The comprehensive Subcortical Atlas of the Human Brain ("SAHB") derived from high-resolution multimodal MRI at 7T.

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Synopsis

Motivation: To develop a detailed 3D atlas to help locate the subcortical subregions for anatomical, functional, and clinical studies.

Goal(s): To generate the comprehensive subcortical atlas of the human brain, using multimodal MRI *ex vivo* at 7T, and register it to an *in vivo* MNI template for 3D segmentation.

Approach: Obtained high-resolution images from the fixed brainstem at 7T using MAP-MRI with 250 µm resolution.

Results: MAP-MRI enabled detailed noninvasive segmentation of deep brain structures at a high spatial resolution.

Impact: Tracing and validating subcortical regions in 3D are imperative for neurosurgical planning for DBS, fMRI studies, cross-species comparison, and establishing brain structure-function relationships.

Introduction

The thalamus, basal ganglia, brainstem nuclei, etc, are subcortical regions that regulate autonomic, sensorimotor, cognitive, and limbic functions. The high-resolution mapping with a comprehensive 3D digital atlas of these subcortical regions in primates based on multimodal MRI[1] is remarkably useful in anatomical, functional, and clinical studies. In particular, registering the 3D atlas to a given human brain MRI scan is of immediate value to determine the regions of interest for tractography studies, the areal location of fMRI responses, and the potential target for deep brain stimulation (DBS) in neurological disorders. This study developed a Subcortical Atlas of the Human Brain (SAHB) in 3D using ultra-high-resolution Mean apparent propagator (MAP)-MRI[2,3], MTR, and T2W images.

Material and Methods

We dissected the entire human brainstem including the thalamus and basal ganglia, but not the cerebellum (**Fig. 1 A**), from a postmortem formalin-fixed adult female brain (age: 24 years old; PMI: 34 hr; fixation time: over six months). The brainstem block was immersed in 0.1M PBS-saline with sodium azide before MRI data acquisition. The specimen was placed inside the custom-made mold and container assembly (**Fig. 1 B- D**) and scanned on a 7T scanner using MAP-MRI with 250 µm resolution. We acquired 104 DWIs with multiple b-values (bmax=10000 s/mm2), and pulse duration and separation were δ=8 ms and Δ=28 ms, respectively. In each voxel, we estimated the MAP and computed microstructural DTI/MAP parameters: fractional anisotropy (FA); mean, axial, and radial diffusivities (MD, AD, and RD, respectively); propagator anisotropy (PA), non-gaussianity (NG), return-to-origin probability (RTOP), return-to-axis probability (RTAP), and return-to-plane probability (RTPP), along with the fiber orientation distribution (FOD)[4] functions. We computed the MT ratio (MTR) from 3D gradient echo images acquired with and without MT preparation. The total duration of the MAP-MRI scan was 62 h and 25 min, and the MT scan was 13 h and 7 min.

The *ex vivo* MAP-MRI dataset and various microstructural parameters were registered to the *in vivo* MNI_icbm152 template[5]. We also registered the direction-encoded color (DEC) volume derived from the *in vivo* human whole-brain connectome diffusion MRI and the BigBrain dataset to the same MNI volume[6,7]. All these volumes registered well to the standard MNI space (**Fig. 2 A- F**), helping us delineate different subcortical nuclei and white matter fiber tracts directly on the MNI template.

Results

We identified and segmented the subregions in the basal ganglia, thalamus, hypothalamus, brainstem (midbrain, pons, and medulla), amygdala, bed nucleus of stria terminalis, and the basal forebrain directly on the *in vivo* MNI template using the warped *ex vivo* MAP-MRI, T2W, and MTR images (**Fig. 3 A- F**, for thalamic subregions as references). In addition, we also distinguished and segmented fiber tracts of different sizes and orientations associated with the basal ganglia, thalamus, brainstem, and cerebellum using the FOD-derived DEC map[6,8] (**Fig. 4 A- F**). This newly segmented volume/template is called the Subcortical Atlas of the Human Brain, or "SAHB". The SAHB atlas in Figure 5 (top row) shows the segmented deep brain regions on the 2D axial, sagittal, and coronal MRI and in 3D. This digital atlas provides a practical standard template for neuroanatomical, functional (fMRI), clinical, and connectional imaging studies.

