Volumetry of the cerebellum and its subregions in genetic frontotemporal dementia

Martina Bocchetta[1,2,3], M. Jorge Cardoso[1], David M. Cash[1], Martin N. Rossor[1], Giovanni B. Frisoni[2,4], Sebastien Ourselin[1], Jonathan D. Rohrer[1]

[1]University College London, UK; [2]Laboratory of Epidemiology, Neuroimaging and Telemedicine, IRCCS Istituto Centro San Giovanni di Dio - Fatebenefratelli Brescia, IT; [3]University of Brescia, IT; [4]Memory Clinic and Laboratory of Neuroimaging of Aging, University Hospitals and University of Geneva, CH.

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 sensory-motor 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, sex 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).

Results

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).

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.