**Supplemental Data**

**Manuscript title:** Blood-Brain Barrier Impairment and Hypoperfusion are linked in Cerebral Small Vessel Disease

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**1.1. Patient inclusion**

Lacunar stroke patients were recruited from the Stroke Unit of the Maastricht University Medical Centre and Zuyderland Hospital, The Netherlands, in the period between April 2013 and December 2014. Lacunar stroke was defined as an acute stroke syndrome with a compatible recent small subcortical infarct on brain MRI. If no such lesion was visible on imaging, established criteria for lacunar stroke syndrome were used consisting of unilateral motor and/or sensory signs that involved the whole of at least 2 of the 3 body parts (face, arm, leg), without disturbance of consciousness, visual fields, language, or other cortical functions.1 Exclusion criteria include a potential cardiac embolic source (e.g. atrial fibrillation), or symptomatic carotid stenosis of ≥50%.2 Lacunar stroke patients were included at least three months post-stroke to avoid acute stroke changes.3 Mild vascular cognitive impairment (mVCI0 patients were recruited from the outpatient clinic of the Department of Neurology and from the Memory Clinic of the Maastricht University Medical Centre, and Zuyderland Hospital, The Netherlands. Criteria of mVCI were met when patients had 1) subjective complaints of cognitive functioning, and 2) objective cognitive impairment in at least one cognitive domain at neuropsychological testing, and 3) a Clinical Dementia Rating of ≤1 and a Mini Mental State Examination score of ≥20, and 4) vascular lesions on brain MRI that suggest a link between the cognitive deficit and cSVD4: moderate to severe white matter hyperintensities (WHM; Fazekas score deep>1 and/or periventricular>2), or mild WMH (Fazekas score deep=1 and/or periventricular=2) combined with lacune(s) and/or microbleeds.5

**1.2. Patient demographics**

Characteristics of all participants were recorded including age, sex, and the presence of cardiovascular risk factors including hypertension (history of hypertension and/or use of blood pressure lowering drugs), hypercholesterolemia (history of hypercholesterolemia and/or use of statin), diabetes mellitus (history of diabetes mellitus or use of blood sugar lowering drugs), smoking (current smoking) and body mass index (BMI: current weight of the subject divided by the square of the current length)

**References**

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