# Volumetry of the cerebellum and its subregions in genetic frontotemporal dementia

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## Background

Frontotemporal dementia (FTD) is a neurodegenerative disorder normally presenting with cognitive and neuropsychiatric features. About 20% of people with FTD have a mutation in one of three genes: *MAPT*, *GRN* and *C9orf72*. The cerebellum is involved in sensorimotor coordination and learning, but has also been shown to take part in the processing of cognition and emotion. Its role in FTD remains unclear.

## Methods

We investigated the volumetry of cerebellar subregions in a sample of 15 genetic FTD patients (9 *MAPT* mutation carriers and 6 *C9orf72* expansion carriers) compared with 18 cognitively-normal controls, to determine whether specific cerebellar regions are associated with genetic mutations in bvFTD. All participants were scanned on a 3T Siemens Trio and matched for age, gender and education. We used an atlas propagation and label fusion strategy of the Diedrichsen cerebellar atlas to automatically extract 33 regions, including the cerebellar lobules, the vermis and the deep nuclei (Cardoso *et al.*, MICCAI 2012;15(Pt2):262–70; Diedrichsen *et al.*, NeuroImage 2009;46:39–46). Cerebellar lobules were classified into four regions, and volumes were corrected for total intracranial volumes (**Figure**).

| | Controls (n=18) | FTD-*MAPT* (n=9) | FTD-*C9orf72* (n=6) |
|---|---|---|---|
| **Gender, male** | 9 (50%) | 7 (78%) | 5 (83%) |
| **Age at scan** | 56 (14) | 60 (9) | 65 (7) |
| **Disease duration** | -- | 8 (6) | 11 (4) |
| **Age at onset** | -- | 51 (6) | 54 (10) |
| **Education** | 14 (3) | 14 (5) | 13 (4) |
| **MMSE** | 29.2 (1.2) | 25.8 (5.0) | 24.0 (4.0) |
| **CBI-R Total** | -- | 76.4 (36.9) | 78.7 (33.4) |

***Table 1. Demographic, clinical and behavioural variables for the bvFTD patients and controls.*** *Values denote mean (standard deviation) or n (%).*

## Results

Subjects' characteristics are summarized in **Table 1.** When compared with controls, *C9orf72* carriers showed a 10% reduction in the whole cerebellar volume (p=0.009, Mann-Whitney U test), mainly located in the superior-posterior portion and specifically in the crus I bilaterally and in the left lobule VI (-18% p=0.027 and -10% p=0.047, respectively). The vermis and the interposed nuclei were also atrophic (-11% p=0.033 and -15% p=0.012, respectively). *MAPT* carriers compared with controls showed a significant reduction in the vermis IX and in the lobule IX bilaterally (-13% p=0.015 and -17% p=0.005, respectively). Comparing FTD subgroups, *C9orf72* carriers showed lower volumes in the crus I bilaterally and in the superior-posterior portion in general, when compared with *MAPT* carriers (-19% p<0.05 and -14% p=0.012) (**Table 2**).

| Comparison | Structure involved | Function |
|---|---|---|
| **FTD-*C9orf72* vs controls** | whole cerebellum (superior-posterior), specifically crus I and left lobule VI | cognition |
| | vermis | Sensorimotor, autonomic/emotional |
| | interposed nuclei and left dentate nucleus | connections to cerebral cortex |
| **FTD-*MAPT* vs controls** | vermis IX | autonomic/emotional |
| | lobule IX | oculomotor , balance, posture |
| **FTD-*C9orf72* vs FTD-MAPT** | superior-posterior, specifically crus I | cognition |

***Table 2. Summary of differences in the volumetry of the cerebellum and its parcellation.***

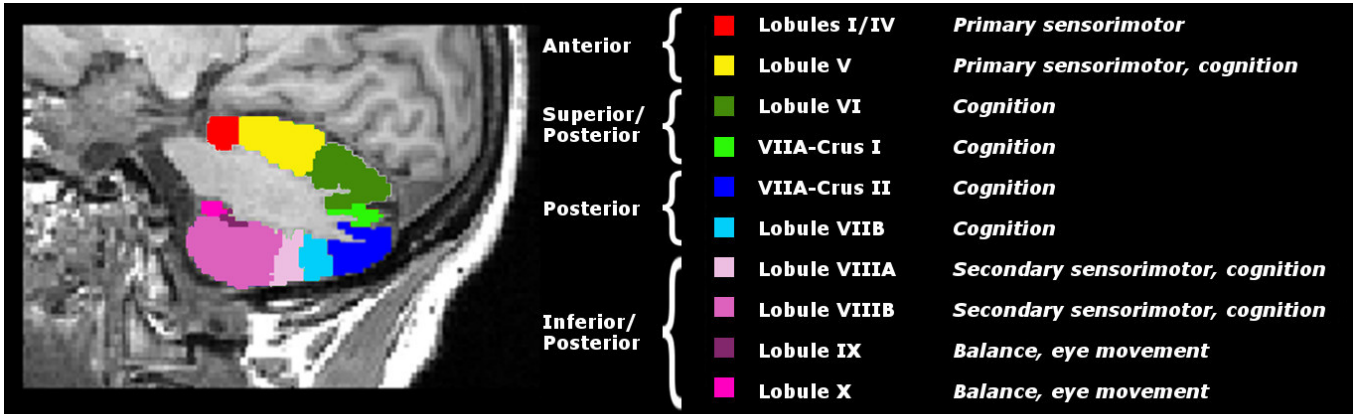


***Figure. Segmentation of the cerebellar lobules (left side) mapped on a 3T T1-weighted MR image of a control subject.*** *Classification was made according to Bogovic et al., NeuroImage 2013;64:616–629 and Pierson et al., NeuroImage 2002;17:61–76. Cerebellar functions were based on Makris et al. Journal of Cognitive Neuroscience 2003;15(4):584–599.*

## Conclusions

*C9orf72* FTD patients showed atrophy in the crus I region which seems to be functionally connected via the thalamus to the dorsolateral prefrontal cortex and involved in cognitive function. Atrophy in *MAPT* carriers was found in cerebellar regions related to the regulation of balance, posture and eye movements, and its relevance remains unclear.

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