Gangliosides are acidic glycolipid compounds widely distributed in vertebrate tissues and fluids. They are present in mammalian milk, where they are almost exclusively associated with the membrane fraction of the fat globule. In human milk, the content and individual distribution of gangliosides changes during lactation, GD3 being the most abundant ganglioside in colostrum, while in mature milk, GM3 is the major ganglioside. Gangliosides are not only one major ionizable ganglioside receptors for bacterial adhesion in specific tissues. After oral administration, they can be putative decoys that interfere with pathogenic binding in the intestine, this being the main mechanism by which these compounds can prevent infection. Ganglioside-supplemented infant formula has been reported to modify the intestinal ecology of preterm newborns, increasing the Bifidobacteria content and lowering that of Escherichia coli. In addition, the influence of dietary gangliosides on several parameters related to the development of intestinal immune system, such as cytokine and intestinal IgA production, has also been observed in animal models. Recently, the influence of GM3 and GD3 on dendritic cell maturation and effector functions has also been reported, suggesting a role for these milk gangliosides, especially GD3, in modulating the process of oral tolerance during first stages of life. In summary, dietary gangliosides may have an important role in the modification of intestinal microflora and the promotion of intestinal immuno development in the neonate, and consequently in the prevention of infections during early infancy.

Schneider JS, Roeltgen DP, Manccall EL,Chopas-Crilly J, Rothblat DS, Tatarian GT.
Parkinson's disease: improved function with GM1 ganglioside treatment in a randomized placebo-controlled study.
Neurology. 1998 Jan;50(1):83-9. Published monthly following open label pilot study. BACKGROUND/OBJECTIVE: Studies in animal models of Parkinson's disease (PD) suggest that GM1 ganglioside treatment can restore neurologic and dopaminergic function. In view of positive preclinical findings and the results of a previous open-label open-study Parkinson's disease study (1995), the present study compared effects of GM1 ganglioside and placebo on motor functions in PD patients. METHODS: Fourty-five patients with mild to moderate PD were studied. The primary efficacy measure was change in the Unified Parkinson's Disease Rating Scale (UPDRS) motor score. At week 24, the early-start group had significant improvement in UPDRS motor scores vs. a significant worsening of scores in the delayed-start group. The early-start group also showed a sustained benefit vs. the delayed-start group at week 72 and at week 120. Both groups had significant symptom worsening during washout. This study provides evidence that GM1 use for 24weeks was superior to placebo for improving motor symptoms and that extended GM1 use (up to 120weeks) resulted in a lower than expected rate of symptom progression. The data from this small study suggest that GM1 may have symptomatic and potentially disease modifying effects on PD.

LIM ST, Esfahani K, Vodovshina V, Muthett J. Exogenous gangliosides increase the release of brain-derived neurotrophic factor.
Neuropsychology. 2011 Jun;60(3):1160-7. Published monthly following open label pilot study. BACKGROUND: Exogenous gangliosides has been shown to lead to neuronal plasticity. Experimental data have shown that exogenous gangliosides exhibit properties similar to the neurotrophins, a family of neurotrophic factors that are important in the survival and maintenance of neurons and prevention of neurodegenerative diseases. Brain-derived neurotrophic factor (BDNF) is the most abundant of the neurotrophins. This work was done to reveal the neurotrophic mechanism of exogenous gangliosides. In particular, we examined whether gangliosides promote the release of BDNF. Rat hippocampal neurons or human neuroblastoma cells were treated with gangliosides, which were then determined by Western blot analysis and a competitive enzyme immunoassay. The depolarizing agent KCl was used as a comparison. In hippocampal neurons, both GM1 ganglioside and KCl evoked within minutes the release of mature BDNF. In human cells, GM1 and other gangliosides released both mature BDNF and pro-BDNF. The effect of gangliosides was structure-dependent. In fact, GT1β preferentially released mature BDNF whereas GM1 released both mature and pro-BDNF. This work provides additional experimental evidence that exogenous gangliosides can be used to enhance the neurotrophic factor environment and promote neuronal survival in neurological diseases.

Park EJ, Suh M, Ramanjarum K, Steiner K, Powell D, Clandinin MT. Diet-induced changes in gangliosides in rat small mucosa and plasma.
Pediatr Gastroenterol Nutr. 2011 Apr;40(4):785-9. Published monthly following open label pilot study. OBJECTIVES: The objective of this study was to determine if dietary gangliosides induce changes in the ganglioside content of intestinal mucosa, plasma and brain and to identify where GM3 and GD3 are localized in the enterocyte membrane. METHODS: Male 18-day-old Sprague-Dawley rats were fed a semipurified diet containing 20% (w/w) fat. The control diet contained triglyceride, reflecting the fat formulation of an existing infant formula. Two experimental diets were formulated by adding sphingomyelin (1% w/w of total fat) or a ganglioside-enriched lipid (0.1% w/w of total fat) to the control diet fat. The ganglioside fraction of ganglioside-enriched lipid was isolated by ethanol precipitation. The ganglioside fraction was loaded into a membrane and internal content was measured in intestinal mucosa, plasma and brain. RESULTS: The ganglioside-enriched lipid diet significantly increased total ganglioside content in the intestinal mucosa plasma and brain compared with the control diet. The ganglioside-enriched lipid diet significantly increased the level of GM3 (75% w/w in the intestine compared with 3.2% w/w in the control) and GD3 in the ganglioside in the intestine. The ratio of cholesterol to ganglioside in the intestinal mucosa significantly in rat decreased in the diet and compared with controls. Conflur monocroab showed that GM3 is exclusively localized in the apical membrane of the enterocyte whereas GD3 is primarily localized in the basolateral membrane.

CONCLUSIONS: The authors conclude that dietary ganglioside is absorbed in the small intestine and transported to different membrane sites, altering ganglioside levels in the intestinal mucosa, plasma and brain and thus possibly having the potential to change developing enterocyte function (and possibly that of other cell lines).
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Gangliosides were shown to enhance the release of acetylcholine from synaptosomes on stimulation. The influx of calcium ion into synaptosomes on membrane depolarization was increased by gangliosides. This was hypothesized to be an underlying mechanisms for the enhancement of acetylcholine release. Studies using calcium channel blockers revealed that four distinct types of voltage-dependent calcium channels occurred in cerebrocortical synapses, and that the N-type was primarily responsible for the evoked release of acetylcholine. An additional result suggests that gangliosides may act mainly on the N-type calcium channel. Cholinergic-specific gangliosides, Chol-1 alpha, were assumed to participate in the mechanism of high-affinity choline uptake. These two different actions of gangliosides were found to be mimicked by synthetic ganglioside analogs. Calcium influx was increased by alpha-sialylcholesterol, and choline uptake was accelerated by beta-sialylcholesterol. Gangliosides and sialycholesterol having these apparently beneficial effects were shown to ameliorate decreased functions of synapses from aged brains.