Abstract #00313 ISMRM ABSTRACT

[USGOV] Multimodal MRI Framework for Cross-Species Cerebellar Mapping and Atlas Construction in Marmoset, Macaque, and Human.

Primary: Preclinical Animal & in vitro MR - Large Animals, Nonhuman Primates 〉 **Secondary:** Contrast Mechanisms - Microstructure 〉 **Presentation:** Oral, Traditional Poster, Digital Poster

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Impact

This work develops a standardized multimodal MRI framework that combines structural, diffusion, and fiber orientation modalities for high-resolution cerebellar mapping and atlas construction across marmoset, macaque, and human brains. This enables cross-species registration, segmentation, and comparative analysis of cerebellar microstructure.

Synopsis

Motivation: A multimodal MRI framework for cross-species cerebellar atlas development in marmosets, macaques, and humans harmonizes high-resolution imaging and analysis in disease models, bridging evolution and function.

Goals: How can advanced multimodal 7T MRI techniques be optimized to create a standardized, high-resolution cerebellar atlas across marmoset, macaque, and human species?

Approach: We acquired MAP-MRI datasets with histology, and the MNI_ICBM T1-weighted template for cerebellum segmentation.

Results: The cross-species cerebellar atlas provides detailed lobular and vermal segmentation, delineates its deep nuclei and fiber orientations in stereotaxic coordinates using MAP-MRI, T2-weighted, and DEC maps, and highlights species-specific MRI signal differences within the deep cerebellar nuclei.

Introduction

Comparative analysis of the cerebellum across primate species is essential for uncovering its evolutionary contributions to motor control and cognition. This work introduces a multimodal MRI framework integrating T1-, T2-weighted, and diffusion (MAP-MRI)[1,2] imaging with histological validation to achieve high-resolution cerebellar mapping across the marmoset, macaque, and human brains. The resulting cross-species atlas enables a detailed investigation of cerebellar structure and microstructural differences among primates.

Materials and Methods

We scanned two perfusion-fixed adult marmoset brains and one macaque brain on a 7T scanner using mean apparent propagator (MAP)-MRI at resolutions of 150 µm and 200 µm, respectively. Diffusion-weighted images (112 or 256 directions) were acquired with multiple b-values (b_{max} = 10,000 s/mm²), gradient durations δ = 6–8 ms, and diffusion times Δ = 20–28 ms. In each voxel, we estimated the MAP and derived both standard diffusion tensor imaging (DTI) and advanced MAP parameters: fractional anisotropy (FA), mean/axial/radial diffusivities (MD, AD, RD), propagator anisotropy (PA), return-to-origin/axis/plane probabilities (RTOP, RTAP, RTPP), non-Gaussianity (NG), and the non-diffusion-attenuated (T2-weighted) image. Fiber orientation distribution functions (fODFs)[3] were also estimated. After scanning, brains were processed histologically using various stains (AChE, Prussian blue, Nissl, SMI-32, parvalbumin, NeuN, ChAT)[4,5], and high-resolution digital images of these stained sections were manually registered to MRI volumes to segment cerebellar lobules and deep cerebellar nuclei in 3D. We also registered these *ex vivo* segmented templates to a multisubject population-based *in vivo* template to generate standard cerebellar atlases in stereotaxic coordinates.

For the human cerebellum, we used the T1-weighted MNI_icbm152 template[6] and registered both the *in vivo* direction-encoded color (DEC)[7] volume from the Human Connectome Project and the BigBrain dataset[8] to MNI space. These registrations aligned well (**Fig. 4B**), enabling accurate segmentation of cerebellar lobules, fiber tracts, and deep nuclei on the MNI template.

Results and Discussion

We observed distinct interspecies differences in cerebellar MR signal characteristics, particularly within the deep cerebellar nuclei (DCN). On T2-weighted images, the DCN appeared significantly more hypointense in macaques and humans relative to marmosets (**Fig. 1A, B, E**), consistent with prior findings associating T2 hypointensity with elevated iron accumulation[9,10]. This interpretation was supported by Perls' Prussian blue staining of histological sections from the same specimens. In macaques, the DCN neuropil exhibited robust iron staining, whereas marmosets showed only minimal labeling, indicating comparatively low iron content (**Fig. 1C, D**). These results point to species-specific differences in cerebellar iron deposition, potentially reflecting evolutionary divergence in cerebellar metabolism, development, or function.

We also present a high-resolution parcellation of the cerebellum in marmosets, macaques, and humans, providing detailed segmentation of lobules (I–X), the vermis, and the deep nuclei (**Figs. 2–4 ▼**). These atlases include standardized anatomical labeling and multi-planar visualizations (coronal, axial, sagittal). Fiber orientation mapping, derived from directionally encoded color (DEC) diffusion MRI, further delineates cerebellar architecture, including white matter tracts and nuclear regions.

Cerebellar size and lobular morphology varied across species, with macaques showing vermal and lobular configurations more similar to marmosets than to humans. Differences were also observed in inter-lobular MR contrast and fiber orientation patterns (**Fig. 5**), reflecting both conserved and divergent features of cerebellar organization across primates.

