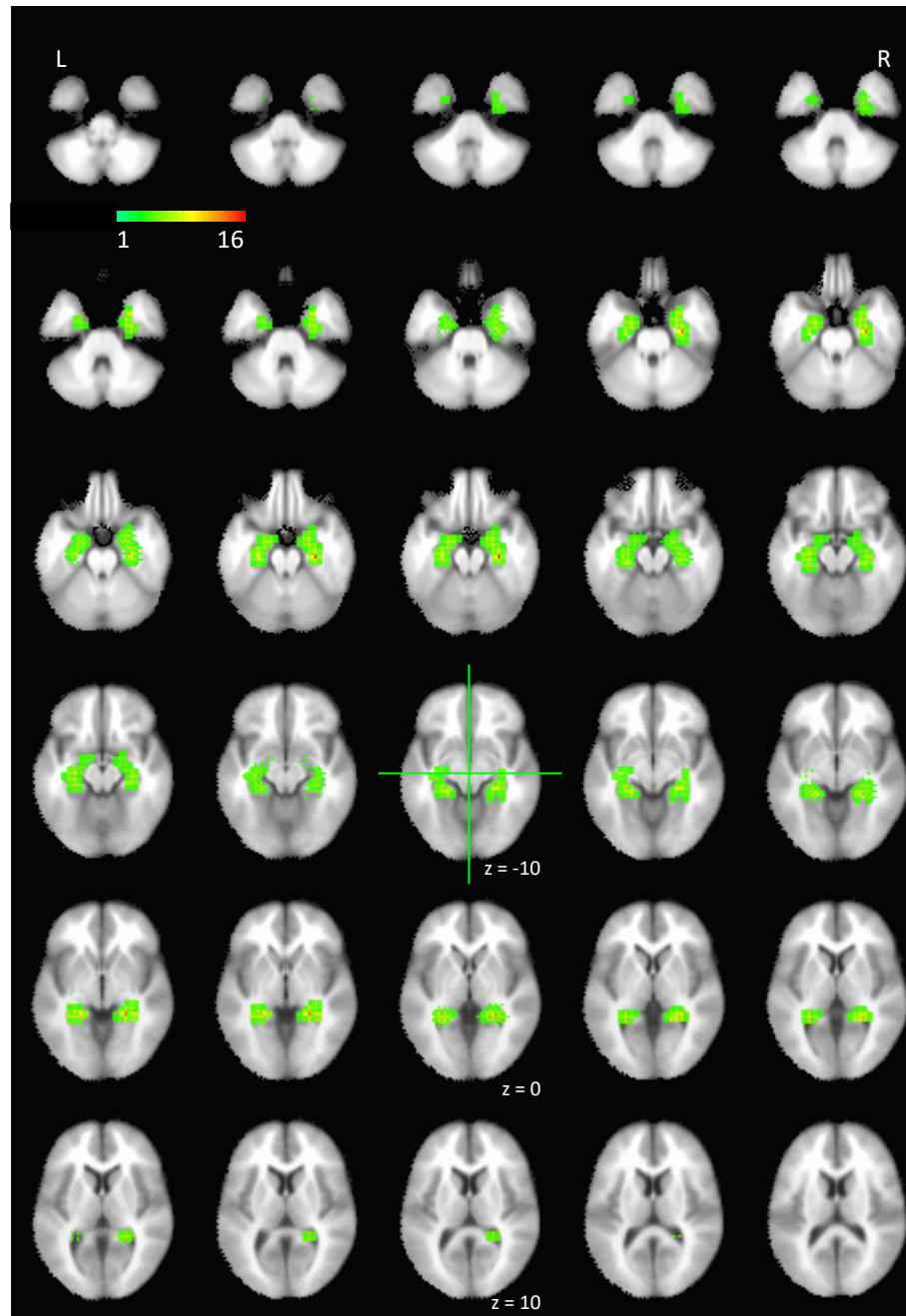


Functional Connectivity Processing Stream

AD = Alzheimer's Disease; AFNI = Analysis of Functional Neuroimages; CN = Cognitively Normal; FDR = False Detection Rate; fMRI = functional Magnetic Resonance Imaging; EMCI = Mild Cognitive Impairment; MNI = Montreal Neurological Institute; MTL = Medial Temporal Lobe; MRI = Magnetic Resonance Imaging; ROI = Region of Interest; rsfMRI = resting-state fMRI; SD = Standard Deviation; SUMA = Surface Mapping; V = Ventricles; WM = White Matter

