Vascular Cognitive Impairment

Introduction

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One of the greatest advances in the understanding of cognitive disorders comes from the realization that Alzheimer disease (AD) and vascular cognitive impairment share common risk factors. This opens the door to a common approach to both and promises that if vascular risk factors are controlled, then not only strokes but also cognitive impairment could be prevented. It also has become evident that AD pathology and vascular lesions often coexist in the brains of the elderly. Less certain is whether the effects are additive or multiplicative.

Gorelick1 reviews and categorizes systematically the different risk factors as demographic, atherosclerotic, genetic, and stroke-related. As our knowledge grows, perhaps another relevant category will be identified, namely protective factors. Not all brains are created equal, varying both in their capacity and in their resistance to injury. Moreover, the brain is molded by experience and environment. We are just beginning to glimpse what strengthens and weakens the brain’s natural resilience.

Amyloid angiopathy has long been recognized in association with cognitive impairment, especially AD. What was not realized is that amyloid deposition is strongly associated with white matter changes and a host of vascular alterations. Greenberg et al2 emphasize that microcirculatory changes long precede the familiar catastrophic hemorrhage, sometimes heralded by small warning leaks. Understanding the mechanisms of amyloid deposition and clearance may hold the key to successful interventions.

Deave et al3 describe the important and interactive roles of the receptor for advanced glycation end products and low-density lipoprotein receptor-related protein-1 in the trafficking of β-amyloid across the blood–brain barrier. Their findings implicate these vascular receptors in the control of the homeostasis of Aβ in brain, highlighting a previously unrecognized role of cerebral blood vessels in “neurodegenerative” pathologies characterized by β-amyloid accumulation. Thus, receptor for advanced glycation end products receptors and low-density lipoprotein receptor-related protein-1 emerge as potential therapeutic targets to enhance β-amyloid clearance from the brain in patients with AD and other conditions associated with cerebral amyloid accumulation.

Three decades ago, atherosclerosis allegedly explained most cognitive decline in the elderly. After being eclipsed by AD as a cause of cognitive impairment, atherosclerosis has regained prominence as a possible culprit in AD itself, as Roher et al4 argue. Although the association of AD and atherosclerosis is clear, their interaction is not. Ischemia and infarction are not the only mechanism through which atherosclerosis can act. It may be that some of the risk factors for atherosclerosis such as hypertension may cause damage through other mechanisms, such as protein leakage into the brain and inflammation. Moreover, both AD change and atherosclerosis may be enhanced by a common factor, such as the presence of the lipoprotein E (e) 4/4 allele.

Whatever the ultimate explanation may be, the fact remains that AD and atherosclerosis have common risk factors and, hence in principle, the potential for similar treatments and prevention.

References


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