| Ganglioside references | | | | |
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| Author(s) | Title | Citation | Web-link | Abstract |
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| Rueda R. | The role of dietary gangliosides on immunity and the prevention of infection. | Br J Nutr. 2007 Oct;98 Suppl 1:S68-73. | http://journals.cambridge.org/action/displayAbstract?fromPage=online&aid=1364092 | Gangliosides are acid glycosphingolipids widely distributed in most 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 individual species. Gangliosides function as "unintended" target 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 described in animal models. Recently, the influence of GM3 and GD3 on dendritic cell maturation and effector functionalities 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 immunity development in the neonate, and consequently in the prevention of infections during early infancy. |
| Yang R, Wang Q, Min L, Sui R, Li J, Liu X. | Monosialoanglioside improves memory deficits and relieves oxidative stress in the hippocampus of rat model of Alzheimer's disease. | Neurol Sci. 2012 Dec 11. | http://link.springer.com/article/10.1007%2Fs10072-012-1263-y | GM-1 ganglioside (GM-1) has been proposed as a new therapeutic agent against Alzheimer's disease (AD). Therefore, in this study we aimed to investigate the effects of GM1 on memory deficits and oxidative stress in the hippocampus of rat model of AD. Wistar rats were randomly divided into three groups (n = 15): control group, model group, and treatment group, which were injected with vehicle, Aβ 1-40, and Aβ 1-40 together with GM-1, respectively. Morris water maze test was performed to evaluate spatial learning and memory of the rats. Brain malondialdehyde (MDA) content was detected by biochemical assay, and 4-hydroxynonenal (4-HNE) level in the hippocampus was examined by immunohistochemistry. The results showed that learning and memory deficits were improved in treatment group compared to model group. Brain MDA content and 4-HNE level in hippocampus CA1 were much lower in treatment group than in model group. In summary, we demonstrate that GM-1 could improve spatial learning and memory deficits in rat model of AD, and this may be mediated by the inhibition of oxidative stress and lipid peroxidation in the neurons. These data suggest that GM-1 is a potential agent for AD treatment. |
| Schneider JS, Gollomp SM, Sendek S, Colcher A, Cambi F, Du W. | A randomized, controlled, delayed start trial of GM1 ganglioside in treated Parkinson's disease patients. | J Neurol Sci. 2013 Jan 15;324(1-2):140-8. | http://www.jns-journal.com/article/S0022-510X(12)00581- | The present single center, double-blind, delayed start study was conducted to examine possible symptomatic and disease-modifying effects of GM1 ganglioside in Parkinson's disease (PD). Seventy-seven subjects with PD were randomly assigned to receive GM1 for 120weeks (early-start group) or placebo for 24weeks followed by GM1 for 96weeks (delayed-start group). Washout evaluations occurred at 1 and 2years after the end of treatment. Seventeen additional subjects who received standard-of-care were followed for comparative information about disease progression. Primary outcome was change from baseline Unified Parkinson's Disease Rating Scale (UPDRS) motor scores. 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. |
| Schneider JS, Roeltgen DP, Mancall EL, Chapas-Crilly J, Rothblat DS, Tatarian GT. | Parkinson's disease: improved function with GM1 ganglioside treatment in a randomized placebo-controlled study. | Neurology. 1998 Jun;50(6):1630-6. | http://www.neurology.org/content/50/6/1630.short | 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 study demonstrating efficacy of GM1 in PD patients, this study compared effects of GM1 ganglioside and placebo on motor functions in PD patients.<br>METHODS: Forty-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. After three independent baseline assessments, patients received IV infusion of the test drug (1,000 mg GM1 or placebo) and then self-administered either GM1 or placebo twice daily (200 mg/day, subcutaneously) for 16 weeks. Patients were examined during monthly follow-up visits.<br>RESULTS: There was a significant difference between groups in UPDRS motor scores at 16 weeks (p=0.0001). The activities of daily living portion of the UPDRS (off-period assessment) also showed a significant effect in favor of the GM1-treated patients (p=0.04). GM1-treated patients also had significantly greater mean improvements than placebo-treated patients in performance of timed motor tests including tests of arm, hand, and foot movements, and walking. GM1 was well tolerated and no serious adverse events were reported.<br>CONCLUSIONS: This study demonstrates that GM1 ganglioside treatment enhances neurologic function significantly in PD patients. Further study is warranted to evaluate long-term effects of GM1 in PD patients and to elucidate further the mechanisms underlying patient improvements. |