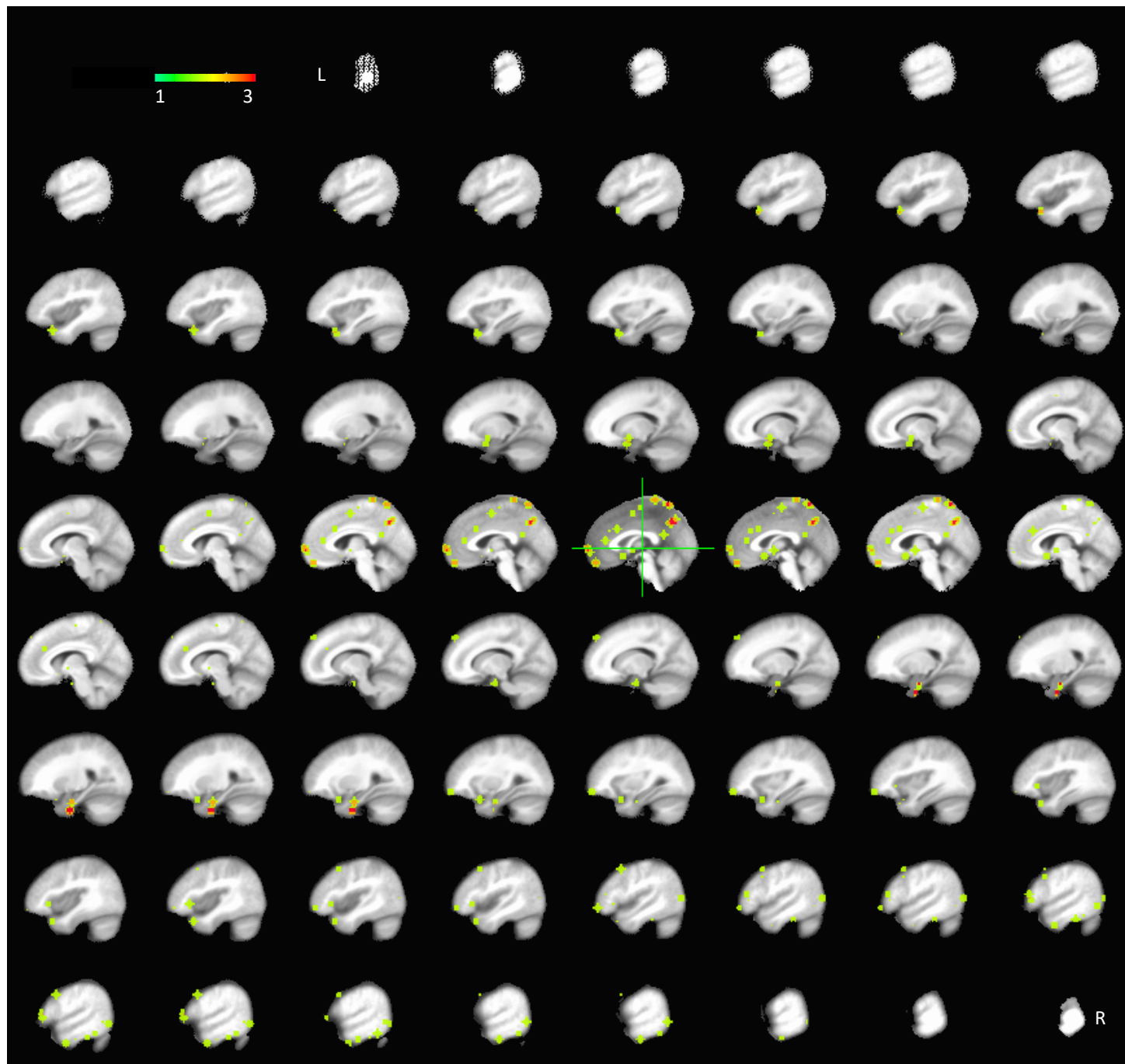




Spatial distribution in left (right) ROI masks sampled from within the global left (right) MTL 3D “bounding box”.

Sum of MTL ROI masks (voxel values set to 0 (not included) or 1 (included)) used as the *starting point* for the MTL ROI identification procedure. At this processing stage, ROI masks overlap due to the 6mm sampling grid.

Crosshair MNI position: 0, -18, -10. Z-direction step size is 2mm.

