Tripping Over Ourselves to Image the Cerebellum

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Introduction: As is now understood, the cerebellum plays a significant role in processing motor, sensory, cognitive, emotional and linguistic information[1,2], relaying information between the cerebral cortex and other gray matter structures, such as the thalamus and red nucleus. The bulk of this information is relayed through the deep cerebellum nuclei, comprised of the dentate, fastigial, globose and emboliform nuclei first identified by Stilling[3]. Given the importance of these nuclei in a wide variety of functions, their study has important clinical applications. Prior post-mortem studies of the cerebellar nuclei have revealed abnormalities in several disorders, including autism, olivopontocerebellar atrophy and Friedreich's ataxia[4]. In some disorders, abnormalities occur early, whilst in others pathological changes are characteristic of more advanced stages and do not correlate well with clinical symptoms (for example, Friedreich's ataxia). The ability to investigate the cerebellar nuclei, as well as the associated inferior olive, both during normal neurological development as well as in disease could therefore offer significant insight into disease pathogenesis. However, the small size of these structures, coupled with their structural similarity to their surrounding environment, has made visualizing them on conventional clinically obtained T_1 or T_2-weighted images a challenge. In this work we report on our efforts to determine the feasibility of visualizing these structures using high resolution quantitative T_1 and proton density (ρ) mapping at 3 Tesla. For the first time we are able to describe the anatomy of the cerebellar nuclei in the living human brain, raising the possibility of performing future clinico-anatomical studies in inherited cerebellar disorders.

Methods: To determine the ability to visualize the deep cerebellar nuclei, a quantitative T_1 and ρ mapping approach was chosen. Unlike conventional T_1-*weighted* imaging, for example, in which the image contrast is primarily a function of T_1, but is also influenced by T_2, ρ and radio-frequency (RF) coil effects, the contrast in a 'pure' T_1 map is solely due to tissue T_1 differences. Consequently subtle variations in T_1 become more apparent in map images. Using the DESPOT1[5] imaging method, high resolution T_1 and ρ maps were acquired of a healthy volunteer with the following parameters: 22cm^2 x 12.5cm field of view (FOV), 440x440x256 matrix (0.5mm isotropic voxels), TE/TR = 3.2ms/9.7ms, and flip angles (α) = 4°, 20°. To account for flip angle errors associated with B_1^+ effects at 3T, the DESPOT1-HIFI[6] method was used, involving a supplementation inversion-prepared spoiled gradient image (IR-SPGR) acquisition with matched FOV and matrix parameters, and α = 5° and inversion time = 450ms. To reduce time, this data were acquired with half the spatial resolution in Y and Z of the DESPOT1 data and interpolated to the full resolution. Imaging time for each DESPOT1 dataset was 20 mins. To increase the signal-to-noise ratio (SNR) of the maps, 12 averages were acquired over the course of 3 days. These data were linearly co-registered and combined to yield the final maps. The data was then interrogated by an expert neuroanatomist with the aim of identifying the cerebellar and inferior olive nuclei.

Results: Slices of interest through the cerebellum and brainstem are shown in Figs. 1 and 2 with reference labeled anatomical images derived from histological studies. While the dentate nucleus (Fig. 1), as the largest of the nuclei, is readily visible in all orientations with a width of approx. 1mm (2 voxels), the smaller fastigial, globose, and emboliform nuclei can only be appreciated in the axial plane with a diameter of approx. 1mm. The inferior olive nuclei (Fig. 2) can also be easily appreciated in both the axial and coronal orientations.

