LUTEIN STUDY 6

IMPROVES SEVERAL PARAMETERS OF COGNITIVE PERFORMANCE

Oxidative and inflammatory processes play a major role in stress-induced neural atrophy. There is a wide body of literature linking oxidative and inflammatory stress with reductions in neurotrophic factors, stress resilience, and cognitive function. Based on their antioxidant and anti-inflammatory capacity, researchers investigated the effect of the dietary carotenoids lutein and zeaxanthin, along with the zeaxanthin isomer meso-zeaxanthin (collectively the "macular xanthophylls" [MXans]) on systemic brain-derived neurotrophic factor (BDNF) and anti-oxidant capacity (AOC), and the pro-inflammatory cytokines TNF-α, IL-6, and IL-1β. To investigate higher-order effects, we assessed cognitive performance. 59 young (18–25 yrs.), healthy subjects participated in a 6-month, double-blind, placebo-controlled trial[10] to evaluate the effects of MXan supplementation on the aforementioned serum parameters and cognitive performance. Subjects were randomly assigned to one of three groups: placebo, 13 mg, or 27 mg/day total MXans; all measures were taken at baseline and 6 months. Blood was obtained via fasting blood draw, and MXan concentration in the retina (termed macular pigment optical density [MPOD]) was measured via customized heterochromatic flicker photometry. Serum BDNF and cytokines were assessed via ELISA. Serum antioxidant capacity (AOC) and serum MXan concentrations were quantified via colorimetric microplate assay, and high-performance liquid chromatography, respectively. Cognitive performance was measured via a computer-based assessment tool (CNS Vital Signs). Results were that BDNF, MPOD, serum MXans, and AOC all increased significantly versus placebo in both treatment groups over the 6-month study period ($p < .05$ for all). IL-1β decreased significantly versus placebo in both treatment groups ($p = .0036$ and $p = .006$, respectively). For cognitive measures, scores for composite memory, verbal memory, sustained attention, psychomotor speed, and processing speed all improved significantly in treatment groups ($p < .05$ for all) and remained unchanged in the placebo group. Several measures were found to be significantly associated in terms of relational changes over the course of the study. Notably, change in BDNF was related to change in IL-1β ($r = −0.47$; $p < .001$) and MPOD ($r = 0.44$; $p = .0086$). Additionally, changes in serum MXans were strongly related to AOC ($r = 0.79$ & 0.61 for lutein and zeaxanthin isomers respectively; $p < .001$). For cognitive scores, change in BDNF was correlated to change in composite memory ($r = 0.32$; $p = .014$) and verbal memory ($r = 0.35$; $p = .007$), whereas change in MPOD was correlated with change in both psychomotor speed ($r = 0.38$; $p = .003$), and processing speed ($r = 0.35$; $p = .007$). Change in serum lutein was found to be significantly correlated to change in verbal memory ($r = 0.41$; $p < .001$), composite memory ($r = 0.31$; $p = .009$), and sustained attention ($r = 0.28$; $p = .036$). Change in serum zeaxanthin isomers was significantly correlated with change in verbal memory ($r = 0.33$; $p = .017$). Lastly,

change in AOC was significantly associated with verbal memory ($r = 0.34$; $p = .021$), composite memory ($r = 0.29$; $p = .03$), and sustained attention ($r = 0.35$; $p = .016$). No significant relational changes in any cognitive parameter were found for the placebo group. In conclusion, six months of daily supplementation with at least 13 mg of MXans significantly reduces serum IL-1β, significantly increases serum MXans, BDNF, MPOD, and AOC, and improves several parameters of cognitive performance. Findings suggest that increased systemic antioxidant/anti-inflammatory capacity (and not necessarily deposition of the carotenoids in neural tissues), may explain many of the effects determined in this study. The significant relationship between change in BDNF and IL-1β over the course of the study suggests that regular consumption of MXans interrupts the inflammatory cascade that can lead to reduction of BDNF. Changes in MPOD and BDNF appear to account for enhancement in cognitive parameters that involve speed of processing and complex processing, respectively.

[10] Stringham NT, Holmes PV, Stringham JM. Effects of macular xanthophyll supplementation on brain-derived neurotrophic factor, pro-inflammatory cytokines, and cognitive performance. *Physiology & Behavior*. 1 November 2019; 211: 112650