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Current Topics in Nutraceutical Research 5 (4): 145-148

145-148 DO POLYPHENOLS AFFECT HUMAN COGNITIVE FUNCTION?

Alexander Collie and Grant Morley

ABSTRACT: Humans are exposed to polyphenols from numerous dietary sources. These polyphenols are rapidly absorbed by the body, and may remain biologically active for many hours after ingestion. Diets rich in polyphenols have numerous health benefits, including improvement in cardiovascular and immune function. The anti-oxidant properties of polyphenols have led some authors to suggest that polyphenols may have a beneficial effect on human cognitive function. The purpose of this review is to summarize the evidence in this field. Animal studies provide convincing evidence that dietary supplementation with polyphenol- rich foods can have both acute and chronic positive effects on cognition. In addition, there is evidence from human randomized, controlled trials that polyphenols and other anti-oxidant rich substances can positively affect cognitive function. Well-designed human clinical trials are required to address the impact of dietary supplementation with polyphenol-rich foods on human cognitive function, and to link any observed cognitive changes with biological markers of polyphenol and anti-oxidant activity.

Current Topics in Nutraceutical Research 5 (4): 149-156

149-156 DIETARY RIBOFLAVIN RESTRICTION AND CHRONIC HEMIN ADMINISTRATION DOES NOT ALTER BRAIN FUNCTION IN RATS: THE IMPORTANCE OF VITAMIN HOMEOSTASIS IN THE BRAIN

Janise DalPai, Andréa Aurélio Borges, Christian Grassl, Luiz Antonio Favero-Filho, Gilberto Fernando Xavier, Virgínia BC Junqueira, Antonio Carlos Lopes, Cícero G Coimbra, Rita Sinigaglia-Coimbra

ABSTRACT: Vitamin B2 deficiency associated with normal dietary intake has been reported in patients with Parkinson's disease (PD), suggesting impaired absorption of this micronutrient. Elevated red meat consumption was thought to contribute as a triggering factor, as the catabolism of hemin (a neurotoxic substance) requires vitamin B2 (Coimbra & Junqueira, 2003). This study tested this hypothesis by verifying the effects of dietary riboflavin restriction associated with hemin administration on rat brain. After 8 months of riboflavin restriction, riboflavin deficiency with or without oral administration of hemin (assessed by erythrocyte glutathione reductase activity) did not impair motor function or spatial learning; neither altered the volume of substantia nigra or brain concentrations of total glutathione. Partial dietary restriction of riboflavin may failed to induce oxidative stress in the rat brain and dopaminergic degeneration in the rat substantia nigra as suggested to occur in humans by Coimbra & Junqueira, (2003), possibly due to an intact mechanism of nutritional privilege that preserves riboflavin content in the normal rat brain during deficiency states. Contrastingly, polymorphic enzymes or receptors involved in the human cellular uptake of riboflavin may conceivably impair the transport of this micronutrient not only through the intestinal wall and renal tubules, but also in the brain of PD patients, thereby annulling the nutritional privilege of the nervous system.

Current Topics in Nutraceutical Research 5 (4): 157-164

157-164 EFFECTS OF PROBIOTIC STRAIN OF *LACTOBACILLUS PARACASEI* ST11 (NCC2461) ON AUTONOMIC NERVE ACTIVITIES, BLOOD PRESSURE AND APPETITE IN RATS
Mamoru Tanida, Yoichi Fukushima, Toshihiko Yamano, Keiko Maeda, Yuko Horii, Jiao Shen and Katsuya Nagai

ABSTRACT: In a recent study, we examined the glycemic and autonomic nervous responses to probiotic strain *Lactobacillus johnsonii* La1, and presented evidence that intraduodenal (ID) injection of this bacteria affected autonomic nerves and lowered blood pressure (BP) in anesthetized rats. In the study presented here, we examined the feeding, autonomic and cardiovascular effects of the *Lactobacillus paracasei* ST11 (NCC2461) in rats, and found that it suppressed food intake. Moreover, ID injection of NCC2461 suppressed gastric vagal nerve activity (GVNA) and accelerated renal sympathetic nerve activity (RSNA) and BP in a dose-dependent manner. Pre-treatment with the histaminergic H1-receptor antagonist diphenhydramine eliminated the effects of NCC2461 on RSNA and BP. Furthermore, bilateral subdiaphragmatic vagotomy did not affect elevating effects of NCC2461, suggesting that vagal afferents are not involved in the pathway of NCC2461 effects. These evidences thus suggest that NCC2461 may exert its hypophagic and hypertensive actions through changes in autonomic neurotransmission via the central histaminergic nerves.