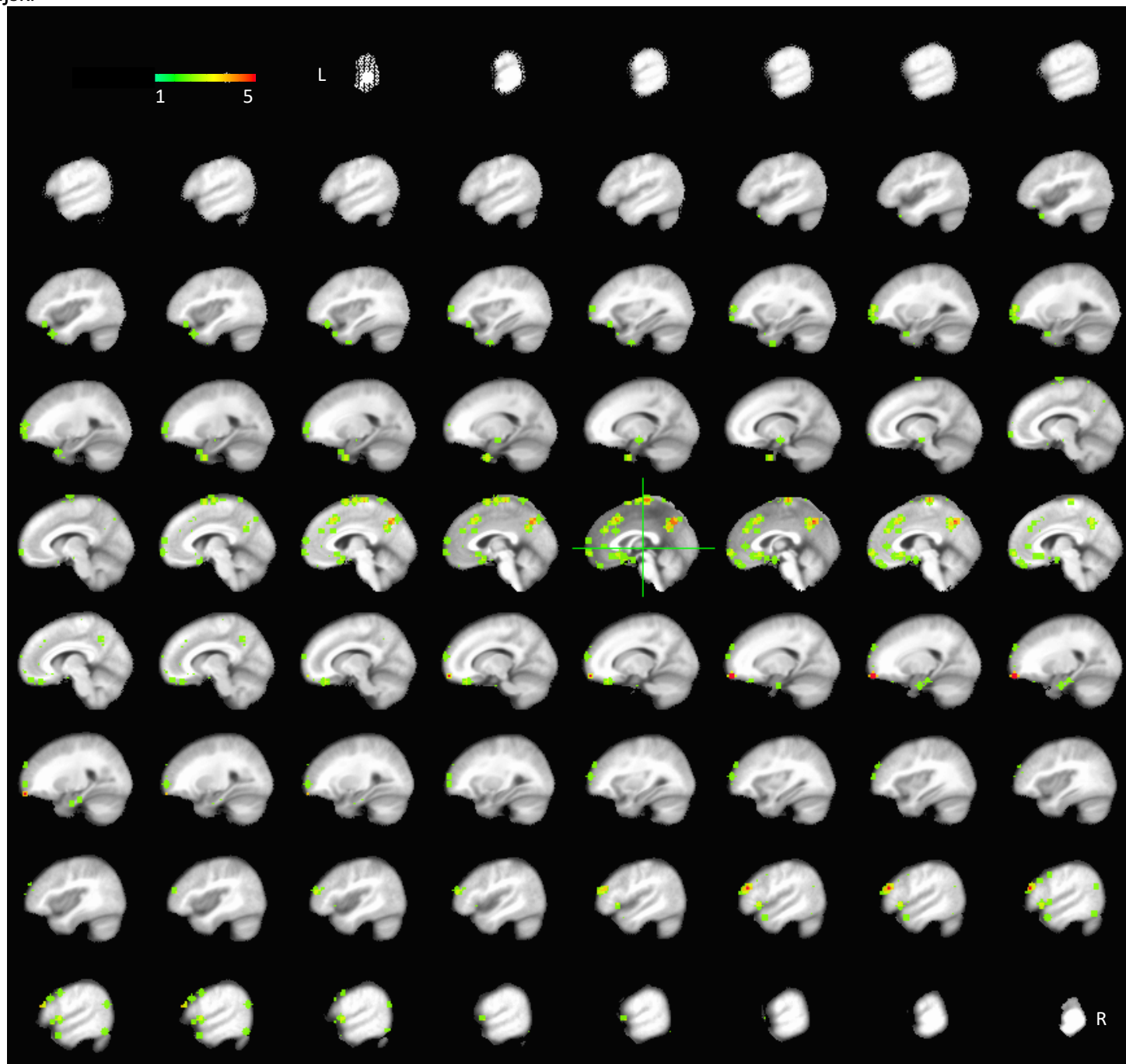


Spatial distribution of ROI masks (each corresponding to the center of mass of an F statistic cluster) identified by 3D ANOVA with a left MTL anchor ROI. 22 anchor ROIs in left hemisphere (*not shown*; see Supplemental Figure 2) comprised the first (“anchor”) element in 50 ROI pairs of interest. The spatial distribution of the sum of the ROI masks corresponding to these 50 ROIs is shown.

In this figure, a value greater than one means that this position comprised an ROI pair of interest with more than one anchor MTL ROI.

ANOVA (with correction for multiple hypothesis testing) is used to determine which of the ROI pairs of interest show significant change as an effect of clinical group.

Sagittal plane step size is 2mm. Cross-hair MNI coordinate (0, -18, 0).

