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Structural and functional cerebellar changes in non-C9orf72 FTD patients

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Background: Cerebellum is known to play an important role in cognition and behavior. In frontotemporal dementia (FTD) cerebellar atrophy is frequently associated with C9orf72 gene mutation while the data on its structural and functional changes in other cases remains lacking. The aim of our study was to assess whether cerebellum atrophy and functional changes occur in FTD without C9orf72 mutation.

Methods: Thirty-six patients with FTD variants (64.5±7.8years, 13 males) and 17 healthy controls (58.2 ± 4.9 years, 5 males) were included in the study. Absence of C9orf72 pathological expansion was verified by repeat primed PCR. All participants underwent brain MRI and cognitive assessment. Voxel-based morphometry (VBM) and ROI-to-ROI connectivity (RRC) analyzes wereconducted in order to assess brain atrophy and functional connectivity (FC) changes. Multiple regression was used to evaluate relationship between clinical data and neuroimaging findings.

Results: VBM revealed a significant grey matter atrophy in cerebellar hemispheres bilaterally compared to controls. There was a positive correlation between left 9 lobule atrophy and disease duration. RRC showed multidirectional changes in FTD compared to controls. FC was reduced between cerebellum and thalami, caudate nuclei, superior temporal gyri; and was increased between cerebellum and nuclei accumbens, temporal poles. Significant correlations were found between cerebellar FC changes and disease severity, disinhibition and cognitive impairment.

Conclusion: Our findings demonstrate that prominent cerebellar grey matter and functional changes are characteristic of FTD even in the absence of C9orf72 mutation. Cerebellar dysfunction is associated with disease duration and severity and contributes to cognitive and neuropsychiatric dysfunction.

Conflicts of interest

Nothing to disclosure