Diffusion Tensor Imaging Enables Robust Mapping of the Deep Cerebellar Nuclei

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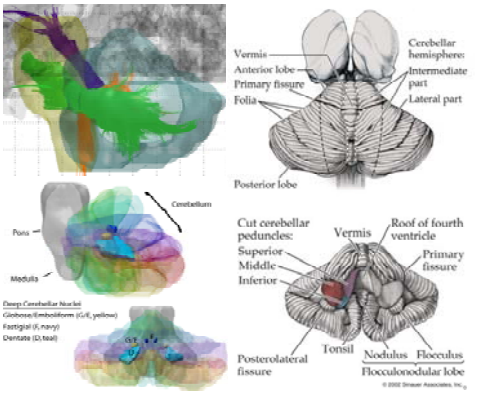
INTRODUCTION

- Deep cerebellar nuclei (DCN) are intimately involved in motor control, balance, and spatial processing, and are sensitive targets of neurodegenerative disease.
- Recent progress in structural and probabilistic assessment has enabled DCN identification[1,2].
- Yet, robust definition of nuclear boundaries and even identification in heterogeneous populations has remained elusive, in part due to highly variable T2, especially in the dentate (e.g., given age and/or pathological iron accumulation)[3].
- Quantitative assessment of DCN could be invaluable to diagnosis, staging, and prognosis in neurodegenerative diseases with cerebellar involvement.
- Diffusion tensor imaging (DTI) investigations of white matter integrity and connectivity have been applied across clinical and aging populations[4,5].
- However, general DTI analyses of gray matter nuclei have been hindered by low signal and contrast.

This study characterizes the DCN using DTI colormaps based on well defined contrast of white matter tracts that encompass the nuclei

GROSS CEREBELLAR ANATOMY

- The cerebellum (top left, light blue) lies in the inferior posterior quadrant of the head beneath the temporal and occipital lobes (top left, gray).
- The spatial relationships of the major white matter tracts (lower left: SCP: purple, MCP: green, ICP: orange) and deep cerebellar nuclei (lower left) are shown.
- The cerebellar surface is composed of highly convoluted folia and divided into hemispheres (right).

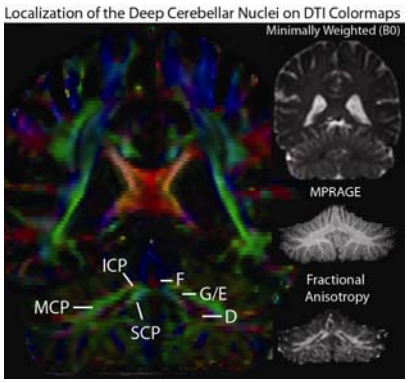


Methods

- A multi-slice, single-shot EPI sequence achieved whole brain coverage (2.2 mm isotropic nominal resolution) in 18 patients (11M/7F) with idiopathic isolated cerebellar disease and 19 controls (6M/13F). Each sequence utilized 32 diffusion encoding directions and five, averaged minimally weighted (b0) volumes with a 3T MR scanner (Intera, Philips Medical Systems, The Netherlands). Fiber tracking of peduncles was performed with DTIStudio (Susumu Mori, Baltimore, Maryland).
- Delineations of the dentate, fastigial, and globose/emboliform nuclei were performed on representative subjects with colormap and b0 (T2-weighted) volumes with MIPAV (NIH, Bethesda, Maryland). Globose and emboliform nuclei could not be individually distinguished, so they were combined into "interposed" nuclei. Accuracy of volume placement was assessed by an expert neurologist with reference to histological and structural MRI sections.
- Bilateral dentate nuclei were manually delineated for all subjects while blind to subject group. Normalized b0 intensities (T2w) and dentate volumes were compared across groups in a general linear framework controlling for age and sex.

