Intra-Cerebellar Mouse Functional Connectivity Echoes Human Functional Connectivity

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Introduction

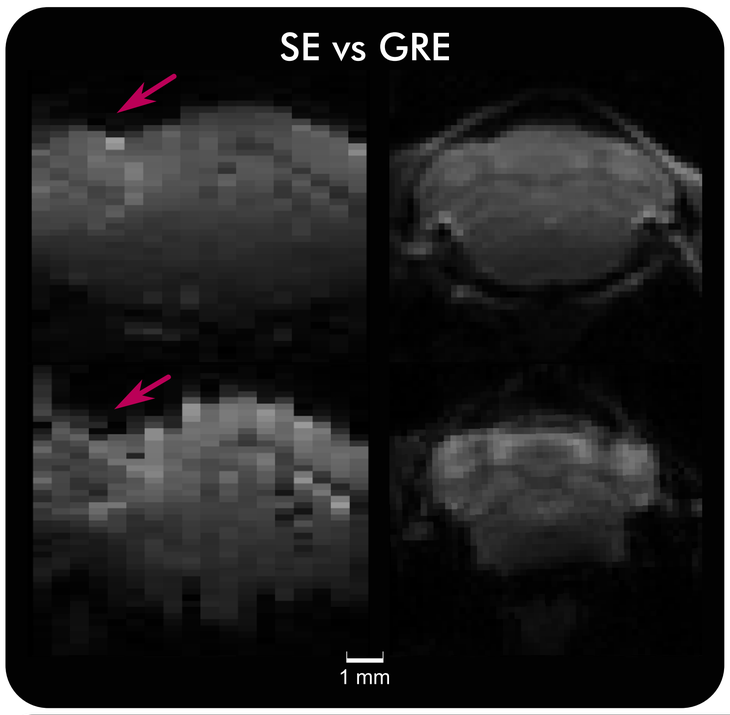
Traditionally associated with motor control, the cerebellum is now known to contribute to cognitive and affective processes, and its dysfunction is linked to pathologies like autism and schizophrenia [1]. While human neuroimaging studies have characterized cerebellar functional connectivity and gradients [2], similar investigations in mice are limited. Here, we present an optimized fMRI protocol for mouse cerebellar imaging, validate connectivity matrices, and derive functional gradients, enabling cross-species comparisons.