We also validated the atlas-based areal boundaries of segmented subcortical areas by registering this *in vivo* "SAHB" template to an individual *in vivo* T1W MRI datasets of adult human subjects of different age groups and genders (control adults), using a sequence of affine and nonlinear registration steps. This procedure resulted in registering the SAHB data to the *in vivo* template space, thereby integrating the segmentation of these subcortical areas into a standard 3D volume (**Fig. 5**; bottom rows, specific to the cerebellum). These results demonstrate that affine and nonlinear warpings are sufficient to distinguish and provide atlas-based estimates of areal boundaries on individual subject-specific brain templates *in vivo.*

Discussion

High-resolution MAP-MRI provides microstructural parameters and directional information (DEC-FOD) that can complement multiple histological stains[1,9]. This study's most important unique feature is the strict adherence to an *ex vivo* MAP- and other MRI scans warped onto the MNI template. As a result, the alignment accuracy between the areal boundaries and the gross anatomical features is optimized for identifying regions-of-interest directly on the MNI template (**Fig. 2**). Taken together, MAP-MRI enables the construction of high-resolution 3D atlases that can improve the precise placement of electrodes in deep brain structures in DBS studies of neurological disorders.

Conclusion

The MAP-MRI enabled noninvasive segmentation of subcortical regions in the human brain. The subcortical 3D atlas provides a readily usable standard for region definition, while the template provides a standard reference and space.

Acknowledgements

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Figures

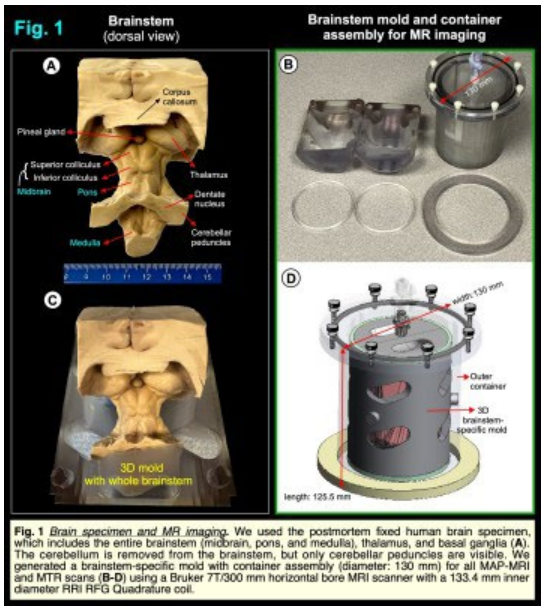

Fig. 1 Brain specimen and MR imaging assembly.

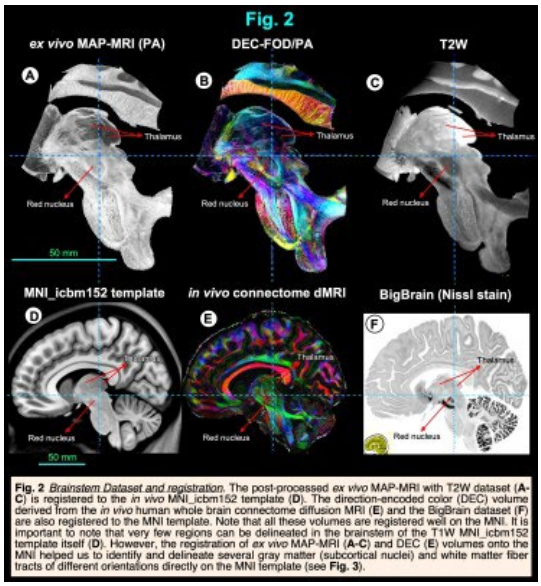

fig. 2 Brainstem dataset and registration.

