Segregated Fronto-Cerebellar Circuits Revealed by Intrinsic Functional Connectivity

Supplementary Materials

Assessing the significance of fronto-cerebellar correlations.

The correlation maps illustrating fronto-cerebellar connectivity all employed a somewhat arbitrary threshold ($r(z) > 0.1$). In order to formally assess how robust these results are, we conducted random effects analyses on the un-thresholded maps. First, we performed two t-tests, one each for the left and right MOT- and DLPFC- correlated maps in order to test the finding that left neocortical seeds are preferentially correlated with right cerebellar regions (and vice versa). Supplementary Figure 1 below displays the seed regions (top row) and results (bottom two rows) of the MOT t-test (A) and DLPFC t-test (B) thresholded at $p<0.001$, corrected for multiple comparisons across the whole brain. The left (red) seed for both MOT and DLPFC maps results in significantly higher correlations with the right cerebellar hemisphere. Conversely, the right (blue) seed produces significantly higher correlations in the left cerebellar hemisphere. Notably, the topography of the effects is qualitatively very similar to the subtraction maps shown in Figure 1 in the text.

Figure 3 in the text shows the result of subtracting a correlation map generated from one frontal site with the correlation map generated from another. The purpose of this analysis was to assess the topography of different fronto-cerebellar connections. For instance, subtracting the DLPFC-correlated map from the MOT-correlated map resulted in a map which clearly dissociated the MOT correlations in lobule V from the DLPFC correlations in Crus I/II. Here again, however, threshold for the correlation coefficient is difficult to interpret. Accordingly, our second random effects analysis computed the significance of these subtraction maps. The correlation maps submitted to this analysis were, as in the original analysis, averages of left and right seeds. T-tests were performed on four pairs of the averaged maps (MOT-DLPFC, DLPFC-MPFC, MPFC-APFC, APFC-MOT), as shown in Supplementary Figure 2. The first two columns represent the placement of the frontal seeds, while the final column shows a representative slice of the cerebellum t-score map. The results are color-coded such that warm colors on the statistical map were significantly more correlated with the seeds in the first column, while blue colors were more correlated with seeds in the second column. Here again the results are thresholded at $p<0.001$, corrected for multiple comparisons.

Overall cerebellar topography is insensitive to the exact placement of frontal seeds.

We preformed an additional control analysis in order to determine whether the pattern of results that emerged from this study was sensitive to the choice of the particular seed coordinates in frontal cortex. To this end, we displaced each of our frontal seeds at least 8mm from their original locations and recomputed the correlation maps for each. This enabled us to assess whether slight variations of the seed regions would have an appreciable effect on the topography of cerebellar correlations.

The results are displayed in Supplementary Figure 3. Panel (A) shows the four pairs of new seeds in the MOT, DLPFC, MPFC and APFC regions. Each new seed location was generated by moving the old seed at least 8mm away from the original coordinate (coordinates of original seeds in Table 2 in the text) while remaining within in the same approximate frontal region as the original. Panel (B) displays representative slices of the resulting cerebellar correlations. Comparing these maps to the original maps in Figure 8 reveals that the displacement appeared to have a negligible effect on the overall topography of the results.

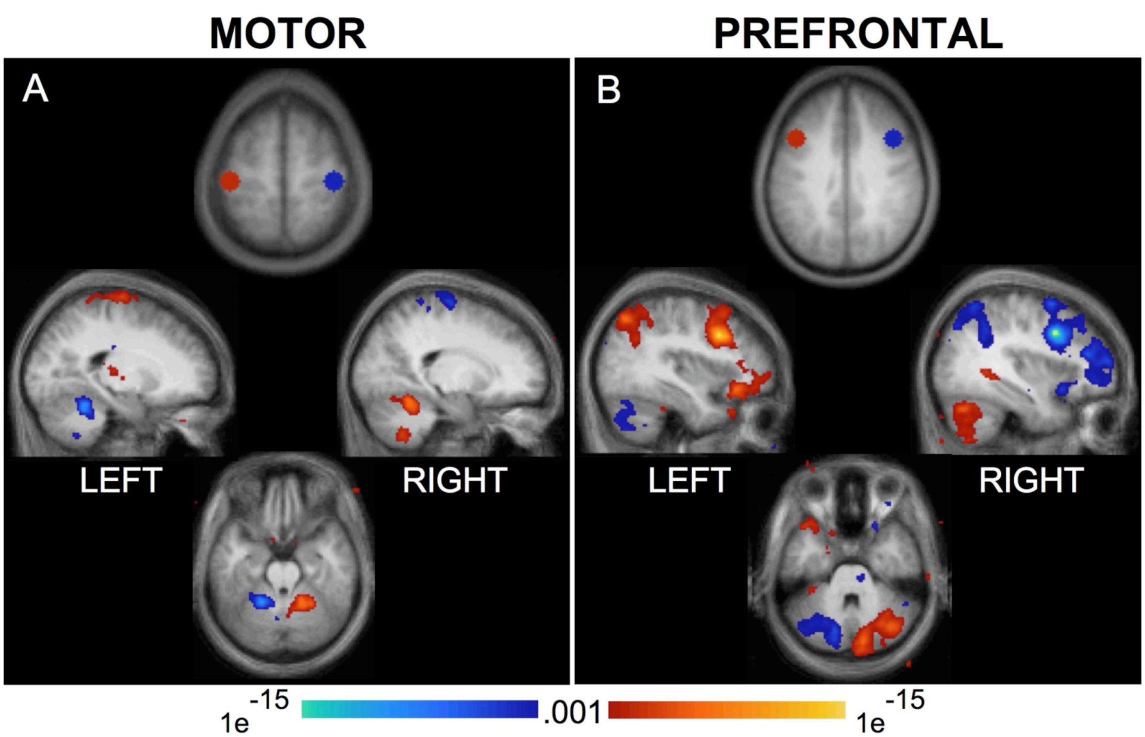
Estimated cytoarchitectonic targets of cerebellar projections.

