The contribution of small vessel pathology to the development of cognitive decline might be even more important than already accepted. In normal aging as well as in the early phases of neurodegenerative diseases when cognitive decline might not yet be present subtle structural changes undetectable to neuroimaging methods are causing functional small vessel changes which alter cerebral blood flow (CBF). Even a mild reduction of CBF might impair learning and memory through disturbed protein and ATP synthesis which lead to diminished synaptic plasticity and inability to generate action potentials. Ischemia promotes amyloid plaque formation and tau phosphorylation. CBF is regulated by neurovascular coupling, a finely tuned system in which neuronal activity and metabolism interact both temporally and spatially. Transcranial Doppler (TCD) is a continuous ultrasound method with high frequency sampling capable of assessing small vessel function in selected brain areas due to excellent temporal resolution. TCD is non-invasive and in comparison to neuroimaging methods it provides relative freedom of movement for subjects and lower costs. Assuming that the changes of mean blood flow velocity reflect changes of CBF different paradigms have been developed to investigate cerebral vasoreactivity, neurovascular coupling and cerebral autoregulation. Besides mean blood flow velocity, pulsatility and resistivity indexes are computed to indicate vasoconstriction or vasodilatation in distal vascular beds. TCD findings correlate well with neuroimaging markers of small vessel disease. Different neurovascular stress tests may identify persons at high risk, follow up of the progression of disease or they can be used to measure the therapeutic effects of different cardiovascular medications.

Except for the already mentioned shortcoming of indirect CBF measurement through the changes of mean blood flow velocities, there are opinions that the complex way in which cognitive functions interrelate are beyond the reach of regionally focused methods and that the theory of neurovascular coupling has its weaknesses. Nevertheless, TCD finds its place as one of the surrogate markers in studies of cognitive dysfunction providing real time data on how ageing and neurodegenerative diseases influence blood flow in small vessels of the brain.