Diffusion Tensor Imaging Enables Robust Mapping of the Deep Cerebellar Nuclei

Bennett A. Landman [a], Annie X. Du [b], Wade D. Mayes [c], Jerry L. Prince [a, c, d], Sarah H. Ying [d, e]

[a] Department of Biomedical Engineering, The Johns Hopkins University School of Medicine, Baltimore, MD, USA
[b] Department of Neurology, The Johns Hopkins University School of Medicine, Baltimore, MD, USA
[c] Department of Electrical and Computer Engineering, Johns Hopkins University, Baltimore, MD, USA
[d] The Russell H. Morgan Department of Radiology and Radiological Sciences, The Johns Hopkins University School of Medicine, Baltimore, MD, USA
[e] Department of Ophthalmology, The Johns Hopkins University School of Medicine, Baltimore, MD, USA

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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]. Yet, general DTI analyses of gray matter nuclei have been hindered by low signal and contrast. In this study, we characterize the DCN using DTI colormaps based on well defined contrast of white matter tracts that encompass the nuclei. We investigate the sensitivity of these DTI derived observations to differences in dentate gray matter between ataxia patients and controls.

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 (**Fig.1**)[6].

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.

Results and Discussion

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)(**Fig.1**). Identified regions visually corresponded to nuclei observed on structural images (when the nuclei were visible on structural volumes). Placement of the DCN agrees with published references both in terms of size and shape relative to the cerebellar anatomy(**Fig.2**). Comparison of the DCN with the cerebellar peduncles reveals that the DCN lie between major tracts, as expected from histology(**Fig.3**), so the areas of reduced anisotropy may be safely interpreted as gray matter rather than fiber crossings.

Ataxia patients exhibited significant decreased dentate volume(p<0.01) and elevated T2w(p<.01)(**Fig.4**). Decreased dentate volume is agreement with atrophy typically presenting in cerebellar disease, and 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. DTI provides contrasts that enable robust identification of DCN and reveal clinically relevant differences in dentate characteristics.

References[1]Dimitrova,A.,et.al.(2002)Neuroimage.17(1):240[2]Dimitrova,A.,et.al.(2006)Neuroimage.30(1):12[3]Maschke,M.,et.al.(2004)J.Neurol.251(6):740[4]Basser,P.J.,et.al.(2002)NMR.Biomed.15(7-8),456[5]Nagae-Poetscher,L.M.,et.al.(2004)AJNR.25(8):1325[6]Duvernoy,H.M.(1995)Springer
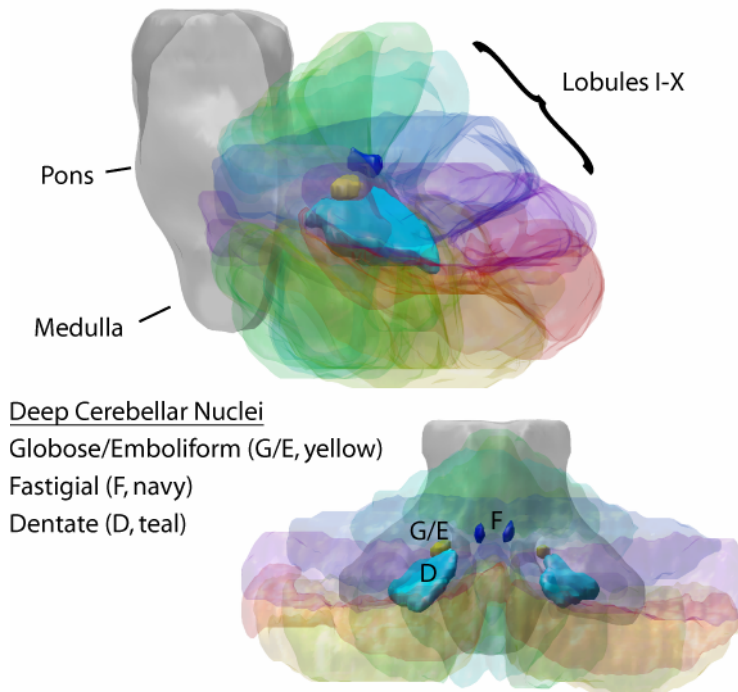
Figure 1

