A Combined High Spatial- and High Angular-Resolution Diffusion MRI Atlas of the Human Brainstem and Thalamus

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Purpose: Recent advances in deep brain stimulation (DBS) have demonstrated that chronic stimulation of small nuclei and white matter tracts in the brainstem and diencephalon can have profound therapeutic effects on a variety of neurologic disorders including Parkinson's disease, Tourette syndrome, and chronic pain. Localization of increasingly precise DBS targets requires accurate 3D maps of brainstem architecture. Diffusion MRI can provide excellent soft tissue contrast as well as detailed 3D anatomy and structural connectivity[1-5]. Unfortunately, clinical studies of the human brainstem are limited by low spatial resolution and/or low angular (diffusion) resolution. Magnetic resonance histology, i.e. MRI of fixed, ex-vivo specimens, can address these limitations. In this study we present the first combined high spatial- and high angular-resolution diffusion MRI atlas of the human brainstem and thalamus. We also demonstrate deterministic and probabilistic tractography of fiber pathways with accurate estimation of intravoxel fiber crossings.

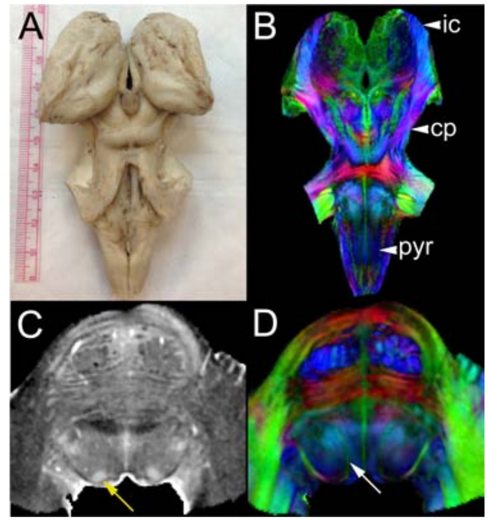

Fig. 1: Anatomic details revealed by DTI. A) The specimen imaged for this study. B) Coronal color FA map showing the pyr/cp/ic complex. C) Diffusion coefficient map highlighting the 6th nerve nucleus (arrow). D) The color map at the same level as C showing the 6th nerve itself (arrow).

Methods: A postmortem brainstem from a 37-year-old male with no neurologic history was immersion fixed in 10% formalin doped with 5 mM gadoteridol. MR imaging was performed on a 7T system using a 65 mm internal diameter quadrature RF coil. Diffusion data were acquired at 200 µm isotropic resolution using a 3D spin echo pulse sequence (TR/TE = 100/24 ms) with 120 diffusion directions (b = 4000 s/mm^2) and 12 non-diffusion weighted images (b0) distributed over a ~227 hr acquisition. Bore temperature was controlled with a water circulation system and monitored using a fiberoptic probe. The dataset was reconstructed using three different models: 1) least squares tensor estimation (DTI)[6], spherical harmonic orientation distribution function (ODF) deconvolution (q-ball)[7], and FSL's BEDPOSTX[8]. Deterministic tractography and tract segmentations were performed on q-ball ODF data using DSI Studio. Probabilistic tractography was carried out using FSL's PROBTRACKX.

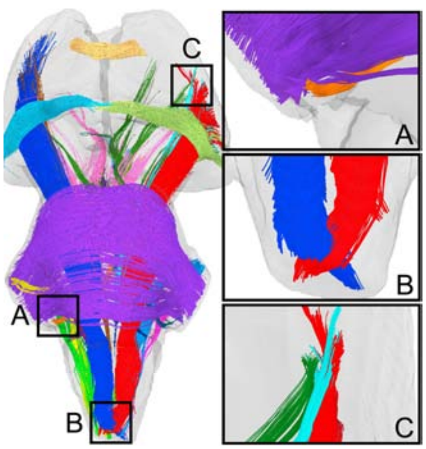

Fig. 2: Deterministic tractography showing 28 tracts in the brainstem. A) The 7th cranial nerve (orange) emerging beneath the transverse fibers of the pons (purple). B) Interdigitating motor fibers in the pyramidal decussation. C) Multiple fiber populations in the internal capsule including corticobulbar fibers (green), somatosensory fibers from the medial lemniscus (cyan), and corticospinal fibers (red).

Results: The entire human brainstem and thalamus (Fig. 1A) are revealed at 200 µm isotropic resolution in DTI-derived images (Fig. 1B-D), allowing visualization of long white matter pathways such as the pyramidal tract (pyr)/cerebral peduncle (cp)/internal capsule (ic) complex (Fig. 1B). Different DTI-derived image contrasts highlight different anatomy. For example, the 6th cranial nerve nucleus stands out in the diffusion coefficient map (Fig. 1C, arrow), while the 6th nerve itself is visible in the directionally encoded color fractional anisotropy (FA) map (Fig. 1D, arrow). Deterministic tractography of q-ball ODF data allows visualization of at least 28 different white matter pathways (Fig. 2). The high spatial resolution allows tracking of small pathways like the 7th cranial nerve (Fig. 2A, orange), and angular resolution is sufficient to resolve interdigitating fibers in the pyramidal decussation (Fig. 2B). At least three different fiber populations are resolved in the internal capsule (ic) (Fig. 2A), corticobulbar fibers (green), somatosensory fibers from the medial lemniscus (cyan), and corticospinal fibers (red). Probabilistic tractography was used to segment the ic based on these different fiber contributions (Fig. 3).

Discussion & Conclusion: We have used magnetic resonance histology to map the human brainstem and thalamus with unprecedented structural detail. We extend previous work by including the thalamus, an important area for DBS, and by modeling intravoxel fiber crossings[1-5]. This atlas allows exploration of 3D spatial relationships and structural connectivity in small brainstem regions including a majority of DBS targets. We have demonstrated probabilistic tractography segmentation of the ic, a current DBS target[9], with ongoing analysis of other common targets including the subthalamic nucleus and ventral intermediate nucleus of the thalamus. These data provide a new 3D map of clinically relevant brainstem anatomy to aid ongoing work in DBS. An expanded atlas built on this approach may well provide surgeons valuable guidance in identifying and localizing new DBS targets.

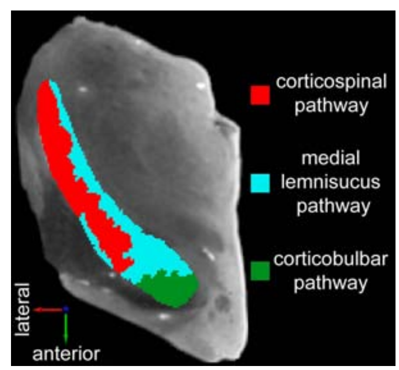

Fig. 3: Probabilistic tractography segmentation of multiple fiber populations in the internal capsule.

References: [1] Aggarwal *et al*, *Neuroimage* 74, 2013. [2] McNab *et al, Neuroimage* 80, 2013. [3] Edlow *et al, J Neuropathol Exp Neurol* 71, 2012. [4] Ford *et al, Front Hum Neurosci* 7, 2013. [5] Prats-Galino *et al, Clin Neurophysiol* 123, 2012. [6] Basser & Pierpaoli, *J Magn Reson B* 111, 1996. [7] Descoteaux *et al*, *Magn Reson Med* 58, 2007. [8] Behrens *et al*, *Neuroimage* 34, 2007. [9] Greenberg *et al*, *Mol Psychiatry* 15, 2008.