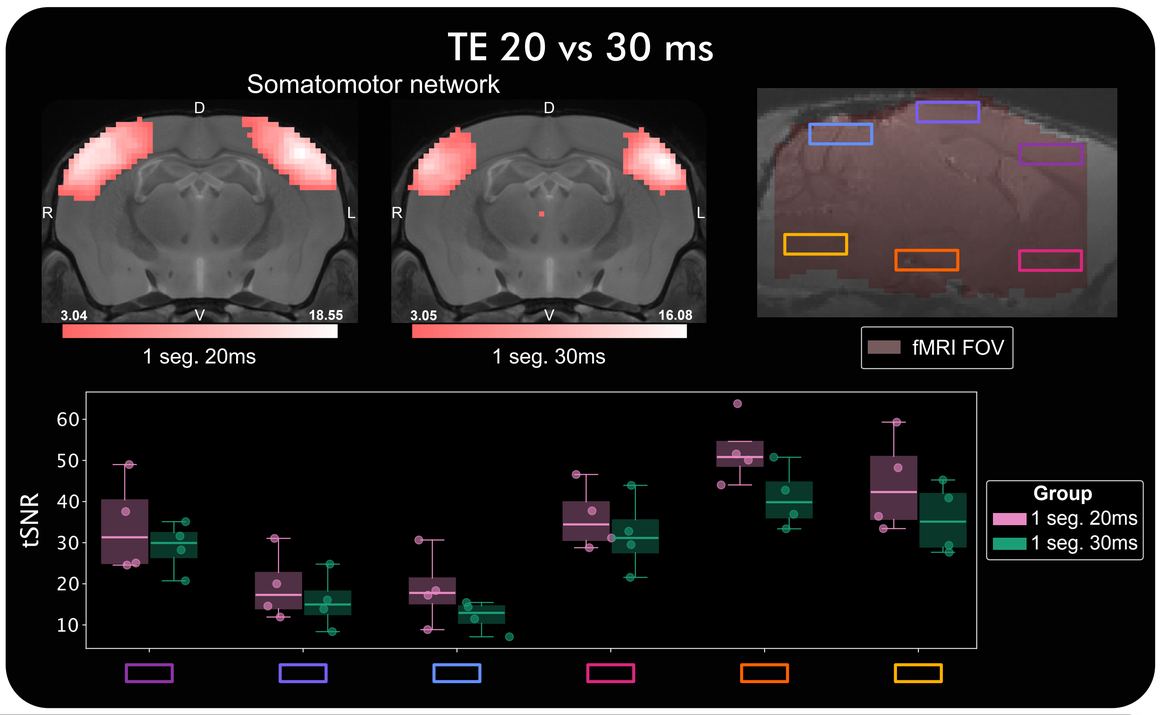
fMRI acquisition

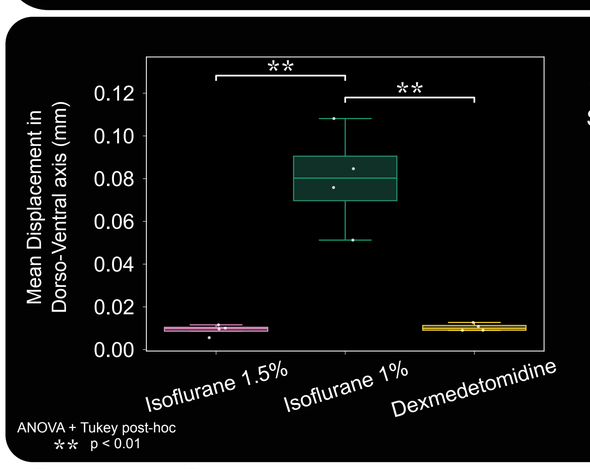
- WT C57BL/6J (2-4 months)
- 4 males for each protocol set-up group
- 3 females, 5 males for connectivity analysis
- 11.7T Bruker scanner with a ^{1}H-cryoprobe
- **Spin-echo (SE)** vs gradient-echo (GRE) EPI
- Chosen sequence : SE-EPI
  - **1 segment** vs 2 segments
  - Echo Time (TE) = **20 ms** vs 30 ms
  - Repetition Time (TR) = 1.5 s
  - Res. 0.18 × 0.18 × 0.5 mm³
  - FOV = 12 × 12 × 9 mm³
  - 400 volumes
- Anatomical RARE seq. (res. 0.05 × 0.05 × 0.5 mm³)
- Anesthesia after isoflurane induction (3%) :
  - Isoflurane (1% vs 1.5%)
  - vs **Dexmedetomidine** (bolus: 0.025 mg/kg; subcutaneous perfusion: 0.1 mg/kg/h)
- Air/Oxygen 1.5:0.3, 1 L/min

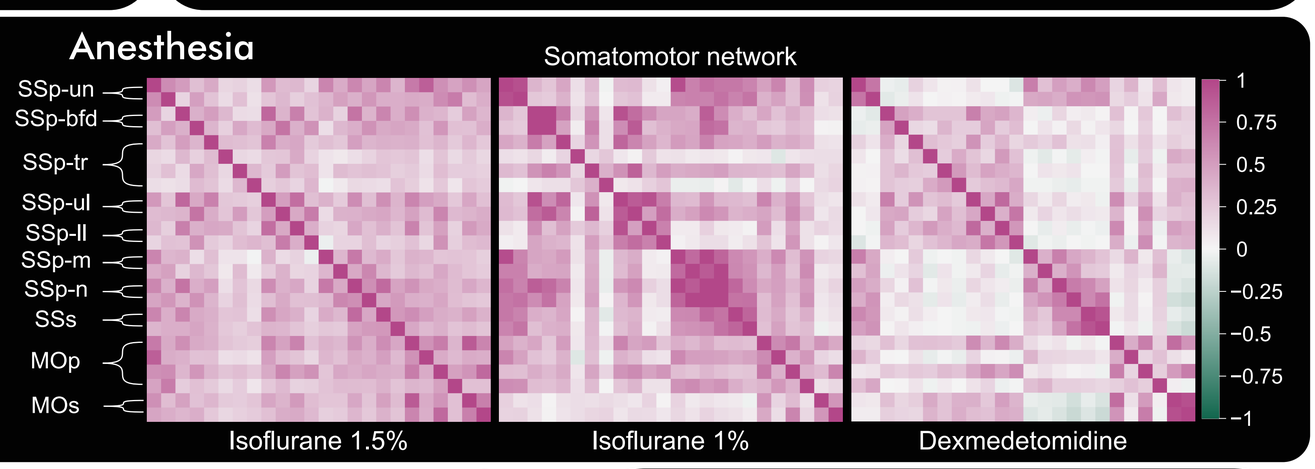
Data Analysis

- Mouse data processed with RABIES [3]
- ICA with fsl melodic (threshold at p<0.05)
- DSURQE atlas [4]
- Human Connectome Project (HCP) Young Adult, n=85, processed with HCP Minimal Preprocessing Pipeline
- 10 functional gradients using BrainSpace [5] (cosine similarity, PCA, Procrustes alignment), averaged across the group