Localization of the Deep Cerebellar Nuclei on DTI Colormaps
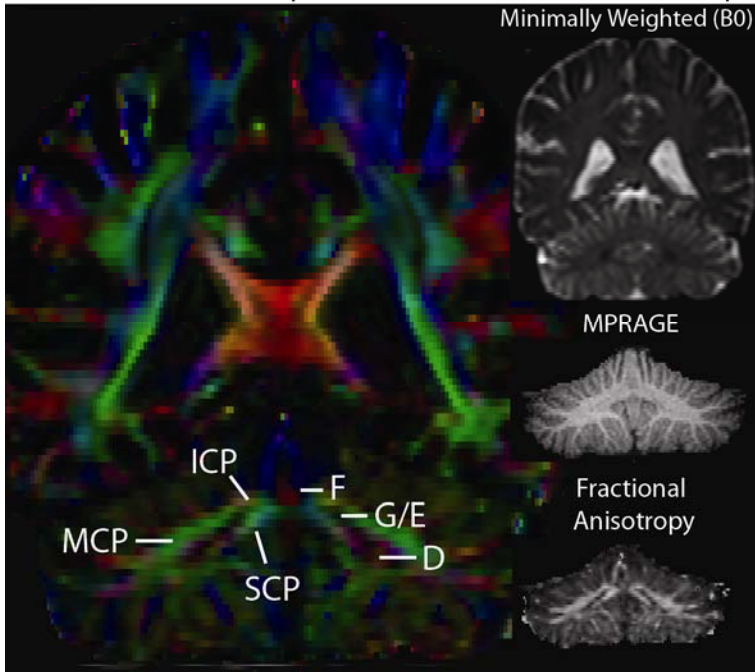

Figure 2

Deep Cerebellar Nuclei Relative to Cerebellar Lobules

Deep Cerebellar Nuclei
Globose/Emboliform (G/E, yellow)
Fastigial (F, navy)
Dentate (D, teal)

Figure 3

Deep Cerebellar Nuclei Relative to Cerebellar Peduncles

Superior Cerebellar Peduncle (SCP)

Cerebellar Cortex

G/E   F

D

Middle Cerebellar Peduncle (MCP)

Inferior Cerebellar Peduncle (ICP)
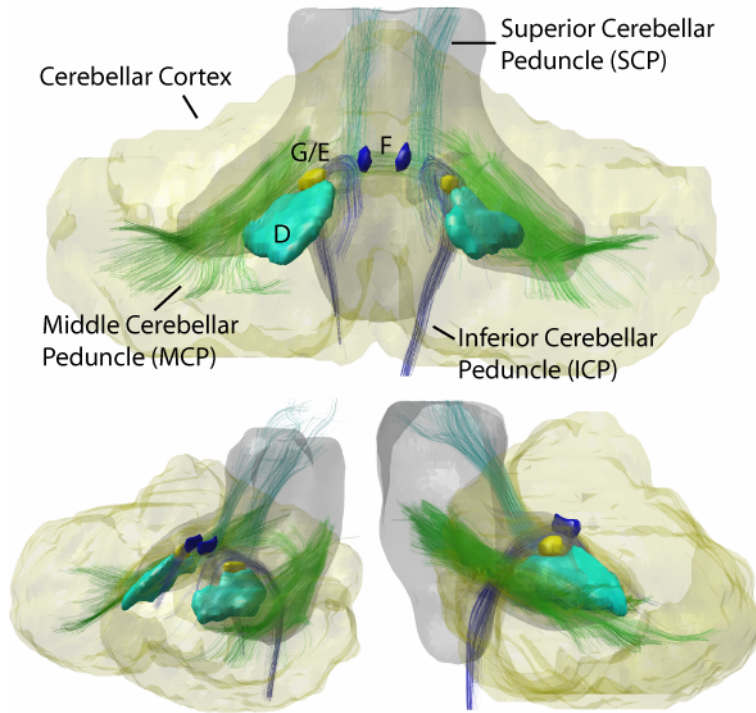
Figure 4

A. Ataxia Patients Exhibit Reduced Dentate Volume

Volume (mm3)
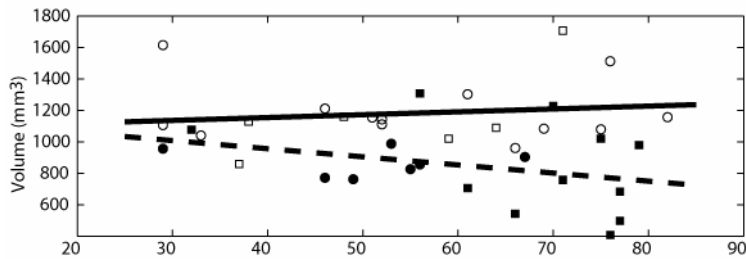
B. Ataxia Patients Exhibit Elevated Dentate T2w Intensity

T2w Intensity

Age (years)
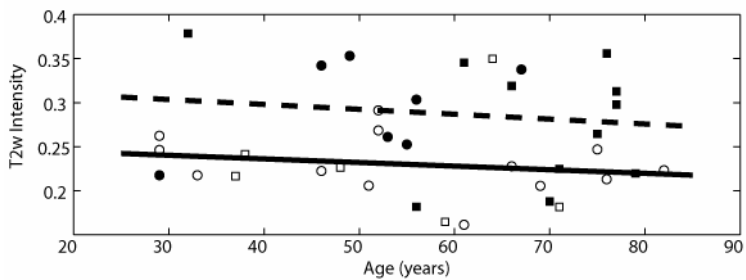
	Male	Female		
Control	□	○	——	Linear Fit to Controls
Ataxia	■	●	– –	Linear Fit to Ataxia Patients