

Adult-diagnosed 47, Xyy Polysomy Presenting As A BvFTD Phenocopy: A Multimodal MRI Case Study

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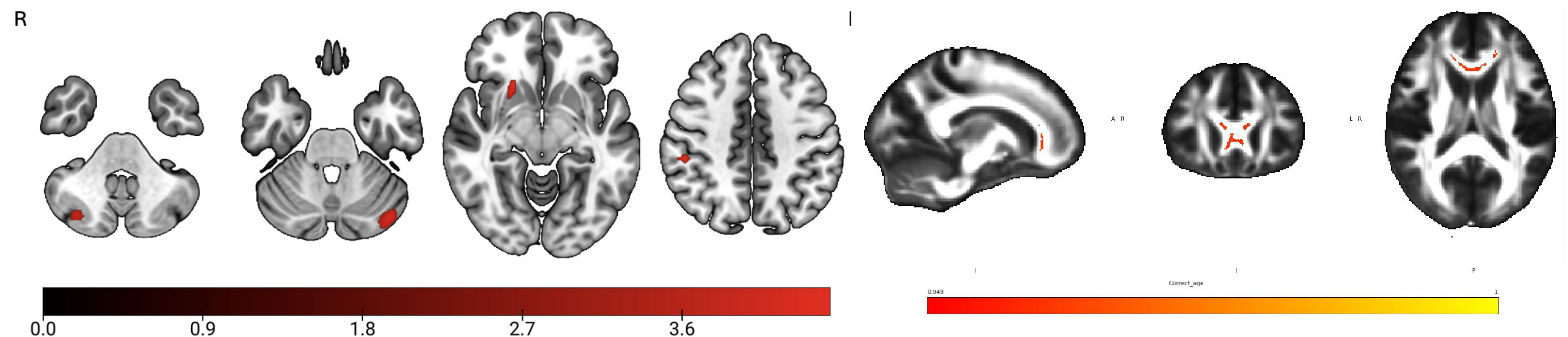
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Background: 47, XYY polysomy (Jacob's syndrome) is a sex chromosome aneuploidy typically diagnosed prenatally and associated with heterogeneous neuropsychiatric features, including impulsivity, emotional dysregulation, and social cognition deficits. Adult diagnosis is uncommon, and its potential overlap with neurodegenerative phenotypes remains poorly characterized. Whether 47, XYY polysomy can give rise to a bvFTD phenocopy-like presentation in adulthood remains unclear.

Results

Methods: We report the case of a 44-year-old male who developed persistent behavioral and personality changes following a traumatic brain injury, initially attributed to the acute event and later raising clinical suspicion of bvFTD. Longitudinal structural MRI showed no post-traumatic lesions and no evidence of progressive neurodegeneration over a five-year follow-up; FDG-PET was negative. Only after an extensive diagnostic workup, a previously unrecognized 47, XYY polysomy was identified. To better characterize the clinical phenotype, a comprehensive multimodal neuroimaging analysis was performed. For neuroimaging analyses, the 47, XYY subject was compared with 26 cognitively healthy controls (HC) and 9 patients with bvFTD. Grey matter (GM) volume was assessed using voxel-based morphometry, and white matter (WM) microstructural integrity was evaluated using tract-based spatial statistics (fractional anisotropy).

Compared with HC, the 47, XYY subject showed **reduced GM volume in the right supramarginal gyrus, right putamen, and bilateral cerebellum. WM analyses revealed a selective disruption of anterior corpus callosum and forceps** in the 47, XYY subject when compared to HC.



Conclusion

This case illustrates a bvFTD phenocopy-like presentation associated with adult-diagnosed 47, XYY polysomy, characterized by selective cortical and subcortical GM alterations in regions implicated in cognitive control, social cognition, and theory of mind, without evidence of neurodegenerative disease. These findings highlight the importance of considering sex chromosome aneuploidies in the differential diagnosis of bvFTD-like syndromes and underscore the value of multimodal neuroimaging to distinguish neurodevelopmental conditions from neurodegenerative disorders.

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