CEREBELLAR FUNCTIONAL CONNECTIVITY IN PATIENTS WITH PEDIATRIC MULTIPLE SCLEROSIS

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Target Audience

Researchers and clinicians in Neurology and Neuroradiology; cognitive Neuroscientists.

Purpose

We explored abnormalities of resting state (RS) functional connectivity (FC) of the dentate nuclei (DN) of the cerebellum in patients with pediatric multiple sclerosis (MS) and healthy controls (HC) and whether they correlate with clinical (disability, disease duration) and MRI measures of structural brain damage (T2 lesion volume and brain atrophy).

Methods

We studied 48 consecutively recruited right-handed pediatric patients with relapsing-remitting (RR) MS (mean age=14.9, range=8.1-18, median Expanded Disability Status Scale=1.5, mean disease duration=1.7 years) and 27 gender- and age-matched HC (mean age=15.2, range=8.5-18). Using a 3 Tesla scanner (Intera, Philips), the following sequences of the brain were acquired from all subjects: a) dual-echo turbo spin echo; b) 3D T1-weighted fast field echo; c) T2*-weighted single-shot echo planar imaging for RS fMRI (TR 3000 ms, TE 35 ms, FOV 240x240 mm; slice thickness 4 mm; 200 sets of 30 contiguous axial slices). FC analysis was performed by computing the cross-correlation between left (L) and right (R) DN (derived from the Automatic Anatomical Labeling atlas) and any other area of the brain. T2 lesion volume (LV) and brain parenchymal fraction (BPF) were also measured. With a non-parametric test we compared demographic and conventional MRI measures between MS patients and HC. Within- and between-group comparison of RS FC, adjusted for age and sex, were performed with SPM8. Correlations of RS FC *vs* clinical and conventional MRI variables were performed with SPM8 and multiple regression models.

Results

In both groups, RS FC of the R DN was significantly correlated with the FC in other portions of the cerebellum, bilateral posterior, middle and anterior cingulate cortices, basal ganglia, bilateral precuneus, bilateral dorsolateral prefrontal cortex and several regions in the parietal and temporal lobes (Fig.1). Similar results were found when analyzing RS FC of the L DN. Compared with controls (Fig.2), pediatric MS patients had a reduced RS FC between the R DN and the bilateral caudate nuclei (a), R parahippocampal gyrus (BA36), L parahippocampal gyrus (BA37) (b), R inferior temporal gyrus (BA20); as well as an increased RS FC with the bilateral precentral gyrus (BA48) (c). Similar results were found when analyzing between group differences of RS FC of the L DN. Longer disease duration correlated with reduced R DN RS FC with the left caudate nucleus (*r=-0.37, p=0.004*) and right hippocampus (*r=-0.37, p=0.005*). Higher T2 LV correlated with reduced R DN RS FC with the left thalamus (*r =-0.36, p=0.007*). No correlation was found between R DN FC *vs* EDSS score and BPF.

Discussion

We found that in both groups the DN is significantly connected with areas involved in sensorimotor control (e.g., basal ganglia, thalamus, primary somatosensory area), high-order functions (e.g., dorsolateral prefrontal cortex) and emotional processing (e.g., cingulum). This finding is consistent with recent studies[1] of functional network connectivity analysis of DN in HC, pointing out the preferential involvement of this nucleus in sensorimotor, emotional and cognitive functions, rather than in motor activity.

Fig. 1. *Significant within-group RS FC between the R DN and all other brain regions in HC and RRMS patients (p<0.001 uncorrected).*

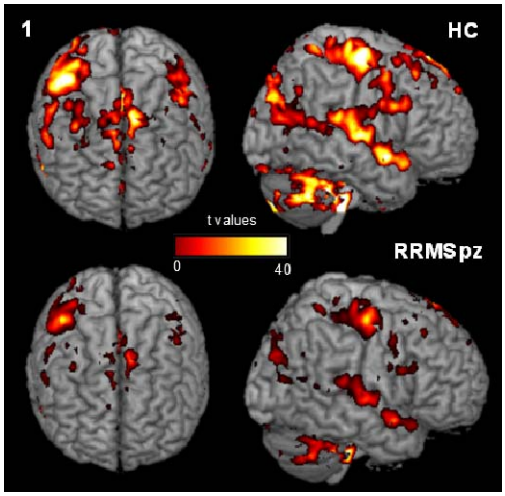
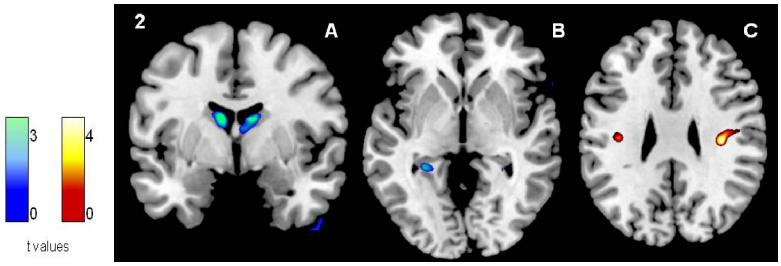


Fig. 2. *Between-groups differences of RS FC of the R DN (p<0.001 uncorrected).*



Conclusion

Pediatric MS patients experience a distributed pattern of reduced RS FC of the DN of the cerebellum, which is influenced by disease duration and accumulation of focal white matter lesions.

References

1. *Habas C. Functional imaging of the deep cerebellar nuclei: a review. Cerebellum. 2010 Mar;9(1):22-8.*

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