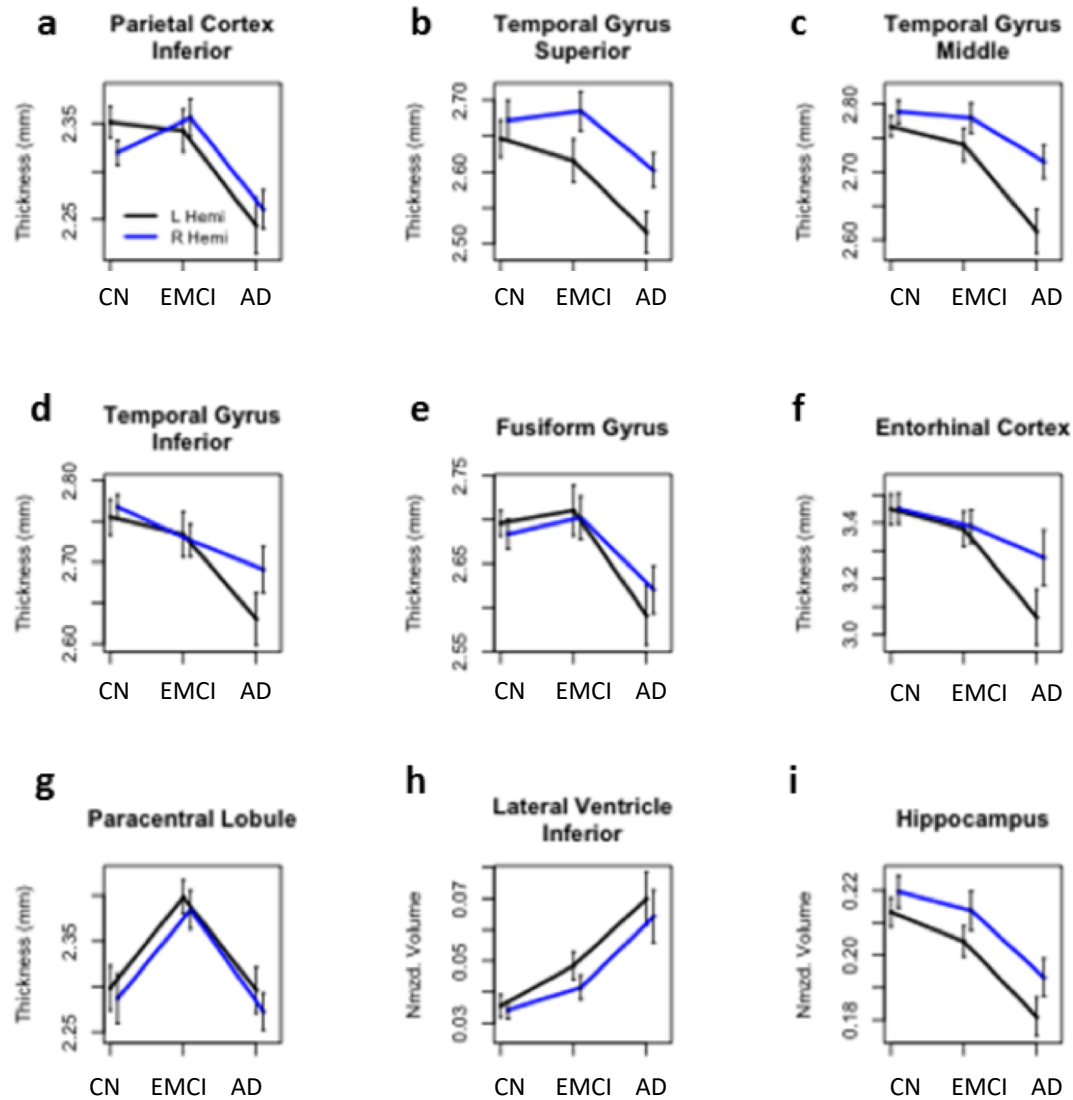


Spatial distribution of ROI masks (each corresponding to the center of mass of an F statistic cluster) identified by 3D ANOVA with a right MTL anchor ROI. 38 anchor ROIs in right hemisphere (*not shown*; see Supplemental Figure 2) comprised the first (“anchor”) element in 82 ROI pairs of interest. The spatial distribution of the sum of the ROI masks corresponding to these 82 ROIs is shown.

