# Quantitative Analyses of Dentate Nuclei and Cerebellar Peduncles Based on DTI in Langerhans Cell Histiocytosis

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## Introduction:

Langerhans cell histiocytosis (LCH) is a rare disorder characterized by the clonal proliferation of immature Langerhans cells that has a variable clinical course[1-2]. Neurologic complications commonly involve the hypothalamic-pituitary axis, parenchymal mass lesions and a neurodegenerative disorder believed to be paraneoplastic in etiology. The neurodegenerative syndrome usually presents with cerebellar peduncle involvement and signs of cerebellar ataxia. Despite increasing understanding of disease, the pathophysiology of LCH remains enigmatic[2], MR abnormalities include absence of posterior pituitary bright spot in T1WI, but diagnosis is difficult because of lack of specific and sensitive imaging markers. In this study, four patients diagnosed with LCH were scanned by routine MRI and diffusion tensor imaging (DTI). The dentate nuclei (DN: deep cerebellar nuclei) of all 4 patients had substantial atrophy on conventional MRI. To confirm our findings, we measured the volume of DN and 3 cerebellar white matter tracts: superior (SCP) , middle (MCP), and inferior cerebellar peduncle (ICP), and compared with age- matched controls.

## Methods:

*MRI:* 4 patients (19-56 years; mean 45±17.5) and 6 age-matched controls (19-58 years; mean 46.3 +/-14.1) were scanned using a 1.5T Philips MRI scanner. MRI included DTI, T2 weighted image, FLAIR, and MPRAGE . For the DTI acquisitions, SS-EPI with SENSE (r = 2.5) was used, with diffusion gradients applied in 30 non-collinear directions. Imaging parameters: FOV=240mm, slice thickness/gap=2.5 mm/0.0 mm, acquisition matrix=96*96, reconstruction matrix=256*256, TR>4s, TE=80 ms, b-value=700s/mm$^2$.

*Data processing*: The AIR program was used to correct for motion. DTI was processed using DtiStudio (Johns Hopkins University, H. Jiang and S. Mori). Fractional anisotropy (FA), vector maps, color-coded maps, average diffusion-weighted images and b0 maps were generated. Fiber tracking was used with a fractional anisotropy threshold 0.2 and an inner product threshold of 0.75.

*Measurement:* Dentate nuclei were delineated using T2, average diffusion-weighted image, and color-map in controls. The SCP, MCP, and ICP were reconstructed using two-ROIs approach[3-5]. After reconstruction, the number of pixels (tract volume), FA and normalized T2 intensity were quantified.

## Results:

In Fig. 1, T2, average DWI, and color maps of a control and a LCH patient are shown, DN could be easily identified in all three image types in control subjects. In LCH patients, DN was difficult to identify on T2. Therefore, average DWI and color maps were used for volume measurements (Fig. 2). Significant volume loss was found for the DN ($t$= -3.8 ~ -4.3, $P$<0.006) and the SCP ($t$= -4.7 ~ -7.2, $P$<0.001). No significant difference was observed for the sizes of ICP and MCP. FA and normalized T2 intensity were not different between the two groups, except for the FA and T2 intensity of SCP ($t$= -2.6 ~ -4.6, $P$<0.033; $t$=3.3~3.6, $P$<0.011).

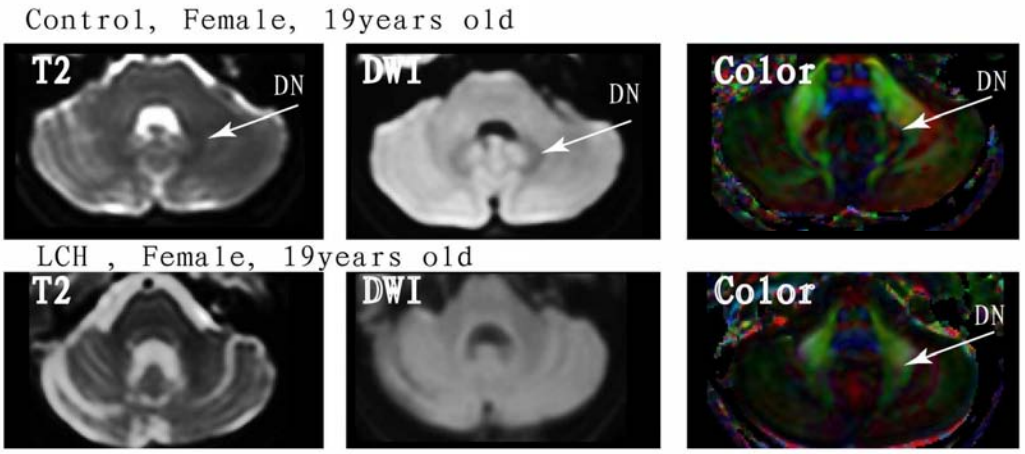


**Fig. 1** T2-weighted, average diffusion weighted, and color maps of a control and a LCH patient. DN was supposed to mixed red color between the green colors of the cerebellar peduncles in colormap.

## Discussion:

The dentate nuclei and SCP in the patients with LCH we studied are significantly smaller than in normals. It is known that all outputs of the cerebellum are relayed by the DN and vestibular nuclei, and the SCP is the efferent tract of the DN. So these findings implicate these structures as a potential source of the clinical cerebellar dysfunction in four patients. The DN is most clearly identified in the color maps both in control subjects and patients due to its characteristic fiber structure, making an effective tool to measure its volume. At this point, the mechanism of the atrophy is not clear and further investigation is needed to characterize the prevalence of this finding in the LCH population. Our preliminary study in 4 patients with LCH confirm that the both DN and SCP are two of the primary target organs of this disease and that DTI may be a sensitive imaging approach to quantify this abnormality. DTI imaging of additional patients at different stages of their disease and correlation with clinical manifestations and outcomes should be pursued.

**References:**

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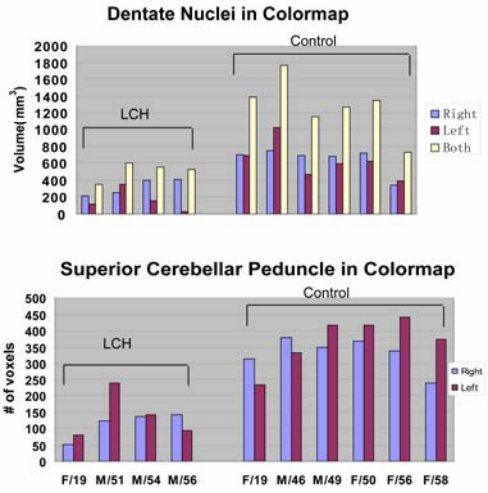


**Fig. 2** Volume measurement results of the DN and the SCP