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The role of dentate nuclei in human oculomotor control: insights from cerebrotendinous xanthomatosis

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Key points

- A cerebellar dentate nuclei (DN) contribution to volitional oculomotor control has recently been hypothesized but not fully understood.
- Cerebrotendinous xanthomatosis (CTX) is a rare neurometabolic disease typically characterized by DN damage.
- In this study, we compared the ocular movement characteristics of two sets of CTX patients, with and without brain MRI evidence of DN involvement, with a set of healthy subjects.
- Our results suggest that DN participate in voluntary behaviour, such as the execution of antisaccades, and moreover are involved in controlling the precision of the ocular movement.
- The saccadic abnormalities related to DN involvement were independent of global and regional brain atrophy.
- Our study confirms the relevant role of DN in voluntary aspects of oculomotion and delineates specific saccadic abnormalities that could be used to detect the involvement of DN in other cerebellar disorders.

Abstract It is well known that the medial cerebellum controls saccadic speed and accuracy. In contrast, the role of the lateral cerebellum (cerebellar hemispheres and dentate nuclei, DN) is less well understood. Cerebrotendinous xanthomatosis (CTX) is a lipid storage disorder due to mutations in *CYP27A1*, typically characterized by DN damage. CTX thus provides a unique opportunity to study DN in human oculomotor control. We analysed horizontal and vertical visually guided saccades and horizontal antisaccades of 19 CTX patients. Results were related to the presence/absence of DN involvement and compared with those of healthy subjects. To evaluate the contribution of other areas, abnormal saccadic parameters were compared with global and regional brain volumes. CTX patients executed normally accurate saccades with normal main sequence relationships, indicating that the brainstem and medial cerebellar structures were functionally spared. Patients with CTX executed more frequent multistep saccades and directional errors during the antisaccade task than controls. CTX patients with DN damage showed less precise saccades with longer latencies, and more frequent directional errors, usually not followed by corrections, than either controls or patients without DN involvement. These saccadic abnormalities related to DN involvement but were independent of global and regional brain atrophy. We hypothesize that two different cerebellar networks contribute to the metrics of

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