Seeding lobule V and Crus I in the cerebellum produced distinct patterns of neocortical correlations. Figure 2A in the text displays the two networks projected onto the PALS inflated neocortical surface (Van Essen, 2005). We identified the peak coordinates of both neocortical networks and list them below in Supplementary Table 1 along with their estimated areal boundaries. These areal boundaries should be considered approximate and are primarily useful as heuristic landmarks. Note that in addition to the correlations with DLPFC, other PFC zones such as anterior PFC including part of pars opercularis also contain peak correlations with this cerebellar region. Lobule V contains peak correlations at or near bilateral premotor and primary motor cortices.

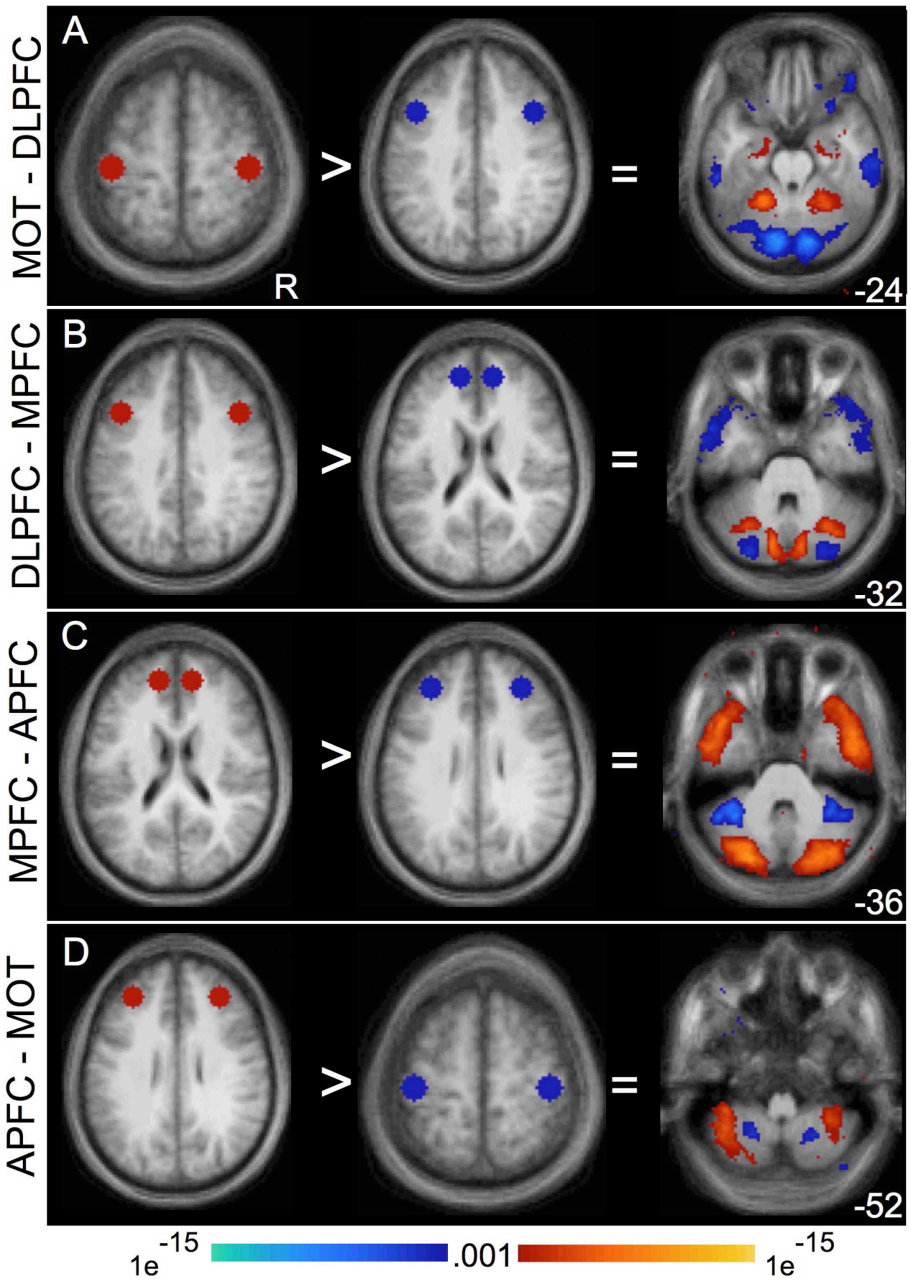
Supplementary Table 1. Peak Correlations in Frontal Cortex.