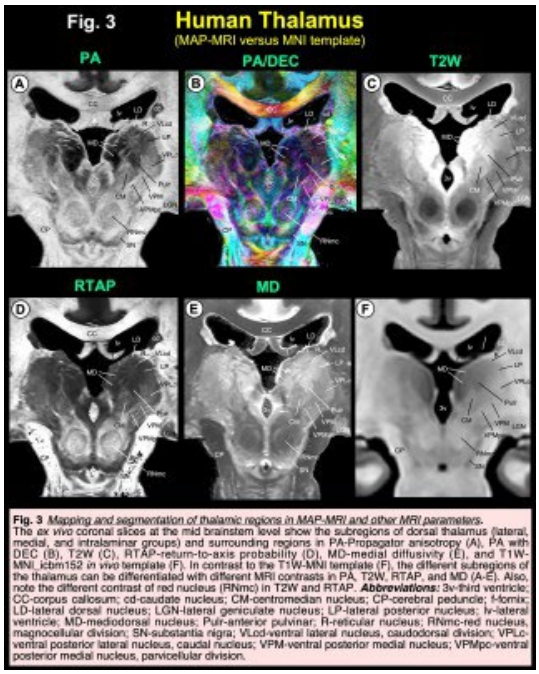

Fig. 3 Mapping and segmentation of thalamic regions in MAP-MRI and other MRI parameters.

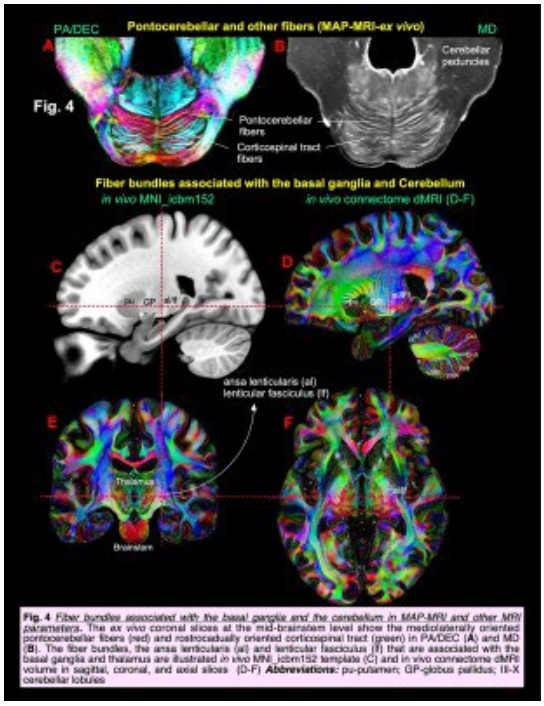

Fig. 4 Fiber bundles associated with the basal ganglia and the cerebellum in MAP-MRI and other MRI parameters.

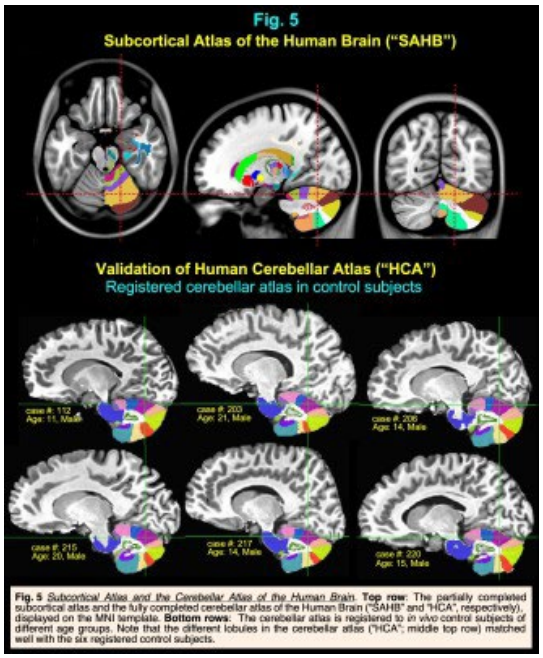

Fig. 5 Subcortical Atlas and the Cerebellar Atlas of the Human Brain.