Using affine and nonlinear registration, we successfully aligned each species-specific cerebellar atlas to individual T1-weighted MRI or population-based datasets from control subjects spanning a range of ages and sexes. The registered atlases demonstrated close correspondence with native cerebellar morphology, enabling accurate delineation of lobular and nuclear boundaries (e.g., **Figs. 2B, 3B, 4D ▼**). These findings validate the use of standard registration pipelines for inter-individual alignment and support the application of our atlases in comparative, developmental, and translational neuroimaging.

Conclusion

Our results reveal fundamental interspecies differences in cerebellar anatomy and iron distribution, particularly within the deep cerebellar nuclei, highlighting evolutionary and metabolic specializations across primates. The accompanying multi-species cerebellar atlases provide a reliable anatomical framework for comparative and developmental neuroimaging research.

Acknowledgements

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Figures and Tables

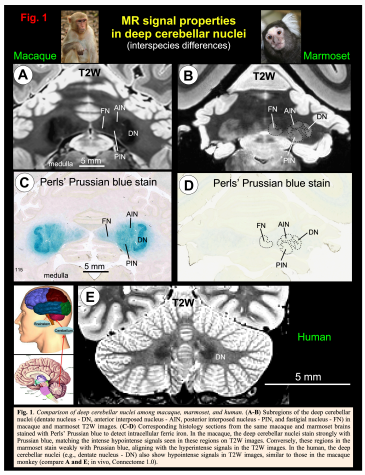

Figure 1: *Comparison of deep cerebellar nuclei among macaque, marmoset, and human.*

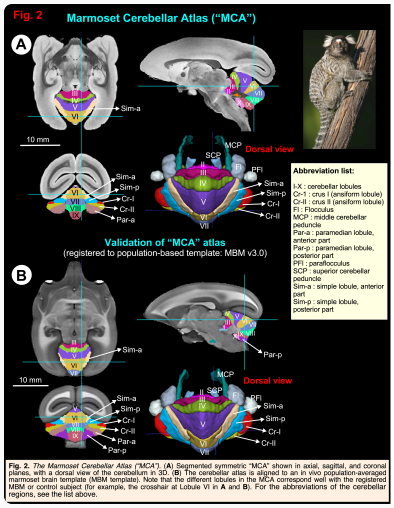

Figure 2: *The Marmoset Cerebellar Atlas ("MCA").*

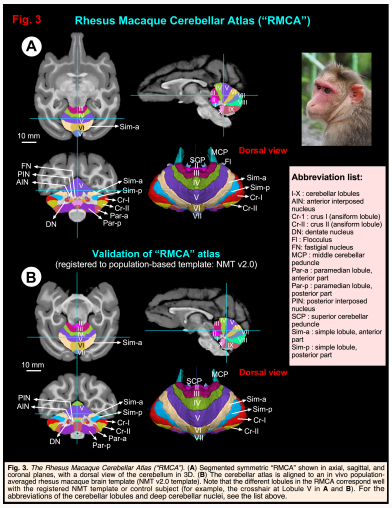

Figure 3: *The Rhesus Macaque Cerebellar Atlas ("RMCA").*

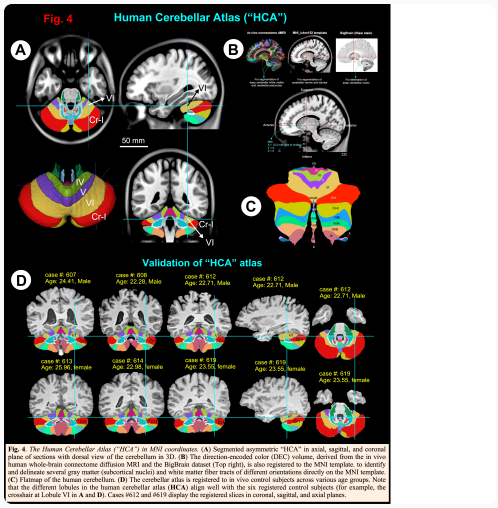

Figure 4: *The Human Cerebellar Atlas ("HCA") in MNI coordinates.*

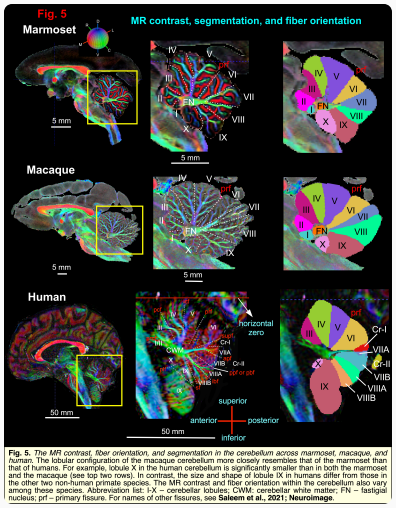

Figure 5: *The MR contrast, fiber orientation, and segmentation in the cerebellum across marmoset, macaque, and human.*