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Leveraging Multimodal Neuroimaging Techniques to in vivo Address Compensatory and Disintegration Patterns in Neurodegenerative Disorders: Evidence from Cortico-Cerebellar Connections in Multiple Sclerosis

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Abstract : Introduction: Advanced structural and functional neuroimaging techniques contribute to the study of anatomical and functional brain connectivity and its role in the pathophysiology and symptoms' heterogeneity in several neurodegenerative disorders, including multiple sclerosis (MS). Aim: In the present study, we applied multiparametric neuroimaging techniques to investigate the structural and functional cortico-cerebellar changes in MS patients. Material: We included 51 MS patients (28 with clinically isolated syndrome [CIS], 31 with relapsing-remitting MS [RRMS]) and 51 age- and gender-matched healthy controls (HC) who underwent MRI in a 3.0T MRI scanner. Methodology: The acquisition protocol included high-resolution 3D T1 weighted, diffusion-weighted imaging and echo planar imaging sequences for the analysis of volumetric, tractography and functional resting state data, respectively. We performed between-group comparisons (CIS, RRMS, HC) using CAT12 and CONN16 MATLAB toolboxes for the analysis of volumetric (cerebellar gray matter density) and functional (cortico-cerebellar resting-state functional connectivity) data, respectively. Brainance suite was used for the analysis of tractography data (cortico-cerebellar white matter integrity; fractional anisotropy [FA]; axial and radial diffusivity [AD; RD]) to reconstruct the cerebellum tracts. Results: Patients with CIS did not show significant gray matter (GM) density differences compared with HC. However, they showed decreased FA and increased diffusivity measures in cortico-cerebellar tracts, and increased cortico-cerebellar functional connectivity. Patients with RRMS showed decreased GM density in cerebellar regions, decreased FA and increased diffusivity measures in cortico-cerebellar WM tracts, as well as a pattern of increased and mostly decreased functional cortico-cerebellar connectivity compared to HC. The comparison between CIS and RRMS patients revealed significant GM density difference, reduced FA and increased diffusivity measures in WM cortico-cerebellar tracts and increased/decreased functional connectivity. The identification of decreased WM integrity and increased functional cortico-cerebellar connectivity without GM changes in CIS and the pattern of decreased GM density decreased WM integrity and mostly decreased functional connectivity in RRMS patients emphasizes the role of compensatory mechanisms in early disease stages and the disintegration of structural and functional networks with disease progression. Conclusions: In conclusion, our study highlights the added value of multimodal neuroimaging techniques for the in vivo investigation of cortico-cerebellar brain changes in neurodegenerative disorders. An extension and future opportunity to leverage multimodal neuroimaging data inevitably remain the integration of such data in the recently-applied mathematical approaches of machine learning algorithms to more accurately classify and predict patients' disease course.

Keywords : advanced neuroimaging techniques, cerebellum, MRI, multiple sclerosis
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