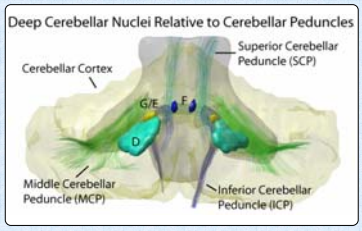
DELINEATION OF THE DEEP CEREBELLAR NUCLEI

- The dentate (**D**) lies medial to the middle cerebellar peduncle (**MCP**) and inferior-lateral to the superior cerebellar peduncle (**SCP**). Typically, the inferior aspect of the dentate is bounded by transverse fibers.
- The globse/emboliform (**G/E**) (interposed) nuclei were found superior-medial to the **D** and lateral-posterior to the **SCP**.
- The fastigial nuclei (**F**) were identified lateral to the superior cerebellar commissure (red), posterior to the fourth ventricle, and medial to the inferior cerebellar peduncle (**ICP**) and **SCP**.
- The nuclei are more clearly visualized on DTI colormaps than on MPRAGE, T2w (b0), or FA contrasts (right).

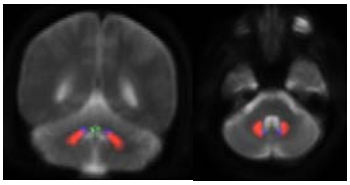


RESULTS

- DTI colormaps enabled identification of DCN on controls and patients despite varying degrees of atrophy and functional deficit.
- Contrast on colormap volumes was superior to T2w(b0) and MPRAGE(T1w).
- Identified regions visually corresponded to nuclei observed on structural images (in the cases when the DCN were visible on structural volumes).
- Placement of the DCN agrees with published MR and histological references both in terms of size and shape relative to the cerebellar anatomy.
- Comparison of the DCN with the cerebellar peduncles reveals that the DCN lie between major tracts, as expected from histology. The areas of reduced anisotropy may be safely interpreted as gray matter as opposed to fiber crossings.



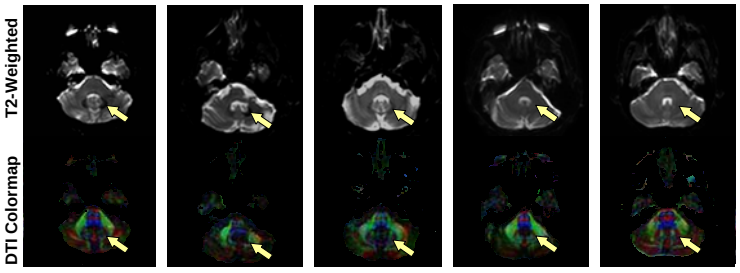
Mean Cerebellar Nuclei Position with Affine Registration (50 subjects)



Dentate (red), globose/emboliform (blue), and fastigial (green).

Dentate Nucleus Visualized on T2w and DT MRI

The dentate is more consistently seen on DTI colormaps than on T2w (b0) images.



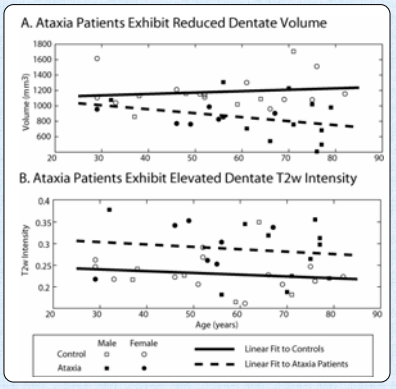
DTI provides contrasts that enable robust identification of DCN and reveal clinically relevant differences in dentate characteristics.

DENTATE CHANGES IN ATAXIA

Ataxia patients exhibited significantly:

- **Decreased dentate volume (p<0.01)**
- **Elevated T2w (p<0.01)**

- Decreased dentate volume is agreement with atrophy typically presenting in cerebellar disease.
- Increased in T2w contrast suggests iron deposition.
- Variable nuclei volumes reduce the precision of probabilistic methods, while variable T2's reduce the reliability of delineation based on T2w contrasts.



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