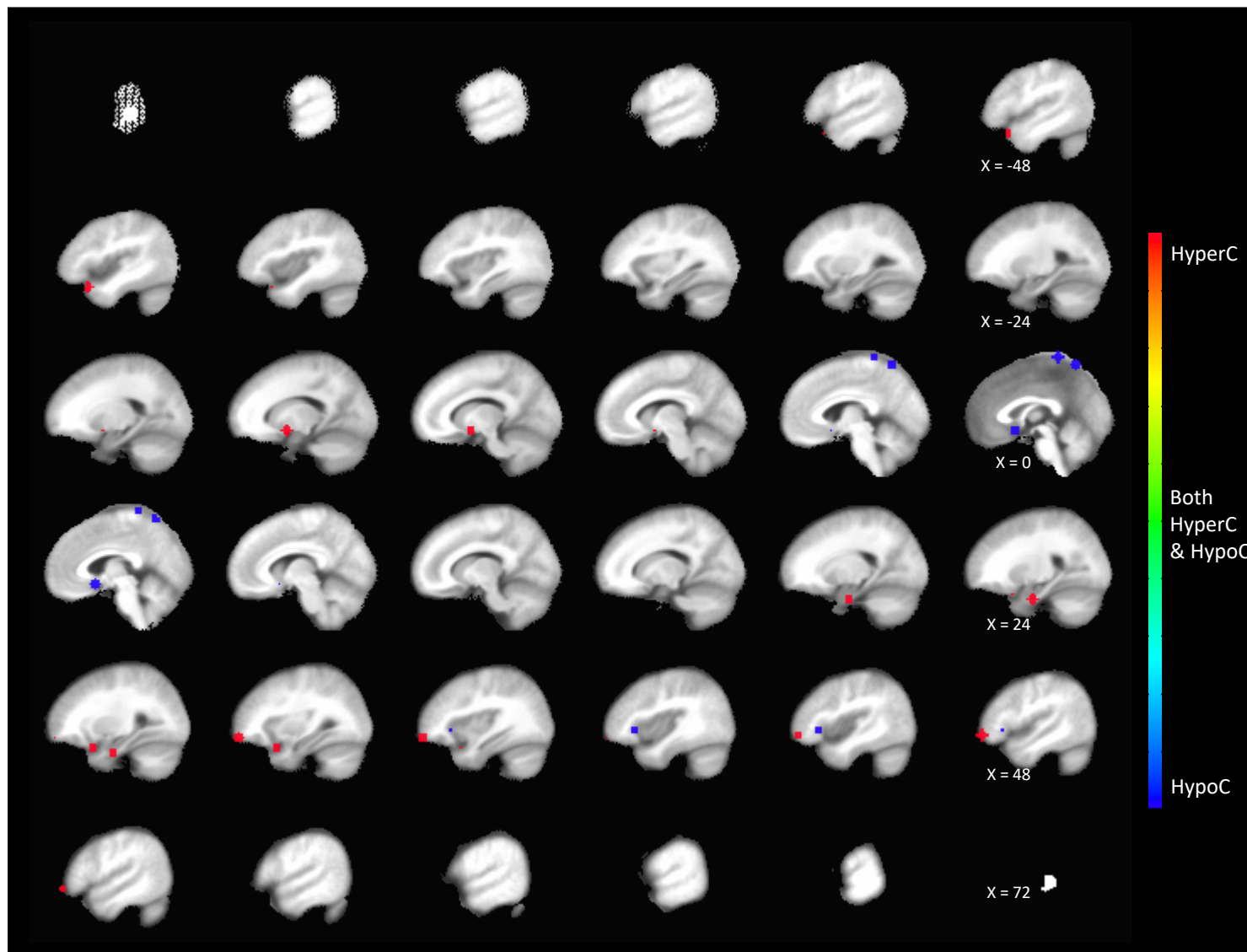
In this figure, a value greater than one means that this position comprised an ROI pair of interest with more than one anchor MTL ROI.

ANOVA (with correction for multiple hypothesis testing) is used to determine which of the ROI pairs of interest show significant change as an effect of clinical group.

Sagittal plane step size is 2mm. Cross-hair MNI coordinate (0, -18, 0).