Seed Region	BA	Description	x	y	z	z(r)
Crus I (CBM_{DLPFC})						
	46	Dorsolateral PFC	-42	50	0	0.3
	10	Anterior PFC	34	62	2	0.29
	9	Dorsolateral PFC	48	16	42	0.28
	44	pars opercularis	50	26	54	0.28
	44	pars opercularis	-50	20	38	0.27
	9	Dorsolateral PFC	40	12	54	0.27
	46	Dorsolateral PFC	42	50	-8	0.24
Lobule V (CBM_{MOT})						
	6	Premotor cortex	30	-14	75	0.22
	6	Premotor cortex	-36	-12	68	0.2
	4	Primary Motor Cortex	-40	-16	64	0.18
	4	Primary Motor Cortex	38	-20	64	0.17

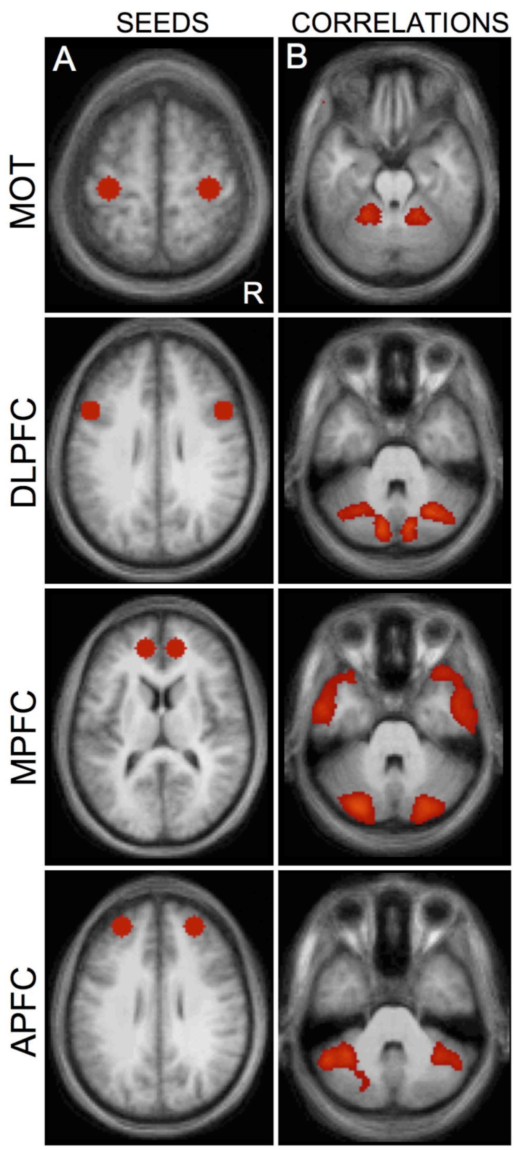
Note: Atlas coordinates (x,y,z) represent the Montreal Neurological Institute (MNI) coordinate system (Evans et al., 1993) based on the MNI152/ACBM-152 target. CBM = seed region placed in cerebellar cortex, MOT = motor cortex, DLPFC = dorsolateral prefrontal cortex, BA = approximate Brodmann's area.



Supplementary Figure 1



Supplementary Figure 2



Supplementary Figure 3