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Study finds B-vitamin deficiency may cause vascular cognitive impairment

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A deficiency of B-vitamins may cause vascular cognitive impairment, according to a new study. Researchers at the Jean Mayer USDA Human Nutrition Research Center on Aging (HNRCA) at Tufts University used an experimental model to examine the metabolic, cognitive, and microvascular effects of dietary B-vitamin deficiency. Their findings appear in the August 26, 2008 issue of *Proceedings of the National Academy of Sciences* (PNAS).

"Metabolic impairments induced by a diet deficient in three B-vitamins -folate, B12 and B6- caused cognitive dysfunction and reductions in brain capillary length and density in our mouse model," says Aron Troen, PhD, the study's lead author. "The vascular changes occurred in the absence of neurotoxic or degenerative changes."

Troen, who is an assistant professor at Tufts University's Friedman School of Nutrition Science and Policy, explains, "Mice fed a diet deficient in folate and vitamins B12 and B6 demonstrated significant deficits in spatial learning and memory compared with normal mice." Troen and colleagues observed similar but less pronounced differences between normal mice and a third group of mice that were fed a diet enriched with methionine.

"The B-vitamin-deficient mice also developed plasma homocysteine concentrations that were seven-fold higher than the concentrations observed in mice fed a normal diet," adds Troen. Homocysteine is produced by the breakdown of a dietary protein called methionine. B-

vitamins, including folate, vitamin B12, and vitamin B6, are required to convert homocysteine back to methionine, thereby reducing the blood concentration of homocysteine.

Studies have linked elevations in plasma homocysteine with an increased risk for cognitive impairment. "However," Troen says, "it has not been determined that homocysteine is directly responsible. Based on the findings of our study, we theorize that a deficiency of B-vitamins induces a metabolic disorder that manifests with high homocysteine, as well as cerebral microvascular dysfunction."

Troen and colleagues divided their study mice into three groups and fed each group a different diet for 10 weeks. While the control (comparison) group was fed a normal diet containing methionine and B-vitamins, the other two diets were designed to induce high homocysteine levels but through different metabolic mechanisms. One was methionine-enriched, and the other was deficient in B vitamins. Researchers measured blood concentrations of B-vitamins and homocysteine and assessed the brain anatomy and vasculature. They also evaluated psychomotor function by a battery of age-sensitive tests, such as holding on to a wire and walking a beam, and assessed spatial learning and memory with the Morris water maze, a well-validated and sensitive test of rodent cognitive function.

"It took longer, on average, for the B-vitamin-deficient mice to maneuver the water maze, compared with controls," says Troen. "Longer latencies were associated with higher plasma homocysteine levels and shorter capillaries, particularly in the brain region called the hippocampus." Troen adds, "Despite the vascular changes, the brain anatomy appeared normal, and there was no evidence of a cellular proliferation process called gliosis, which typically accompanies neurodegeneration."

Irwin Rosenberg, MD, director of the Nutrition and Neurocognition

Laboratory at the HNRCA, notes, "The elevated levels of homocysteine that were associated with vascular cognitive impairment in the mice in our study are comparable to the levels that are associated in older adults with an increased risk for Alzheimer's disease and cerebrovascular disease, the latter of which manifests with conditions such as stroke and atherosclerosis. These findings may indicate that microvascular changes mediate the association between high homocysteine levels and human age-related cognitive decline."

Troen and colleagues write that their study helps to "…define more precisely the mechanisms underlying cerebral microvascular disease, independent of or prior to the onset of irreversible neurodegeneration." According to Troen, this work, which was funded by the U.S. Department of Agriculture, "may provide a model system in which to study the role of the brain's microvascular circulation in cognitive function."

Source: Tufts University