Untangling Vascular Cognitive Impairment

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See related articles, pages 783–830.

Vascular pathology is often the cause of cognitive impairment and dementia. The entities implicated include large cortical infarcts; single strategically-placed or multiple small infarcts, cerebral hemorrhage, cortical changes due to hypoperfusion (eg, hippocampal sclerosis, ischemic-anoxic damage, cortical laminar sclerosis), and a variety of vascular pathologies (eg, lipohyalinosis, CADASIL, cerebral amyloid angiopathy). Vascular cognitive impairment (VCI) is an umbrella term that encompasses these instances of cognitive decline due to vascular factors, and includes patients with mixed vascular and neurodegenerative pathologies.1–2 It is an evolving concept, and as our understanding grows, new questions arise, including two that are addressed by studies published in this issue of Stroke: do white matter lesions and silent infarcts lead to a specific pattern of cognitive impairment, and if so, how?3 and do changes in the microvasculature precede and potentially lead to the development of Alzheimer pathology?

The effect of silent infarcts and CT- and MRI-detected white matter changes on cognition is still controversial. On the one hand, these lesions are commonly seen in healthy individuals with intact mental functions, and some researchers in the field question whether they play a role in cognitive decline in the elderly.4 On the other hand, the results of many clinical, epidemiological, and pathological studies suggest that people with white matter changes and silent infarcts are more likely to have varying degrees of cognitive impairment and dementia.4–5 The mechanisms through which these pathologies lead to cognitive decline are not well understood. One putative mechanism is the interruption of frontal-subcortical circuits that link specific regions of the frontal lobes, particularly the dorsolateral prefrontal, orbitofrontal and anterior cingulate cortices, to the striatum, globus pallidus and ventral anterior and mediodorsal thalamus.6 Interruption of these circuits leads to three well-defined “frontal” cognitive syndromes: dorsolateral (executive dysfunction and impaired recall), orbitofrontal (behavioral and emotional changes), and anterior cingulate (abulia and akinetic mutism). The thalamus is a key component, not only of these frontal-subcortical circuits, but also of temporo-limbic circuits important for memory storage and retrieval: thalamic pathology may lead to dementia.7–8 Several articles published in this issue of Stroke confirm that white matter lesions are associated with executive dysfunction, and that the extent and location of the white matter changes determine the neuropsychological profile among healthy community-dwelling individuals, stroke patients, and memory clinic patients with mild cognitive impairment and dementia.9–12 Other studies in this issue highlight the critical role of the thalamic pathology in the development of cognitive impairment in patients seen in a stroke and a memory clinic: patients with thalamic changes (due to local lesions or subcortical diaschisis) perform poorly in multiple cognitive behaviors with frontal and temporal lobe function.9,12,13 Among patients with VCI, multiple pathologies may affect structures that are critical for cognition: white matter hyperintensities are reflective of the presence of vascular disease, whereas cortical gray matter volume is reflective of the presence of Alzheimer and vascular disease.14

Many patients diagnosed with Alzheimer disease may in fact have vascular cognitive impairment. There is an interaction between cerebral infarcts and Alzheimer pathology: people with multiple pathologies are more likely to have dementia, and patients with infarcts and Alzheimer-type changes have a greater degree of cognitive impairment than those with similar severity of either pathology.15 In addition, epidemiological studies show that traditional vascular risk factors, such as hypertension and diabetes, are also risk factors for Alzheimer disease.16 Some authors argue that because cerebral hypoperfusion and changes in the microcirculation may precede the onset of the clinical and neuropsychological changes of Alzheimer disease, and coexisting vascular and neurodegenerative changes are found in most patients with dementia, Alzheimer disease is in effect a vascular disorder.17 While not making that claim, an article in this issue of Stroke by Stopa and colleagues provides further evidence that vascular factors may play a role not only in the expression but also in the development of Alzheimer pathology. These investigators found that patients with Alzheimer disease had biochemical (substantial loss of arteriolar smooth muscle actin and deposition of β amyloid) and structural (increase arteriolar wall and luminal diameter) changes that lead to altered vasoreactivity, impaired autoregulation, and a greater degree of arterial pressure transmittal to the capillaries, predisposing them to microvessel damage, and that these changes were severe in the earliest stages, before the onset of major neuronal and interstitial degeneration.18 It is intriguing that, as this study implies, vascular factors involved in Alzheimer disease go beyond the traditional ones—stroke, white matter changes and vascular risk factors—and may be involved in the development of neurodegenerative changes. These findings broaden the concept of vascular cognitive impairment.
We need to understand the relationship between vascular factors and cognition better: mixed dementia may be the most common type of dementia, and unless we develop strategies to prevent and treat vascular cognitive impairment, the burden of cognitive decline will increase exponentially when the “vascular tsunami” arrives. But vascular cognitive impairment is preventable, at least in some people. As stroke researchers and clinicians, we must become familiar with the sophisticated clinical, imaging, neuropsychological, pathological, and statistical techniques that, as shown by the articles discussed in this editorial, are necessary to study the effect of vascular disease on cognition. This need is heightened by recent calls to make cognitive function an important outcome in future clinical trials of stroke therapies. For these reasons, it is fitting that Stroke has become an important forum for VCI research: a search of PubMed using the terms “cognitive impairment OR dementia AND stroke” revealed that the number of these publications increased from 58 in 1993 to 1997 to 163 in the last 5 years. We in the stroke community must lead to charge against VCI, otherwise our patients will lose.

Disclosures

None.

References


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