Appendix A.1: Pseudo-codes of creating multiple subsets for RSMFC

Assume there are p voxels in the brain and each subset contains p_0 voxels (a subspace size of p_0 voxels).

Step 1: Randomly permute the original p voxels and store the correspondence between the permuted and the actual voxel indices

Step 2: Take the first p_1 voxels from the permuted voxel sequence and append them to the end of the permuted voxel sequence. p_1 is the smallest number such that $(p + p_1)$ is a multiple of p_0 $(p_1 \leq p_0)$

Step 3: Partition the newly created voxel sequence ($p + p_1$ voxels) into $\frac{p+p_1}{p_0}$ subsets such that the first p_0 voxels belong to the first subset, the second p_0 voxels belong to the second subset and etc.

Step 4: To perform multiple partitions, repeat step 1 – step 3.

Appendix A.2 Estimating functional connectivity of PCC using anatomical component base noise reduction method (aCompCor)

We applied aCompCor on the same experimental fMRI dataset used in RSMFC. Out of 22 subjects, 19 subjects with good quality structural MRIs were included for the analysis. We first segmented each subject's MNI-normalized structural MRI into grey matter, white matter and CSF. Then we set the partial volume threshold for white matter and CSF images at 0.9 and further eroded the two thresholded images by 2 voxels in each direction to make sure that the white matter and CSF mask is less likely to contain BOLD signals with neuronal origins. This approach is similarly used to define white matter and CSF mask in Wong et al. (2012). The first 5 principal components suggested by Chai et al. (2012) were extracted from the white matter and CSF mask and subsequently regressed out as nuisance covariates. To illustrate the substantial influence of mask creation as well as the number of principal components used as nuisance regressors, we created one additional white matter and CSF mask by setting the partial volume threshold at 0.9 but eroding the images by 1 voxel, and further extracted the first 5 principal components as nuisance regressors. Finally, we also extracted the first 50 principal components instead of 5 from the first mask (eroded by 2 voxels) as nuisance regressors.

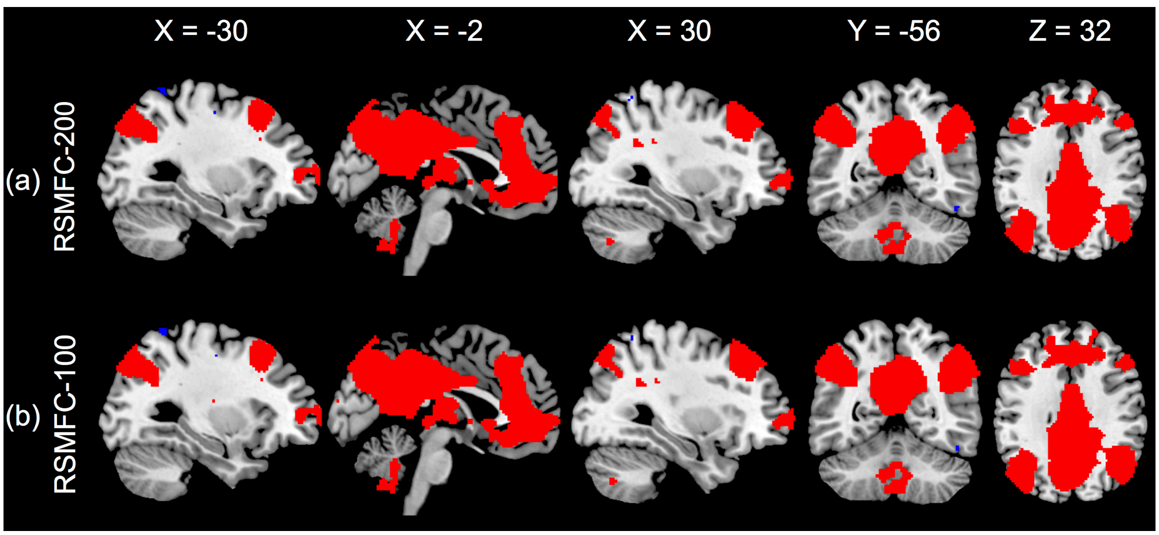


Figure S1: Comparisons between RSMFC with 200 partitions and 100 partitions on the simulated dataset. (a) RSMFC with 200 partitions. **(b)** RSMFC with 100 partitions. In both cases, RSMFC accurately identifies the same positively correlated network (marked in red color) and correctly excludes the uncorrelated network. Both connectivity maps are thresholded under FDR < 0.001 and then masked by the two preset networks. RSMFC = random subspace method functional connectivity.

