FRUIT POLYPHENOLS PREVENT KAINIC ACID-INDUCED DECREMENTS IN COGNITION BY ALTERING GENE EXPRESSION IN THE HIPPOCAMPUS OF AGED FISHER RATS

F.C. Lau[1] (P), B. Shukitt-Hale[1], A.N. Carey[1], D.F. Bielinski[1], E.L. Spangler[2], D.K, Ingram[2], and J.A. Joseph[1]

[1]USDA, HNRC on Aging Tufts Univ., Boston, MA 02111 and [2]Laboratory of Experimental Gerontology, NIA, Baltimore, MD, 21224

Age-related cognitive deficits in neurodegenerative diseases such as Alzheimer's disease (AD) and Parkinson's disease (PD) may be attributable to chronic exposure and/or increased susceptibility to inflammatory insults. The current study investigates if the polyphenols in blueberries (BBs) can reduce the deleterious effects of inflammation induced by kainic acid (KA). Central administration of KA induces a characteristic behavioral syndrome and neurodegeneration in several brain areas including the hippocampus. Briefly, 4 month old male F344 rats were fed a control, 0.015% piroxicam (PX) or 2% BB diet for 8 weeks before either Ringers (R) or KA (300ng in 0.5 microliter Ringers) was bilaterally microinfused into the hippocampus. Two weeks later, following behavioral evaluations, the rats were sacrificed, their brains removed and dissected. Total RNA from the hippocampus was extracted and used in real-time quantitative RT-PCR (qRT-PCR) to analyze the expression of genes that are involved in inflammatory response. Behavioral studies showed that KA had deleterious effects on cognitive behavior. KA-injected rats on the control diet exhibited increased latencies to find the hidden platform in the Morris water maze (MWM) on days 1-3 and on day 4 during reversal learning, compared to R-injected rats. These deficits were improved by BB supplementation: latencies to find the platform on days 2-4 in the BB-KA group were not different than the control diet-R group. Immunohistochemical analyses of OX-6 expression revealed that KA produced an inflammatory response by increasing the OX-6 positive areas in the hippocampus of KA-injected rats. qRT-PCR analysis showed that KA up-regulated the expression of inflammatory cytokines IL-1beta and TNF-alpha, the neurotrophic factor IGF-1 and the transcription factor NF-kappaB. BB supplementation was found to reduce the expression of all but IGF-1. These results indicate that BB polyphenols exert anti-inflammatory actions via alteration of gene expression. *(Supported by USDA Intramural & Alzheimer Assoc.)*