Dysfunction of the neurovascular unit in patients with subcortical vascular disease

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Vascular cognitive impairment (VCI) is a broad diagnostic category that includes all forms of vascular disease. Because VCI is a heterogeneous group of illnesses, few clinical trials have been done. Biomarkers from clinical, imaging and biochemical studies provide a means to select homogeneous cohorts of patients with a similar natural history. There is a growing consensus that the optimal form to focus on for the initial clinical trials is patients with white matter injury secondary to small vessel disease (SVD). These patients generally have progressive damage to the white matter often secondary to inflammation with blood-brain barrier (BBB) disruption. Biomarkers from multiple modalities can be used to classify patients. The multimodal approach involves: 1) clinical and neuropsychological features, such hyperreflexia and executive dysfunction; 2) ischemic injury to the white matter as shown by reduced N-acetylaspartate on proton NMR spectroscopy and reduced fractional anisotropy on diffusion tensor imaging; 3) disruption of the BBB demonstrated by dynamic contrast-enhanced MRI; and 4) increased CSF albumin ratio and abnormal matrix metalloproteinases in the CSF. These biomarkers can be used to classify patients based on statistical clustering methods. Those subgroup with inflammatory damage to the white matter who have the progressive form of SVD form the optimal group for treatment trials.