| Ando S. | Neuronal dysfunction with aging and its amelioration. | Proc Jpn Acad Ser B Phys Biol Sci. 2012;88(6):266-82 | http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3410143/ | The author focused on the functional decline of synapses in the brain with aging to understand the underlying mechanisms and to ameliorate the deficits. The first attempt was to unravel the neuronal functions of gangliosides so that gangliosides could be used for enhancing synaptic activity. The second attempt was to elicit the neuronal plasticity in aged animals through enriched environmental stimulation and nutritional intervention. Environmental stimuli were revealed neurochemically and morphologically to develop synapses leading to enhanced cognitive function. Dietary restriction as a nutritional intervention restored the altered metabolism of neuronal membranes with aging, providing a possible explanation for the longevity effect of dietary restriction. These results obtained with aging and dementia models of animals would benefit aged people. |
| Lim ST, Esfahani K, Avdoshina V, Mocchetti I. | Exogenous gangliosides increase the release of brain-derived neurotrophic factor. | Neuropharmacology. 2011 Jun;60(7-8):1160-7. | http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3045641/pdf/nihms252484.pdf | Gangliosides are lipophilic compounds found in cell plasma membranes throughout the brain that play a role in neuronal plasticity and regeneration. Indeed, absence or abnormal accumulation of gangliosides has been shown to lead to neurological disorders. 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 neurological 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 transduced with a recombinant adenovirus expressing BDNF-flag to facilitate detection of BDNF. Release of BDNF was then determined by Western blot analysis and a two-site immunoassay of culture medium. 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, GT1b preferentially released mature BDNF whereas GM1 released both mature and pro-BDNF. Ceramide and sphingosine did not modify the release of 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, Ramanujam K, Steiner K, Begg D, Clandinin MT. | Diet-induced changes in membrane gangliosides in rat intestinal mucosa, plasma and brain. | J Pediatr Gastroenterol Nutr. 2005 Apr;40(4):487-95. | http://journals.lww.com/jpgn/pages/articleviewer.aspx?year=2005&issue=04000&article=00017&type=abstract | 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.<br>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 diet contained more than 80% GD3. After 2 weeks of feeding, the total and individual ganglioside and cholesterol content was measured in small intestinal mucosa, plasma and brain.<br>RESULTS: The ganglioside-enriched lipid diet significantly increased total gangliosides in the intestinal mucosa, plasma and brain compared with the control diet. The ganglioside-enriched lipid diet significantly increased the level of GD3 (7.5% w/w) in the intestine compared with control (3.2% w/w) while decreasing the level of GM3, the major ganglioside in the intestine. The ratio of cholesterol to ganglioside in the intestinal mucosa, plasma and brain decreased significantly in rats fed the ganglioside-enriched lipid diet compared with controls. Confocal microscopy showed that GM3 is exclusively localized in the apical membrane of the enterocyte whereas GD3 is primarily localized in the basolateral membrane.<br>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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| Ando S, Tanaka Y, Waki H, Kon K, Iwamoto M, Fukui F. | Gangliosides and sialylcholesterol as modulators of synaptic functions. | Ann N Y Acad Sci. 1998 Jun 19;845:232-9. | http://onlinelibrary.wiley.com/doi/10.1111/j.1749-6632.1998.tb09676.x/abstract;jsessionid=02EB4CCA6464E7696EF2136D0D763CCB.d02t03 | 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 sialylcholesterol having these apparently beneficial effects were shown to ameliorate decreased functions of synapses from aged brains. |