Current Topics in Nutraceutical Research 5 (4): 165-176

165-176 MOLECULAR CHARACTERIZATION OF PIG UDP-N ACETYLGLUCOSAMINE-2 EPIMERASE/NACETYLMANNOSAMINE KINASE (GNE) GENE: EFFECT OF DIETARY SIALIC ACID SUPPLEMENTATION ON GENE EXPRESSION IN PIGLETS
Bing Wang, Honghua Hu, Bing Yu and Frederic A. Troy II

ABSTRACT: The UDP-N-acetylglucosamine-2-epimerase/N-acetylmannosamine kinase (Gne) gene encodes a key bifunctional enzyme important in initiating and regulating sialic acid (Sia) synthesis. Sia is commonly expressed as a terminal (non-reducing) sugar residue on oligosaccharide side chains on cell surface glycoconjugates where it mediates many carbohydrate receptor interactions, particularly in the neural and immune systems. The myriad of functions include nerve cell transmission, memory formation, cell-cell adhesion and communication, and lymphocyte extravasation. Sia is also a major component of human milk oligosaccharides where its level has been correlated with enhanced cognitive function and memory. There is no information, however, if early dietary Sia supplementation that increases the intracellular levels of Sia, may regulate Gne gene expression in developing piglets. To study this possible regulation, we cloned and sequenced a 4.3 kb of pig Gne cDNA (4326 nt), including 2169- nucleotides in the coding region. The Gne cDNA showed 91.9% and 98.9% identities to the human counterparts in the nucleotide and protein sequences, respectively. There are only eight amino acid differences between human and pig Gne, making the pig cDNA closer in homology to the human than the orthologs from mouse, rat, hamster, chicken, frog or zebrafish. The piglets Gne gene is highly expressed in the hippocampus, liver, and thymus followed by the pancreas, frontal cortex, lungs, kidneys, heart and spleen. The lowest level of expression was in skeletal muscle. Importantly, we have now shown that dietary Sia supplementation in developing piglets with a Sia-rich glycopeptide and active learning increased the Gne mRNA expression levels 2 to 3-fold in brain hippocampus and liver. These findings suggest that normal brain development and active learning increases the requirement for sialylated glycoconjugates, including neural cell adhesion molecules (N-CAM), and brain gangliosides. They further show that dietary supplements of Sia can modulate Gne gene expression, and that Sia is an essential nutrient during periods of rapid neural growth and brain development in piglets.

Current Topics in Nutraceutical Research 5 (4): 177-182

177-182 THE EFFECT OF FLAXSEED SUPPLEMENTATION ON HORMONAL LEVELS

ASSOCIATED WITH POLYCYSTIC OVARIAN SYNDROME: A CASE STUDY

Debra A. Nowaka, Denise C. Snydera, Ann J. Brownb, and Wendy Demark-Wahnefried

ABSTRACT: Flaxseed is a rich source of lignan and has been shown to reduce androgen levels in men with prostate cancer. Polycystic ovarian syndrome (PCOS), a common endocrine disorder among women in their reproductive years, also is associated with high levels of androgens and is frequently accompanied by hirsutism, amenorrhea and obesity. This clinical case study describes the impact of flaxseed supplementation (30 g/ day) on hormonal levels in a 31-year old woman with PCOS. During a four-month period, the patient consumed 83% of the flaxseed dose. Heights, weights, and fasting blood samples taken at baseline and 4-month follow-up indicated the following values: BMI (36.0 vs. 35.7m/kg²); insulin (5.1 vs. 7.0 uIU/ml); total serum testosterone (150 ng/dl vs. 45 ng/dl); free serum testosterone (4.7 ng/dl vs. 0.5 ng/dl); and % free testosterone (3.1% vs. 1.1%). The patient also reported a decrease in hirsutism at the completion of the study period. The clinically significant decrease in androgen levels with a concomitant reduction in hirsutism reported in this case study demonstrates a need for further research of flaxseed supplementation on hormonal levels and clinical symptoms of PCOS.

