Tracking the roots of human mental retardation: cognitive impairments in Gdi1 knockout mice are associated with anomalous synaptic vesicles

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X-linked non-specific mental retardation (XLMR) is a common human disorder characterized by mental handicap as the only clinical symptom. Among the recently identified genes is GDI1, which encodes alpha-Gdi, one of the proteins controlling the activity of the small GTPases of the Rab family, in vesicle fusion and intracellular trafficking. To gain insights into the specific role of GDI1 in MR, we generated a . A detailed study of learning and behavior in a mouse mutant deficient in Gdi1 revealed cognitive impairments chiefly in two tests: the eight arm radial maze and trace fear conditioning, both depending partially on intact short term memory.
The deficit in trace fear conditioning disappeared when the mice were subjected to training sessions with long intertrial intervals (spaced training sessions). We then investigated synaptic morphology in somatosensory cortex, hippocampus and amygdala. This revealed visible anomalies: Gdi1 knockout mice showed much less synaptic vesicles that were moreover lumped at the synaptic cleft.
These data suggest that one main factor in mental retardation is the inability of rapid recycling of vesicles.

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