Expanding the phenotypic spectrum associated with OPHN1 mutations: Report of 17 individuals with intellectual disability but no cerebellar hypoplasia

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Résumé en anglais	Mutations in the oligophrenin 1 gene (OPHN1) have been identified in patients with X-linked intellectual disability (XLID) associated with cerebellar hypoplasia and ventriculomegaly, suggesting it could be a recognizable syndromic intellectual disability (ID). Affected individuals share additional clinical features including speech delay, seizures, strabismus, behavioral difficulties, and slight facial dysmorphism. OPHN1 is located in Xq12 and encodes a Rho-GTPase-activating protein involved in the regulation of the G-protein cycle. Rho protein members play an important role in dendritic growth and in plasticity of excitatory synapses. Here we report on 17 individuals from four unrelated families affected by mild to severe intellectual disability due to OPHN1 mutations without cerebellar anomaly on brain MRI. We describe clinical, genetic and neuroimaging data of affected patients. Among the identified OPHN1 mutations, we report for the first time a missense mutation occurring in a mosaic state. We discuss the intrafamilial clinical variability of the disease and compare our patients with those previously reported. We emphasize the power of next generation techniques (X-exome sequencing, whole-exome sequencing and targeted multi-gene panel) to expand the phenotypic and mutational spectrum of OPHN1-related ID.

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