

Behavioral analysis of GDI1 knockout mice

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GDI1 is one of the genes responsible for non-specific X-linked mental retardation. GDI1 encodes GDI, a protein highly expressed in brain, and the major role should be to bind to and retrieve the GDP-bound forms of Rab3A and Rab3C, the Rab proteins highly enriched in the synapses, involved in synaptic vesicle fusion and neurotransmitter release. GDI1 is expressed and upregulated during mouse brain development in the postmitotic cell layers suggesting that it may also play a role in neuron differentiation and/or migration through its interaction with different Rab proteins. To understand the mechanisms leading to mental retardation, we have generated a mouse knockout (KO) for GDI1. GDI KO males were generated, in the F2 generation, in two different backgrounds: B6D2/F1 and C57/B16. KO mice were viable and fertile and exhibited no obvious phenotype. To investigate the role of GDI1 in learning and memory events, Gdi1 KO mice have been subjected to behavioral tests. Depending on the genetic background learning impairment was observed in the Morris Water Maze test. The observed differences were not due to a deficit in spatial memory but rather to a reduced behavioral flexibility and insufficient adaptation to the test situation. The lower performance of GDI KO mice in the Morris Water Maze Test suggested a less efficient strategy in solving tasks. Accordingly, differences were found between wild type and KO mice in conditioning tests (conditioned taste aversion and two-way avoidance tests), confirming a behavioral difference between the two genotypes.

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