Vascular dysregulation in AD

C. Iadecola

There is increasing evidence that vascular factors play a significant role in the pathogenesis of Alzheimer's dementia (AD). Whereas the structure of cerebral blood vessels is altered in AD, cerebral blood flow (CBF) is reduced even in the early stages of the disease. Epidemiological studies have shown that cerebrovascular diseases and AD share similar risk factors, suggesting a pathogenic commonality. Furthermore, small ischemic lesions amplify the cognitive dysfunction linked to amyloid plaques and neurofibrillary tangles, the neuropathological hallmarks of AD. These observations have suggested an interaction between vascular insufficiency and the clinical expression of AD, raising the possibility that cerebrovascular dysfunction promotes the disease process underlying the dementia. Recent experimental studies have provided critical evidence supporting a role of vascular dysfunction in AD. Studies in mouse models of AD have revealed that amyloid-b (Ab), the amyloid precursor protein (APP)-derived peptide central to AD pathogenesis, has profound cerebrovascular effects that disrupt the brain's blood supply and render the brain more vulnerable to injury. Taken together, these epidemiological, pathological and experimental observations indicate that cerebrovascular dysfunction may contribute to the structural and functional alterations underlying the pathogenesis of AD.