

Figure S1. Effects of regression of principle components on mediation analyses. Related to Figure 5.

(A) Percent of variance explained by each principle component (frontal = magenta; parietal = lime green; cerebellar = cyan) in the discovery sample. (B) *Top*: Percent change in cerebellar mediation estimate when regressing out frontal (magenta) and parietal (lime green) principle components [Δ Mediation %tage = (original mediation effect – mediation effect after regression of *n* PCs)/original mediation effect × 100]. Change in frontal lobe mediation estimate when regressing out cerebellar principal components is shown in cyan. *Bottom*: Similar results were obtained in the independent replication sample (n=24). Cerebellum_{Frontal} = Effect of partialling frontal PCs on cerebellar mediation; Cerebellum_{Parietal} = Effect of partialling parietal PCs on cerebellar mediation; Cerebellum_{Parietal} = Effect of partialling parietal PCs on frontal mediation.

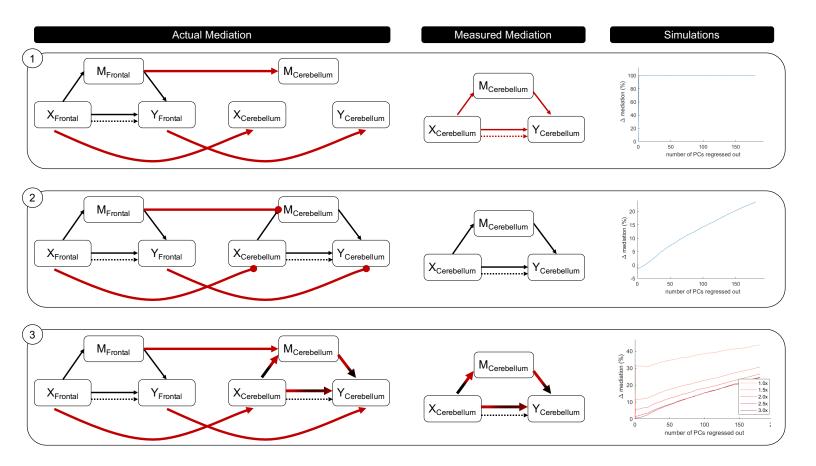


Figure S2. Simulations of effects of principle component regression on mediation analyses. Related to Figure 5.

Three models were tested using simulated data: (1) Cerebellar mediation is entirely reflective of frontal mediations: M_{frontal} mediates the relationship between X_{frontal} and Y_{frontal}. These signals are sent to M_{cerebellum}, X_{cerebellum}, and Y_{cerebellum}, respectively. No actual signals are exchanged among cerebellar regions such that measured mediation in the cerebellum entirely reflects the relayed frontal mediation. In this case, regressing a single frontal PC from each cerebellar areas (i.e. M_{frontal} from M_{cerebellum}, X_{frontal} from M_{cerebellum}, etc.) eliminates the observed mediation in the cerebellum. (2) Cerebellar mediation is completely local: M_{cerebellum} mediates the relationship between X_{cerebellum} and Y_{cerebellum}. X_{frontal}, Y_{frontal}, and M_{frontal} signals are sent to respective cerebellar regions, but these signals are not exchanged among cerebellar regions. In this case, removal of the first few frontal PCs actually improves the measured mediation effect, while removal of additional PCs slowly reduces the mediation. (3) Cerebellar mediation reflects both local and relayed frontal mediation: Cerebellar X, Y, and M regions receive input from the frontal lobe. These signals are mixed with local cerebellar signals so that mediation measured in the cerebellum reflects both local and relayed mediation effects. Depending on the weight given to incoming frontal signals (1X = equally mixed frontal and cerebellar; 3X = more cerebellar), there is less of an effect of frontal PC regression on the cerebellar mediation. In most cases, there is an abrupt decline in mediation after removing the first frontal PC. Collectively, the simulations indicate that if cerebellar mediation is driven entirely by relays from the frontal lobe, regressing frontal PCs from cerebellar signals should quickly extinguish the cerebellar mediation.

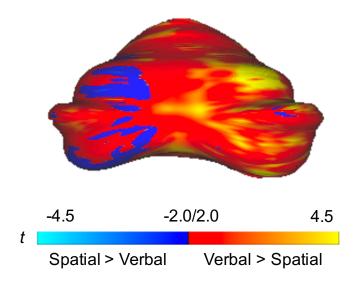


Figure S3. Domain specific effects. Related to Figure 3.

Unthresholded maps of domain effects (verbal > spatial in reds, spatial > verbal in blues). Verbal processing was right-lateralized in the cerebellum and spatial processing was left-lateralized in the cerebellum consistent with known contralateral cerebro-cerebellar connectivity.