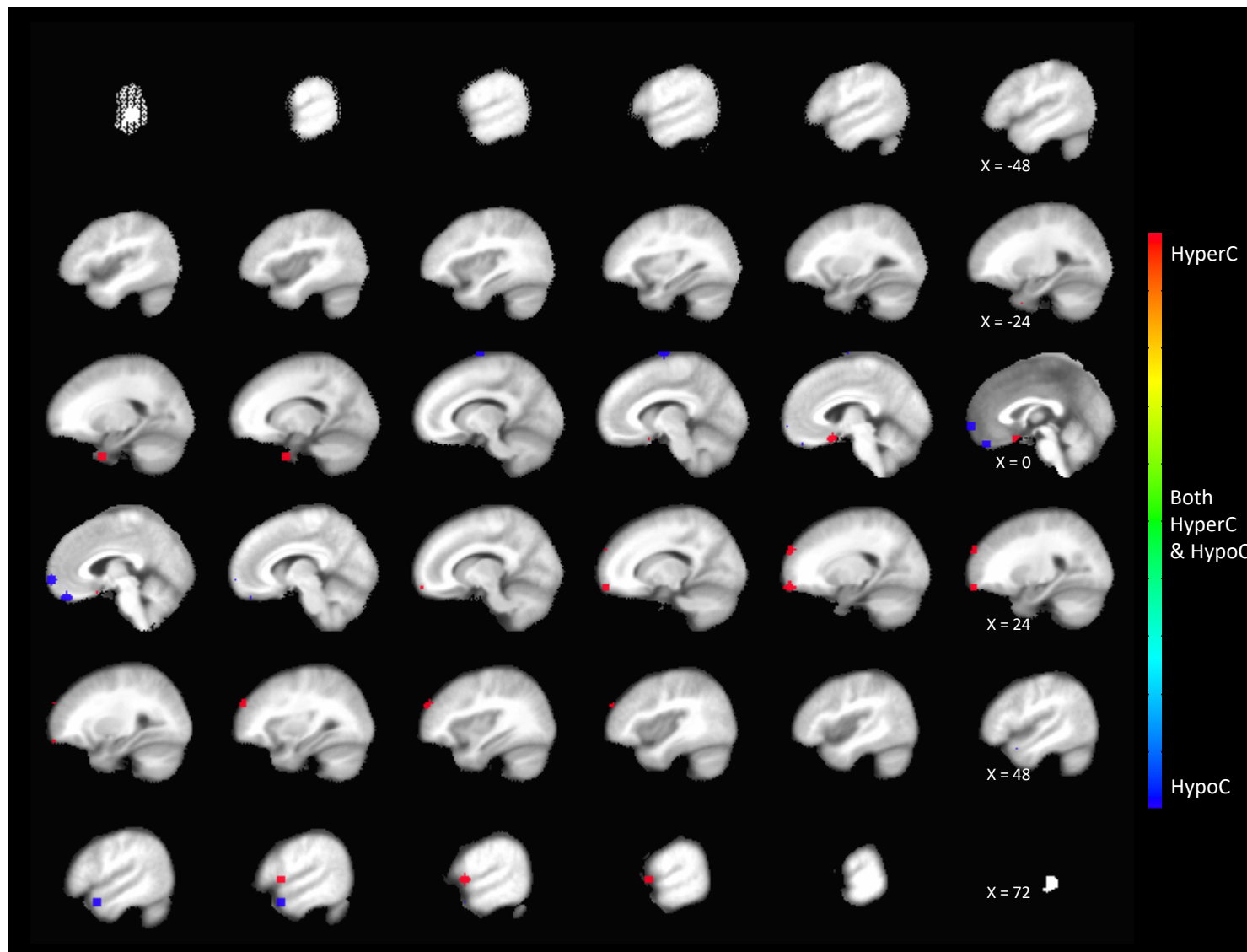


Representative progression of cortical thinning and subcortical structure volume changes with clinical group. **(a-g):** Representative left and right hemisphere CN, EMCI and D diagnosis group average and standard error of FreeSurfer 6.0 estimates of labelled regional cortical layer thickness where one or both hemispheres were significant in a one-way, three-factor (CN, EMCI, D), ANOVA, FDR-corrected ($q=0.1$, 68 tests). **(h-i):** Representative left and right hemisphere CN, EMCI and D clinical group average and standard error of FreeSurfer 6.0 estimates of labelled subcortical structure volume where one or both hemispheres were significant in a one-way, three-factor (CN, EMCI, D), ANOVA, FDR-corrected ($q=0.1$, 16 tests).