Current Topics in Nutraceutical Research 5 (4): 183-188

183-188 **WILD ALASKAN BLUEBERRY EXTRACTS INHIBIT A MAGNESIUM-DEPENDENT NEUTRAL SPHINGOMYELINASE ACTIVITY IN NEURONS EXPOSED TO TNF α**
Sally J. Gustafson, Brian M. Barth, Colin M. McGill, Thomas P. Clausen And Thomas B. Kuhn

ABSTRACT: The proinflammatory cytokine tumor necrosis factors α (TNF α) is key to initiating and orchestrating inflammation, which substantially contributes to the progression of many chronic and acute CNS pathologies. TNF α can stimulate a magnesium (Mg²⁺)-dependent neutral sphingomyelinase (nSMase) resulting in the accumulation of ceramide, a lipid messenger implicated in oxidative stress and apoptosis. Dietary polyphenols were shown to alleviate CNS inflammation largely attributed to their antioxidant properties. We found that preincubation of human SH-SY5Y neuroblastoma cells with organic or aqueous extracts prepared from wild Alaskan bog blueberries completely negated Mg²⁺-nSMase activation upon TNF α exposure. This specific and potent inhibition of Mg²⁺-nSMase activity was non-antioxidant in nature. This study demonstrated for the first time that wild Alaskan bog blueberries harbor the capacity to interfere with a key step in the progression of inflammation, the activation of Mg²⁺-nSMase, in neuronal cells further providing evidence for the therapeutic potential of blueberries.

Current Topics in Nutraceutical Research 5 (4): 189-196

189-196 **EFFECTS OF CONTROLLED DIETS ENRICHED WITH ALPHA-LINOLENIC ACID, EICOSAPENTAENOIC ACID OR DOCOSAHEXAENOIC ACID ON SOLUBLE ADHESION MOLECULES AND ENDOTHELIN-1 CONCENTRATIONS IN HEALTHY VOLUNTEERS**
Sarah Egert, Fausi Rassoul, Christine Boesch-Saadatmandi, Volker Richter, Gerald Rimbach, Helmut F. Erbersdobler, Veronika Somoza, and Ursel Wahrburg

ABSTRACT: The consumption of omega-3 polyunsaturated fatty acids may protect against atherosclerotic diseases, and the blood concentrations of soluble cellular adhesion molecules (sCAMs) and endothelin-1 (ET-1) possibly reflect the inflammatory processes underlying atherosclerosis. However, knowledge of the differential effects of dietary n-3 fatty acids on markers of inflammation is incomplete. Our aim was to compare the effects of dietary alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) on serum levels of soluble E-selectin (sE-selectin), soluble intercellular adhesion molecule-1 (sICAM-1), soluble vascular cell adhesion molecule-1 (sVCAM-1), and plasma levels of endothelin-1 (ET-1). Therefore, a randomized strictly

controlled dietary study in 48 healthy volunteers (mean age 25.9 years) with three dietary groups and a parallel design, consisting of two consecutive periods was conducted. Subjects received a 2- week wash-in diet rich in monounsaturated fatty acids followed by experimental diets enriched with equal amounts of ALA, EPA, or DHA for 3 weeks. The concentrations of sICAM-1, sVCAM-1 and sE-selectin, as well as ET-1, did not significantly change after consuming the ALA-, EPA- or DHA-diet. In conclusion, in healthy young subjects without established cardiovascular risk factors and under the condition of a three- week intervention period, neither ALA nor EPA nor DHA significantly affected levels of sCAM or ET-1.