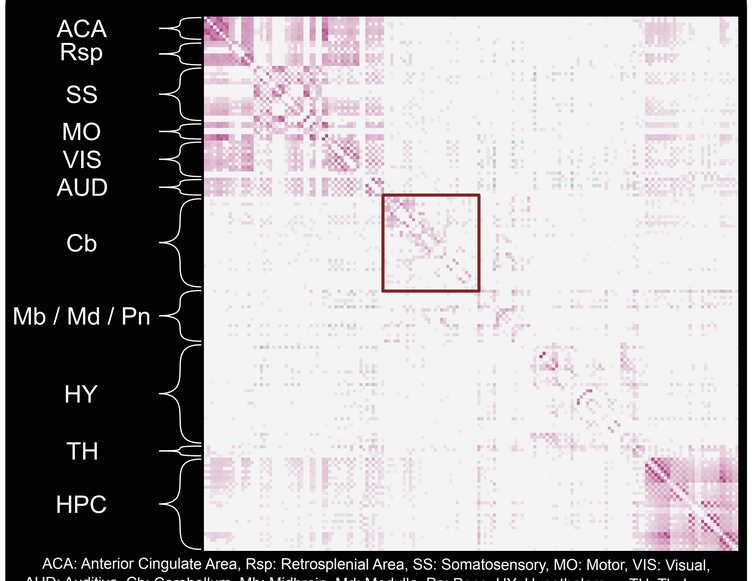




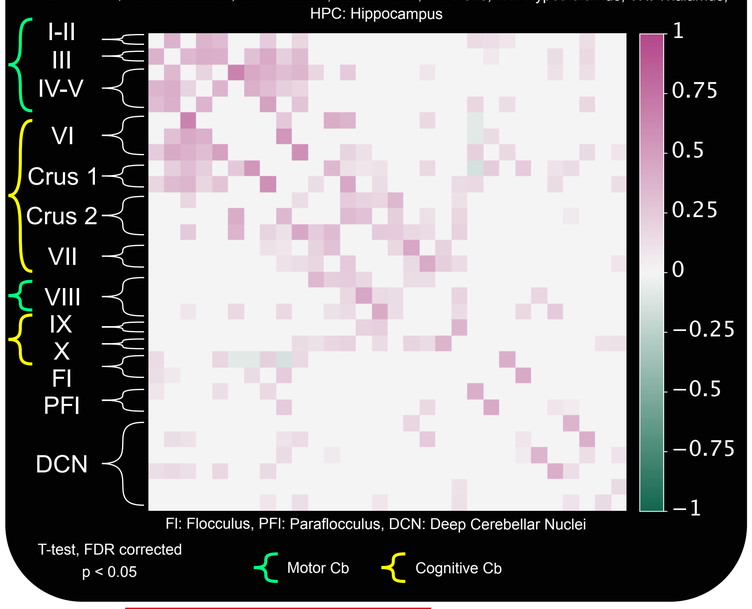




Brain-wide and Cerebellar Correlation



ACA: Anterior Cingulate Area, Rsp: Retrosplenial Area, SS: Somatosensory, MO: Motor, VIS: Visual, AUD: Auditive, Cb: Cerebellum, Mb: Midbrain, Md: Medulla, Pn: Pons, HY: Hypothalamus, TH: Thalamus, HPC: Hippocampus



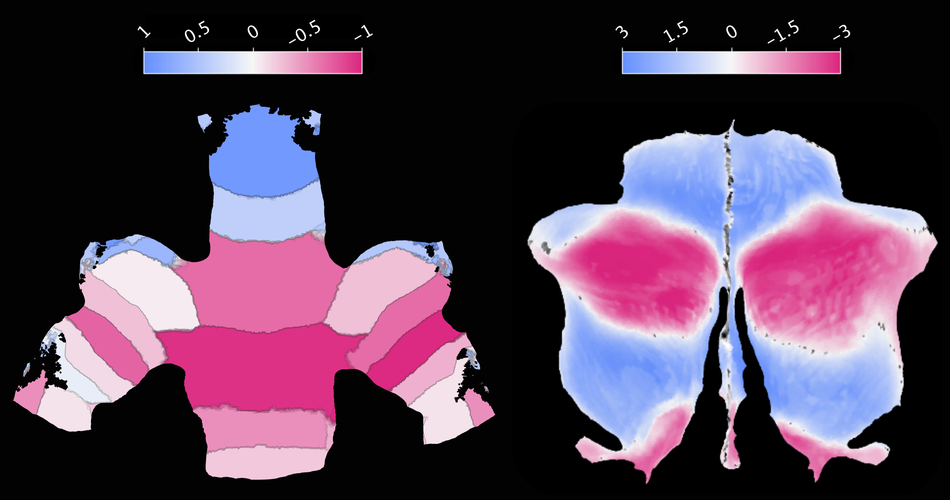
Fl: Flocculus, PFl: Paraflocculus, DCN: Deep Cerebellar Nuclei

