Intracranial stenosis in cognitive impairment and dementia

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Abstract
Intracranial stenosis is a common vascular lesion observed in Asian and other non-Caucasian stroke populations. However, its role in cognitive impairment and dementia has been under-studied. We, therefore, examined the association of intracranial stenosis with cognitive impairment, dementia and their subtypes in a memory clinic case-control study, where all subjects underwent detailed neuropsychological assessment and 3 T neuroimaging including three-dimensional time-of-flight magnetic resonance angiography. Intracranial stenosis was defined as ≥50% narrowing in any of the intracranial arteries. A total of 424 subjects were recruited of whom 97 were classified as no cognitive impairment, 107 as cognitive impairment no dementia, 70 vascular cognitive impairment no dementia, 121 Alzheimer’s Disease, and 30 vascular dementia. Intracranial stenosis was associated with dementia (age/gender/education – adjusted odds ratios (OR): 4.73, 95% confidence interval (CI): 1.93–11.60) and vascular cognitive impairment no dementia (OR: 3.98, 95% CI: 1.59–9.93). These associations were independent of cardiovascular risk factors and MRI markers. However, the association with Alzheimer’s Disease and vascular dementia became attenuated in the presence of white matter hyperintensities. Intracranial stenosis was associated with dementia (age/gender/education – adjusted odds ratios (OR): 4.73, 95% confidence interval (CI): 1.93–11.60) and vascular cognitive impairment no dementia (OR: 3.98, 95% CI: 1.59–9.93). These associations were independent of cardiovascular risk factors and MRI markers. However, the association with Alzheimer’s Disease and vascular dementia became attenuated in the presence of white matter hyperintensities. Intracranial stenosis was associated with vascular cognitive impairment no dementia independent of MRI markers. In Alzheimer’s Disease and vascular dementia, this association is mediated by cerebrovascular disease. Future studies focusing on perfusion and functional markers are needed to determine the pathophysiological mechanism(s) linking intracranial stenosis and cognition so as to identify treatment strategies.

Keywords
Cognitive impairment, cerebrovascular diseases, dementia, intracranial stenosis, magnetic resonance angiography

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Introduction
Cerebrovascular diseases (CeVD) have been increasingly implicated as a cause and contributor to cognitive impairment and dementia with a strong association reported between infarcts and white matter hyperintensities (WMH) with cognitive decline.1 In this context, intracranial stenosis (ICS) has gained increasing attention due to its role in causing ischemic damage and hence cognitive dysfunction.2 The occurrence of ICS has been attributed to vascular risk factors such as hypertension and diabetes3,4 – the same risk factors which are also linked with Alzheimer’s disease (AD) and vascular dementia (VaD). Previous post-mortem studies have shown that severe arterial atherosclerosis of the Circle of Willis is common in dementia, being found in 53% of VaD and 34% of AD cases.5

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