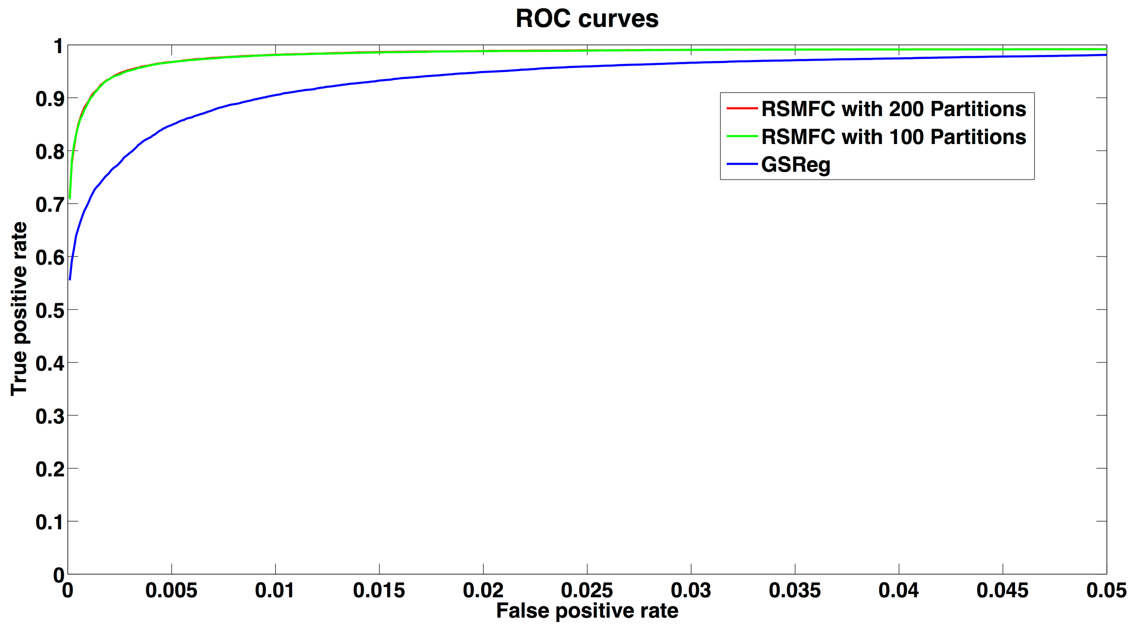


Figure S2: ROC curves for RSMFC with 200 partitions and 100 partitions as well as GSReg on the simulated dataset. RSMFC performs significantly better than GSReg in terms of area under the curve, and ROC curves for RSMFC with 200 partitions are almost identical to the ROC curve of RSMFC with 100 partitions. Red line shows ROC curve for RSMFC with 200 partitions; green line shows ROC curve for RSMFC with 100 partitions; blue line shows ROC curve for GSReg. ROC = Receiver Operating Characteristic. RSMFC = random subspace method functional connectivity. GSReg = global signal regression method.

