Translational Models of Vascular Cognitive Impairment and Vascular Dementia

Overview: pre-clinical models of vascular dementia
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Vascular contributions to cognitive impairment and dementia (VCID) in humans reflects a multitude of clinicopathological states. These range from pure genetic small vessel arteriopathy (CADASIL, CARASIL, COL4A1/2 mutations) to post-stroke dementia following large artery stroke. The most common source of VCID is diffuse white matter pathology with focal lacunar lesions due to small artery disease (“small vessel disease”). At present no experimental model replicates all features of VCID. Systematic reviews of the experimental animal literature have concluded that existing animal models of VCID are far from ideal, in that they do not typically reflect underlying clinical pathology [1]. A recent US-based roundtable concluded: “the need for new model systems with metabolic similarity to humans, such as animal models with white matter vascular injury, animal models of hypertension or the potential utility of stem cell/induced pluripotent models are in need of further exploration” [2].

A translational experimental model should faithfully reflect at least one of the pathological processes involved in human VCID. This would be useful for: i) prospective studies of the temporal and spatial development of the disease and identification of molecular and cellular mechanisms; ii) preclinical testing of drugs and other interventions.

References