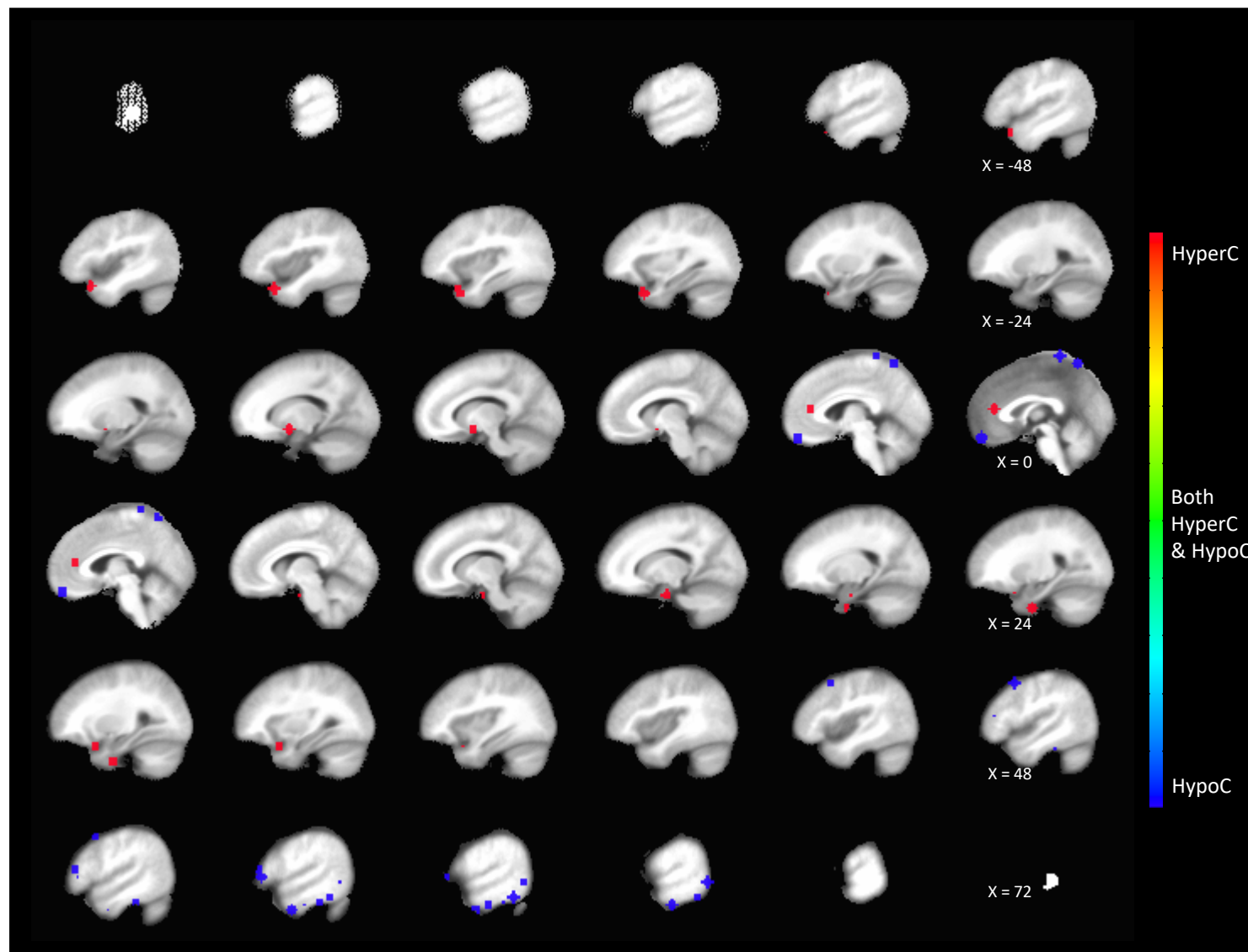
Position of ROI pair of interest non-anchor elements in 10 ROI pairs of interest that were significant in the left hemisphere EMCI–CN contrast. The anchor ROIs were in left MTL. Shown are ROI masks consisting of a 6-mm radius volume centered at the ROI seed.

Direction of ROI pair functional change is color-coded for hyperconnected (hyperC) (*red*), hypoconnected (hypoC) (*blue*), and hyperconnected and hypoconnected (*green*).