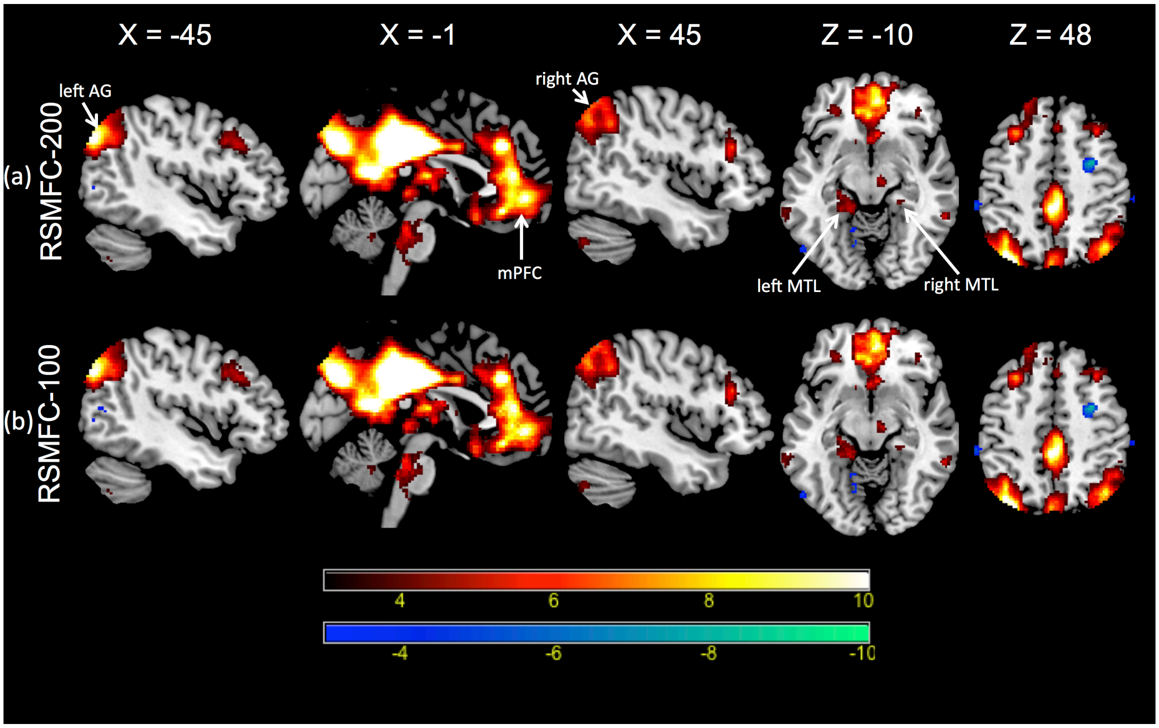


Figure S3: Comparisons between PCC functional connectivity determined by RSMFC with 200 partitions and 100 partitions on the experimental dataset. (a) PCC functional connectivity determined by RSMFC with 200 partitions. **(b)** PCC functional connectivity determined by RSMFC with 200 partitions. RSMFC with different number of partitions yield almost identical PCC functional connectivity patterns. Both connectivity maps are thresholded using a voxel-wise height threshold of $p < 0.001$ and a spatial extent threshold of 42 voxels, corresponding to an overall $p < 0.01$ for a family-wise correction. PCC = posterior cingulate cortex. DMN = default mode network. AG = angular gyrus. mPFC = medial prefrontal cortex. MTL = medial temporal lobe. RSMFC = random subspace method functional connectivity.