T-test, FDR corrected
p < 0.05

{ Motor Cb { Cognitive Cb

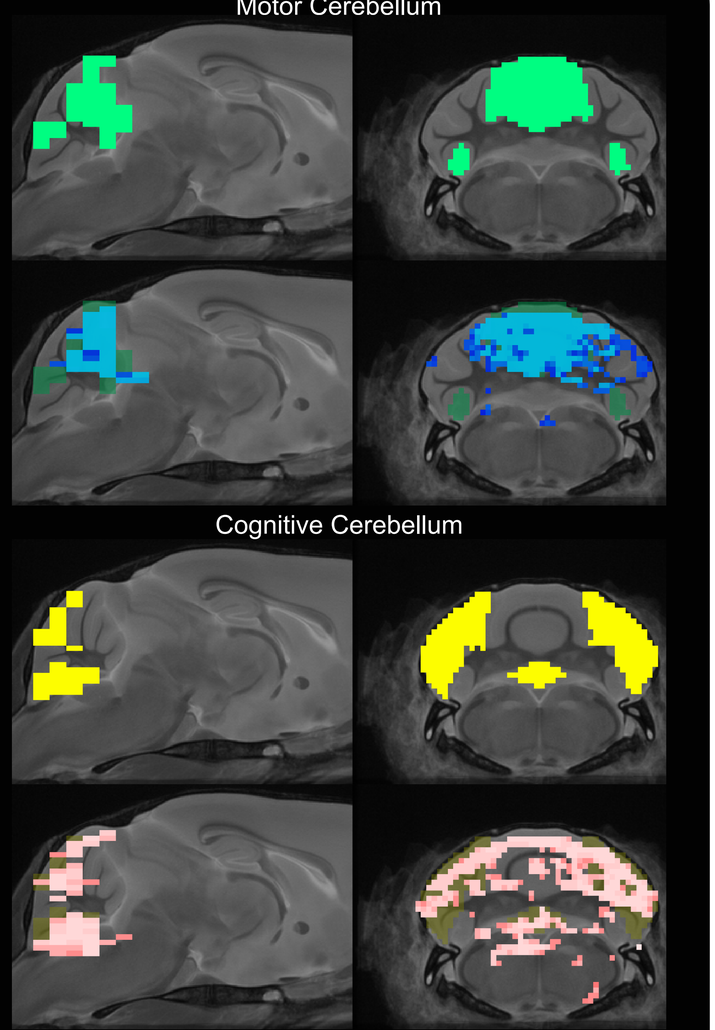
Cerebellar Connectivity Gradients

Flatmap of the mouse cerebellum generated from the DSURQE atlas. Landmarks were manually placed, to cut the cerebellum, between the posterior vermis and hemispheres, between lobule X and lobules I–II, and between the hemispheres of lobules VI–VII and lobules I–V. It was then flattened with Least Squares Conformal Maps.



Second gradient of the mouse cerebellum, separating motor from cognitive lobules (left). However, lobule VIII, typically motor-related, is clustered with cognitive lobules. The separation between motor and non-motor lobules is less distinct in mice. Notably, Crus I showed intermediate connectivity, correlating more with motor lobules than expected. First gradient of the human cerebellum, computed on HCP Young Adult, and corresponding to the one found in [2] (right).

Seed Based Analysis



Region-wise seed-based connectivity analysis of motor and cognitive cerebellar territories. Strong within-region autocorrelation was observed for each seed. Motor and cognitive territories exhibited distinct connectivity patterns with minimal overlap, indicating functional segregation between cerebellar regions.

Randomise with Threshold-Free Cluster Enhancement, FWE corrected
p < 0.05

Conclusion

Our study presents an optimized SE-fMRI protocol for mouse cerebellar imaging, enabling robust functional connectivity analysis. By validating SE-EPI and dexmedetomidine anesthesia, we overcame key technical challenges (motion artifacts and inhomogeneity artefacts) to reveal conserved connectivity patterns in mice. The intra-cerebellar correlation matrix and functional gradients mirrored human findings. Crus 1 and lobule VIII showed species-specific connectivity probably due to voxel resolution tradeoffs. The conserved gradients suggest that mouse models can inform human cerebellar dysfunction in pathology.

References

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