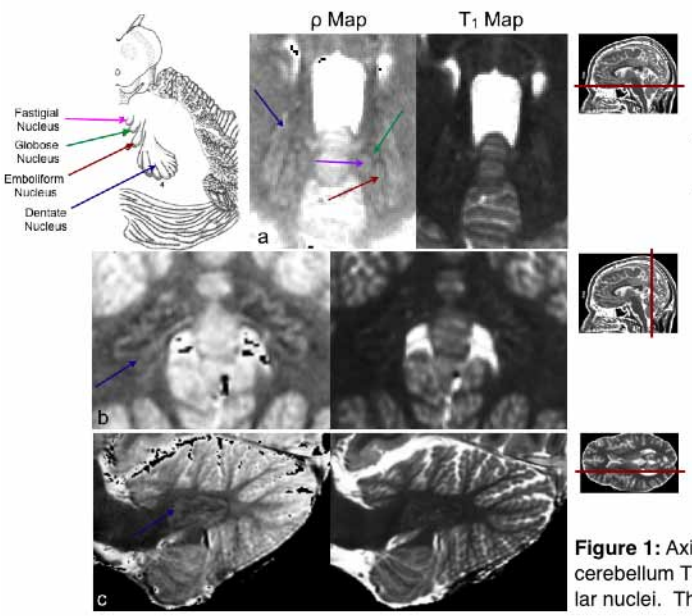

Figure 1: Axial (**a**), coronal (**b**) and sagittal (**c**) sections through the cerebellum T_1 and proton density maps revealing the deep cerebellar nuclei. The top left image is a reference histological cartoon.

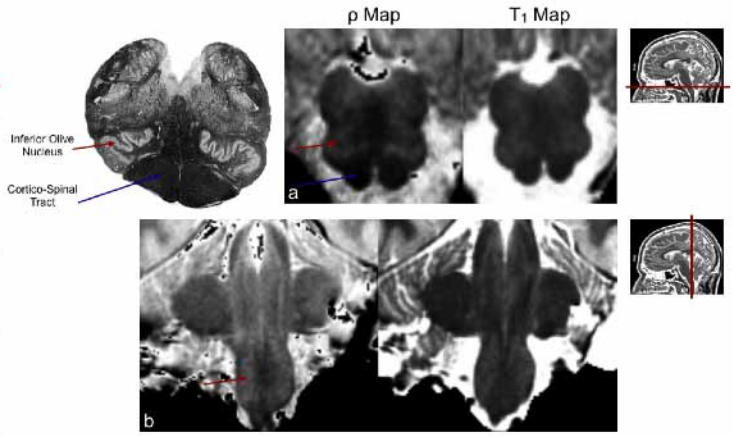

Figure 2: Axial (**a**) and coronal (**b**) sections through the brainstem T_1 and proton density maps inferior olivenuclei. The top left image is a reference histological cartoon.

Discussion / Conclusions: The results shown in Figs. 1 and 2 demonstrate the ability to visualize and discriminate the deep cerebellum and inferior olive nuclei. Whilst the data presented represents a clinically impractical 4hrs of scanning, exam time can be shortened considerably by acquiring non-isotropic voxels. In this work, isotropic voxels were utilized since the orientation and geometry of the structures of interest was not well understood. In future studies, however, resolution in one dimension could be traded for SNR, allowing considerable reductions in acquisition time. In addition to investigating abnormalities in these structures with disease, the ability to visualize these important structures also introduces the possibility of using them as seed points for diffusion tensor imaging tractography studies to further elucidate and confirm hypothesized pathways between them and other brain regions, such as ipsilateral connections between the cerebellum and olive, or between the olive and brainstem.

References: [1] Kim SG et al. Science. 1994. 265:949-951, [2] Dum RP, Strick PL. J. Neurophysiol. 2003. 89:634-639, [3] Stilling B. 1864. Untersuchungen über den Bau des kleinen Gehirns des Menschen. Kassel. Teune, T.M., 1999, [4] Wallesch CW, Bartels C. Inherited cerebellar diseases. In: The cerebellum and cognition (Schmahmann, ed). Int Rev Neurobiol, Academic Press, 1997. [5] Christensen JA et al. J. Phys. Chem. 1974;78:1971-1977, [6] Deoni SCL. submitted 2007 ISMRM, abstract #306.