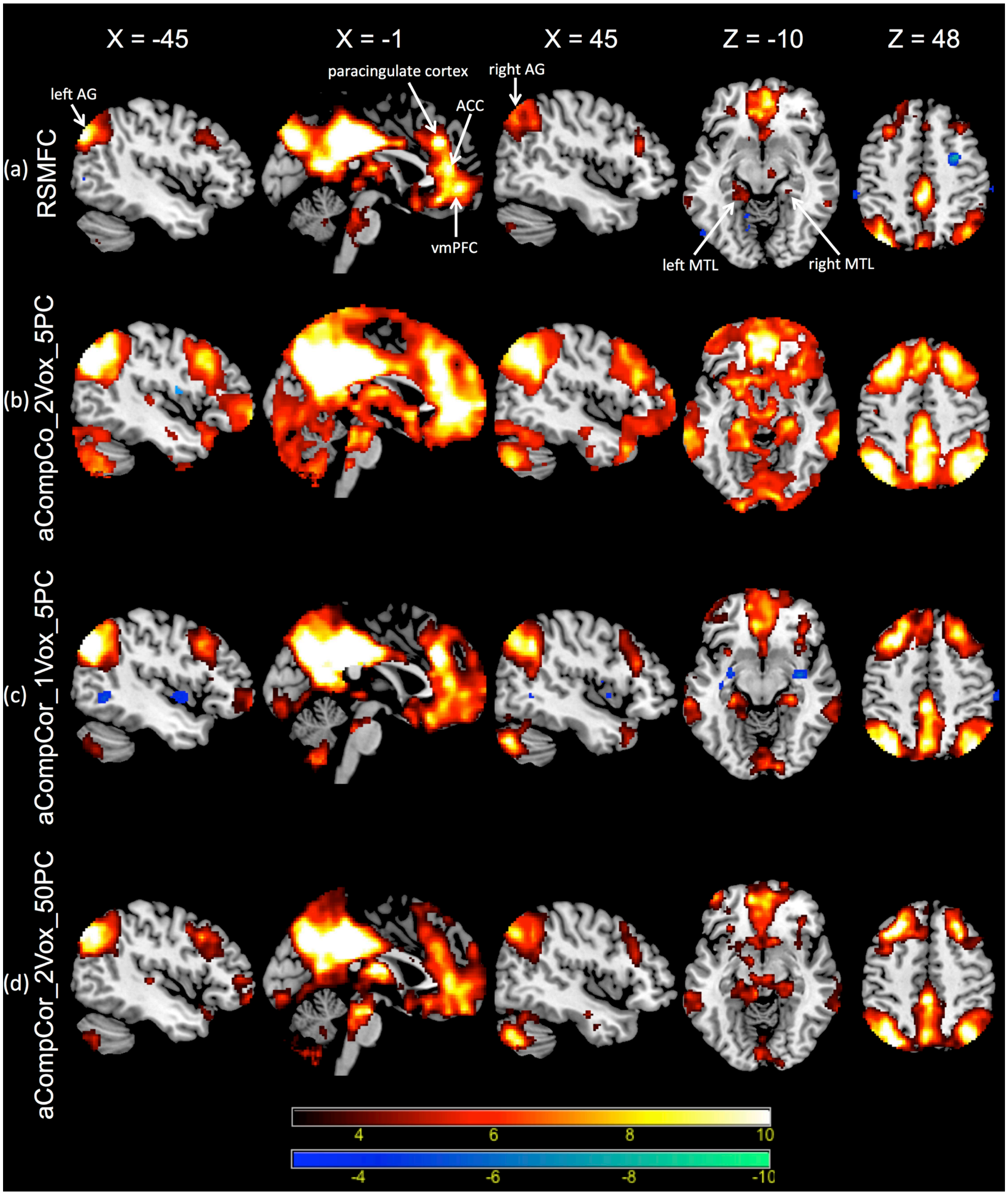
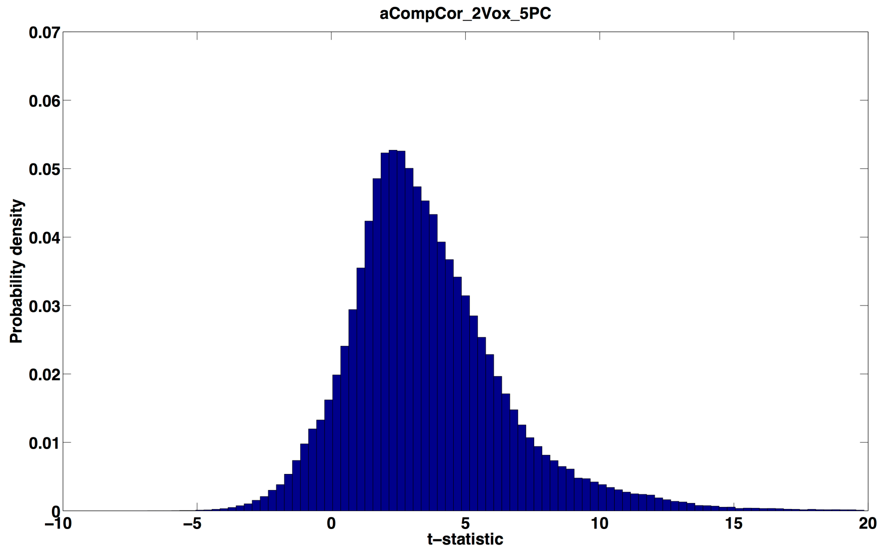


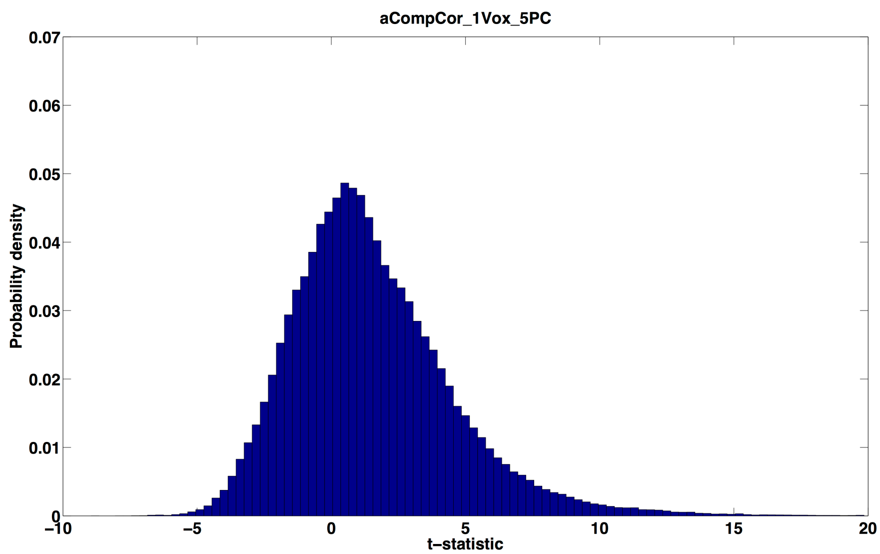
Figure S4: Functional connectivity maps of PCC using RSMFC and aCompCor with different white matter and CSF masks and different numbers of principal components as nuisance regressors. **(a)** Functional connectivity map of PCC using RSMFC. **(b)-(d)** Functional connectivity map of PCC using aCompCor. For aCompCor, the functional connectivity map varies depending on the white matter and CSF mask and the number of extracted principal components. All connectivity maps are thresholded using a voxel-wise height threshold of $p < 0.001$ and a spatial extent threshold of 42 voxels, corresponding to an overall $p < 0.01$ for a family-wise error correction. aCompCor = anatomical component base noise reduction method.

