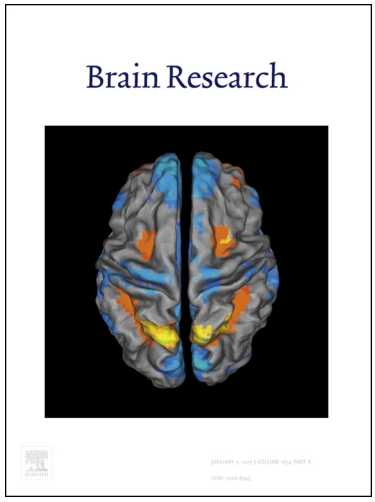

Research report

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Pleiotropic Neuropathological and Biochemical Alterations Associated with Myo5a Mutation in a Rat Model.

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Abstract

In this study, we analyze the neuropathological and biochemical alterations involved in the pathogenesis of a neurodegenerative/movement disorder during different developmental stages in juvenile rats with a mutant *Myosin5a (Myo5a).* In *mutant* rats, a spontaneous autosomal recessive mutation characterized by the absence of *Myo5a* protein expression in the brain is associated with a syndrome of locomotor dysfunction, altered coat color, and neuroendocrine abnormalities. *Myo5a* encodes a myosin motor protein required for transport and proper distribution of subcellular organelles in somatodendritic processes in neurons. Here we report marked hyperphosphorylation of alpha-synuclein and tau, as well as region-specific buildup of the autotoxic dopamine metabolite, 3,4-dihydroxyphenyl-acetaldehyde (DOPAL), related to decreased aldehyde dehydrogenases activity and neurodegeneration in *mutant* rats. Alpha-synuclein accumulation in mitochondria of dopaminergic neurons is associated with impaired enzymatic respiratory complex I and IV activity. The behavioral and biochemical lesions progress after 15 days postnatal, and by 30-40 days the animals must be euthanized because of neurological impairment. Based on the obtained results, we propose a pleiotropic pathogenesis that links the *Myo5a* gene