Characterization of the FBXO7 (PARK15) protein

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Background

Mutations in the *F-box only protein 7* gene (*FBXO7*) cause PARK15, an autosomal recessive neurodegenerative disease presenting with severe levodopa-responsive parkinsonism and pyramidal disturbances. Understanding the pathogenesis of PARK15 might provide clues on the mechanisms of maintenance of brain dopaminergic neurons. The expression of the FBXO7 protein in the human brain remains poorly characterized, while its expression in idiopathic Parkinson's disease or different common neurodegenerative diseases was never explored.

Methods and tissues used

Our aim was to perform detailed biochemical and immunohistochemical studies of the pattern of the FBXO7 protein expression in human brain from normal controls and patients with Parkinson's disease and atypical degenerative parkinsonisms.

Results and conclusion

We studied FBXO7 protein expression in brain samples of normal controls (n = 9) and from patients with PD (n = 13), multiple system atrophy (MSA) (n = 5), Alzheimer disease (AD) (n = 5), and progressive supranuclear palsy (PSP) (n = 5) using immunohistochemistry with 2 anti-FBXO7 antibodies. We detected widespread brain FBXO7 immunoreactivity, with the highest levels in neurons of the cerebral cortex, putamen, and cerebellum. There were no major differences between normal and PD brains overall, but FBXO7 immunoreactivity was detected in large proportions of α-synuclein-positive inclusions (Lewy bodies, Lewy neurites, glial cytoplasmic inclusions), where it colocalized with α-synuclein in PD and MSA cases. By contrast, weak FBXO7 immunoreactivity was occasionally detected in tau-positive inclusions in AD and PSP. These findings suggest an important role for FBXO7 in the pathogenesis of the synucleinopathies.