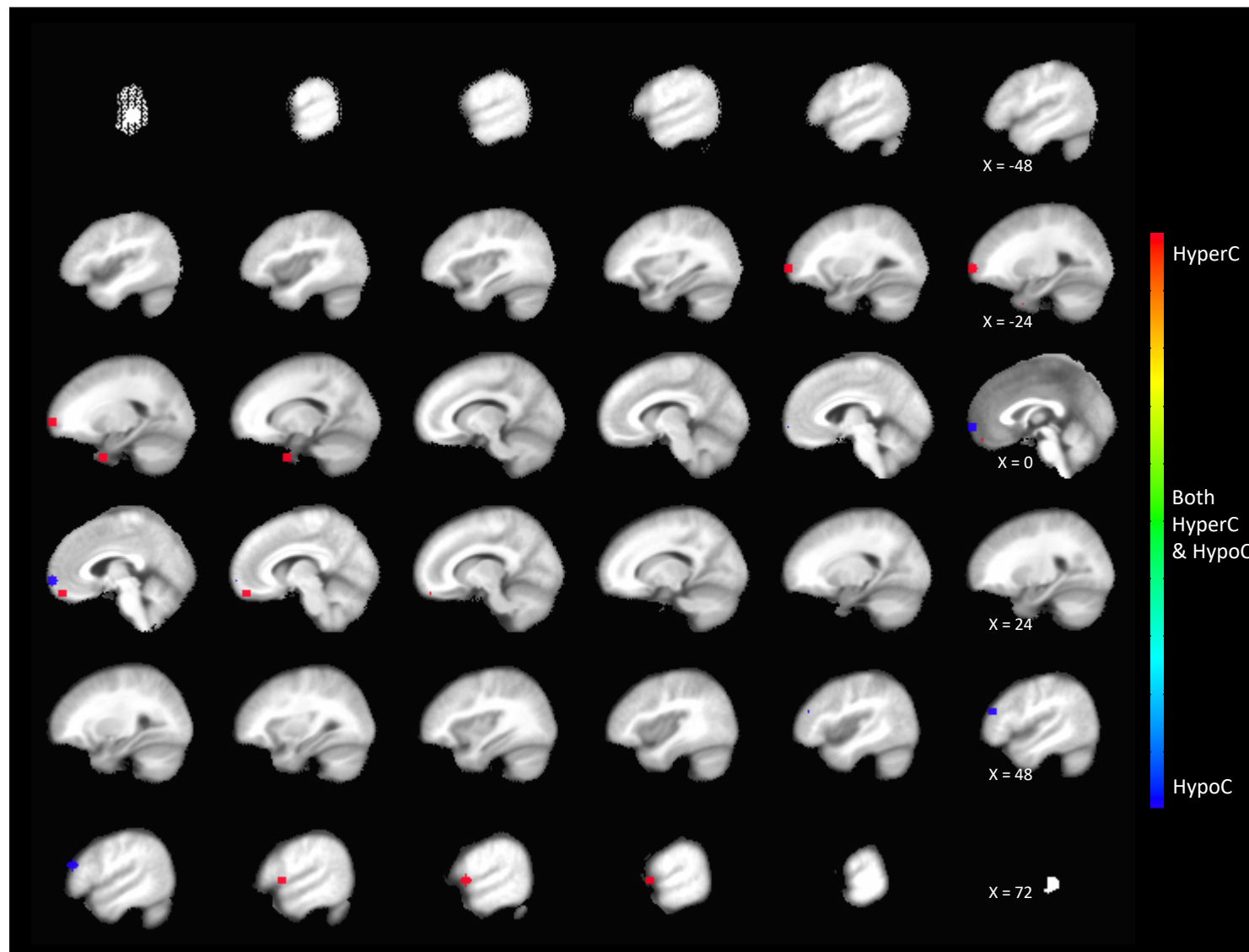
Position of ROI pair of interest non-anchor elements in 13 ROI pairs of interest that were significant in the right hemisphere EMCI–CN contrast. The anchor ROIs were in right MTL. Shown are ROI masks consisting of a 6-mm radius volume centered at the ROI seed.

Direction of ROI pair functional change is color-coded for hyperconnected (hyperC) (*red*), hypoconnected (hypoC) (*blue*), and hyperconnected and hypoconnected (*green*).



Position of ROI pair of interest non-anchor elements in 21 ROI pairs of interest that were significant in the left hemisphere AD–CN contrast. The anchor ROIs were in left MTL. Shown are ROI masks consisting of a 6-mm radius volume centered at the ROI seed.

Direction of ROI pair functional change is color-coded for hyperconnected (hyperC) (*red*), hypoconnected (hypoC) (*blue*), and hyperconnected and hypoconnected (*green*).



Position of ROI pair of interest non-anchor elements in 6 ROI pairs of interest that were significant in the right hemisphere AD–CN contrast. The anchor ROIs were in right MTL. Shown are ROI masks consisting of a 6-mm radius volume centered at the ROI seed.

Direction of ROI pair functional change is color-coded for hyperconnected (hyperC) (*red*), hypoconnected (hypoC) (*blue*), and hyperconnected and hypoconnected (*green*).