Characterization of cerebrovascular changes in the hyperhomocysteinemia model of vascular dementia

Elizabeth Grau [1] • *David Braun, PhD* [1] • *Linda VanEldik, PhD* [1]

[1]Neuroscience, University of Kentucky

Vascular dementia, though being the most common form of dementia following Alzheimer's disease, has received minimal attention. As a result, very little is known regarding its underlying mechanism and the resulting implications. This experiment characterizes vascular changes in a hyperhomocysteinemia (HHcy) model of vascular dementia. Elevated homocysteine levels in the blood has been identified as a risk factor for vascular disease and dementia in patients, and in rodents it can induce cognitive impairments, neuroinflammation, and microhemorrhages. In the present study, mice were fed a diet deficient in B12, B6, and folate while simultaneously supplemented with excess methionine for 4, 8, or 12 weeks. We found that the blood protein immunoglobulin G (IgG), normally excluded from the brain, was elevated in the cortical and hippocampal parenchyma by 4 weeks on diet. Interestingly, this putative "leakiness" of the blood brain barrier (BBB) recovered in the hippocampus, despite continuation on diet. In the cortex, however, BBB dysfunction was progressive. We are currently exploring whether these changes in BBB integrity are also associated with infiltration of peripheral immune cells or vascular remodeling in these regions. Better understanding of the vascular pathology and inflammatory responses in this model will assist in the development of treatments for vascular cognitive impairment and dementia.