aCompCor_2Vox_5PC = using a white matter and CSF mask eroded by 2 voxels and the first 5 principal components. aCompCor_1Vox_5PC = using a white matter and CSF mask eroded by 1 voxel and the first 5 principal components. aCompCor_2Vox_50PC = using a white matter and CSF mask eroded by 2 voxels and the first 50 principal components. PCC = posterior cingulate cortex. DMN = default mode network. AG = angular gyrus. ACC = anterior cingulate cortex. vmPFC = ventral medial prefrontal cortex. MTL = medial temporal lobe. RSMFC = random subspace method functional connectivity.

(a)


aCompCor_2Vox_5PC
Probability density
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
−10
−5
0
5
10
15
20
t−statistic

(b)


aCompCor_1Vox_5PC
Probability density
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
−10
−5
0
5
10
15
20
t−statistic

(c)

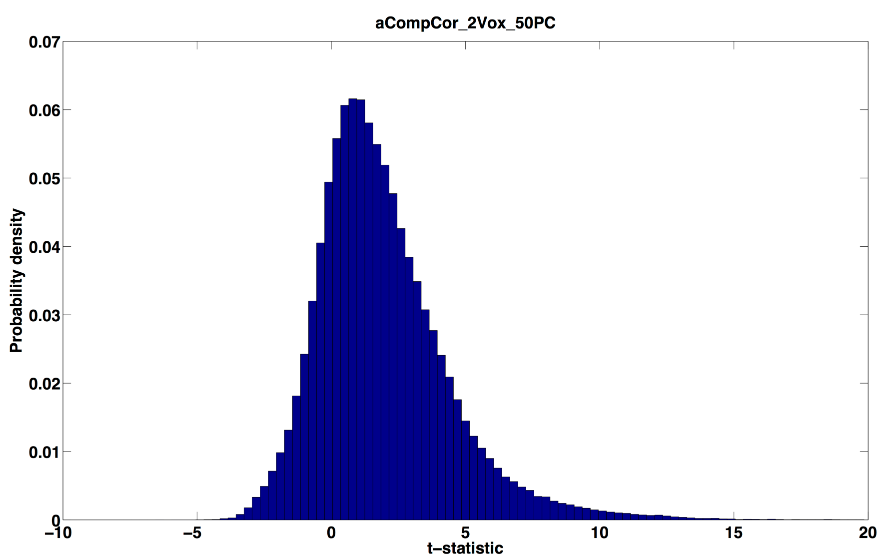

aCompCor_2Vox_50PC
Probability density
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
−10
−5
0
5
10
15
20
t−statistic

Figure S5: Histogram of group-level whole-brain voxel-wise t-statistics on the experimental rsfMRI dataset using aCompCor with different white matter and CSF masks as well as different numbers of principal components. For the approach of aCompCor_2Vox_5PC, the mode of the distribution is significantly biased towards a positive t-statistics of 2.3, indicating widespread overestimating of functional connectivity. For aCompCor_1Vox_5PC, the mode of the distribution is centered around zero. For aCompCor_2Vox_5PC, the mode of the distribution is shifted towards zero and centered around 0.9. aCompCor = anatomical component base noise reduction method. aCompCor_2Vox_5PC = using a white matter and CSF mask eroded by 2 voxels and the first 5 principal components. aCompCor_1Vox_5PC = using a white matter and CSF mask eroded by 1 voxel and the first 5 principal components. aCompCor_2Vox_50PC = using a white matter and CSF mask eroded by 2 voxels and the first 50 principal components.

Reference

Chai, X.J., Castanon, A.N., Ongur, D., Whitfield-Gabrieli, S., 2012. Anticorrelations in resting state networks without global signal regression. Neuroimage 59, 1420-1428.

Wong, C.W., Olafsson, V., Tal, O., Liu, T.T., 2012. Anti-correlated networks, global signal regression, and the effects of caffeine in resting-state functional MRI. Neuroimage 63, 356-364.