GM1 GANGLIOSIDE DEFICIENT MOUSE AS MODEL OF PARKINSON'S DISEASE

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Introduction: GM1 ganglioside plays important roles in stabilizing neuronal functions. GM1 treatment has been reported as beneficial to PD patients and animal models of PD. LIGA-20, a membrane permeable derivative of GM1, was even more effective in animals. To further identify GM1 role in PD development, we examined PD-like symptoms in GM2/GD2 synthase knockout (KO) (GalNAcT⁻/⁻) and heterozygous (HT) (GalNAcT⁺/-) mice.

Methods: Movement impairment was determined with rod-hanging and adhesive removal tests. Rescue was attempted with IP injection of L-dopa, GM1, and LIGA-20. Dopaminergic (DA) neuron loss in SNpc was determined with unbiased stereology. α-Synuclein (aSyn) accumulation was assayed by immunostaining and immunoblot. GM1 was determined in brain sections from these mice and from sporadic PD patients by immunostaining with cholera toxin B subunit (CtxB) linked to FITC.

Results: KO mice lacking GM1, as well as HT mice with reduced GM1, showed movement impairment in both tests that was reversed by L-dopa and LIGA-20 but not GM1. Stereology revealed specific loss of DA neurons of SNpc. Increased aSyn was diminished by LIGA-20. Significant reduction of GM1 was observed in SNpc DA neurons of 9/9 sporadic PD patients, similar to HT mice.

Conclusions: GM1 deficiency in DA neurons of SNpc induces PD symptoms in genetically altered mice and correlates with similar GM1 deficiency in such neurons of PD patients. HT mice, which show no other symptomatology, appear to provide an excellent PD model based on the actual pathophysiology of PD. Membrane permeability is essential for rescue: LIGA-20 vs GM1.