The enigma of vascular depression

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Late-life depression (LLD) is frequently associated with cognitive impairment and increases the risk of subsequent dementia. Cerebrovascular disease (CVD), deep white matter lesions, Alzheimer disease (AD) and dementia with Lewy bodies (DLB) have all been hypothesized to contribute to this increased risk, and a host of studies have looked at the interplay between cerebrovascular disease and LLD. This has resulted in the concept of "vascular depression", but despite multiple magnetic resonance imaging (MRI) studies in this field, the relationship between structural changes in human brain and LLD is still controversial. While postmortem studies of suicide in elderly persons revealed multiple lacunes, small vessel CVD or AD-related lesions, recent autopsy data challenged the role of subcortical lacunes and white matter lesions as major morphological substrates of depressive symptoms in aged persons. Several neuropathological studies, including a personal clinico-pathological study in elderly persons with LLD and age-matched controls confirmed that lacunes, periventricular and deep white matter demyelination as well as AD-related lesions are usually unrelated to the occurrence of LLD. In the same line, neuropathological data show that early-onset depression is not associated with an acceleration of age-related neurodegenerative changes. Recent data on the critical role of glia-modulating neuronal dysfunction and degeneration in depression are discussed.