Cerebrovascular fragility

Cerebrovascular fragility and cerebral microhemorrhages (CMH) contribute to age-related cognitive impairment, mobility defects, and vascular cognitive impairment and dementia, impairing healthspan and reducing quality of life in the elderly. Insulin-like growth factor 1 (IGF-1) is a key vasoprotective growth factor that is reduced during aging. Circulating IGF-1 deficiency leads to the development of CMH and other signs of cerebrovascular dysfunction.

The goal of Miller et al. was to understand the contribution of IGF-1 signaling on vascular smooth muscle cells (VSMCs) to the development of CMH and associated gait defects. They used an inducible VSMC-specific promoter and an IGF-1 receptor (Igf1r) floxed mouse line (Myh11-CreERT2 Igf1rf/f) to knockdown Igf1r. Angiotensin II in combination with L-NAME-induced hypertension was used to elicit CMH. We observed that VSMC-specific Igf1r knockdown mice had accelerated development of CMH, and subsequent associated gait irregularities. These phenotypes were accompanied by upregulation of a cluster of pro-inflammatory genes associated with VSMC maladaptation. Collectively the findings support an essential role for VSMCs as a target for the vasoprotective effects of IGF-1, and suggest that VSMC dysfunction in aging may contribute to the development of CMH [1].

1)
Miller LR, Bickel MA, Vance ML, Vaden H, Nagykaldi D, Nyul-Toth A, Bullen EC, Gautam T, Tarantini S, Yabluchanskiy A, Kiss T, Ungvari Z, Conley SM. Vascular smooth muscle cell-specific Igf1r deficiency exacerbates the development of hypertension-induced cerebral microhemorrhages and gait defects. Geroscience. 2024 Feb 23. doi: 10.1007/s11357-024-01090-7. Epub ahead of print. PMID: 38388918.