Assessing the Impact of Vascular Disease in Demented and Nondemented Patients

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That vascular diseases can induce dementia has been known for more than a century. For example, in the 19th and early 20th centuries, the major differential diagnosis of patients with dementia was neurosyphilis versus vascular disease. Also, it is a little known fact that Alzheimer himself wrote 5 articles on vascular dementia and that many of Alzheimer’s observations with respect to vascular dementia subtypes, and the effect of vascular disease on behavior and cognition, have withstood the test of time.1

For a few decades interest in vascular dementia (VaD) waned, but there is now keen interest in how cerebrovascular disease influences cognition. Beginning in the early 1990s, new algorithms for the diagnosis of VaD were developed and proposed.2,3 However, subsequent research has shown that the relationships between Alzheimer disease (AD) and VaD are far more complex than previously believed.4,5 For example, risk factors traditionally associated with stroke/VaD are now also considered risk factors for AD. Numerous longitudinal, population-based studies have demonstrated links between vascular risk factors, such as atherosclerosis,6 diabetes,7 hyperlipidemia,8 and stroke9 and the development of AD. Although AD and VaD are usually associated with different forms of cognitive impairments (eg, declarative memory and executive control, respectively), investigators have reported considerable overlap in the neuropsychological and the neuropsychological profiles of these syndromes.10,11

Much works needs to be done to better delineate and characterize these two common dementia syndromes. The role of vascular disease in producing various forms of cognitive impairment still needs to be better elucidated.

The purpose of this special topics project is to investigate how cerebrovascular disease influences the clinical presentation of patients with mild dementia and mild cognitive impairment (MCI). This issue of Stroke contains 6 articles,3 of which examined how neuroradiological evidence of vascular disease is associated with specific patterns of neuropsychological impairment in patients presenting with mild dementia and stroke. Libon and colleagues replicated their previous findings12 and provide further evidence that, irrespective of clinical diagnosis, a threshold regarding the total burden of MRI-leukoaraiosis is related to different patterns of impairment on tests of declarative and working memory. In a second article Swartz and coworkers studied a large cohort of AD and VaD patients, as well as older adults without dementia. They quantified total brain atrophy, leukoaraiosis, and strategic thalamic and cortical gray matter infarcts on MRI. Their results demonstrated that each neuroradiological alteration was associated with a specific type of neuropsychological deficit. Finally, Stebbins and colleagues examined a sample of nondemented, poststroke patients who were divided into groups presenting with either no evidence of cognitive impairment or evidence of impairment in at least 1 neuropsychological domain. Results based on voxel-based morphology showed that a reduction in thalamic volume was highly associated with the presence of impairment in at least 1 cognitive domain. Decreased volume in the cingulate gyrus and cortical gray matter also contributed to this model. Collectively, these 3 articles document differential patterns of neuropsychological impairment among patients, presumably with different neuropathological aetiologies (AD, stroke, leukoaraiosis).

Bowler and Hachinski13,14 have commented that vascular disease and risk factors for stroke are quite common in middle-aged and elderly individuals, and suggested that evidence of vascular disease can contribute to mild or prodromal cognitive impairment (MCI).15 Two articles in this special topics project examined this issue. Delano-Wood and colleagues used a rigorous methodology to identify a cohort of patients with MCI and then subsequently applied volumetric MRI to measure both deep and periventricular, white matter pathology. She and her colleagues found that, in MCI, increased deep white matter alterations were related to impaired performance on tests of executive control, information processing speed, and visual construction. In a population-based study, Wright and colleagues measured MRI-leukoaraiosis and infarctions in a group of MCI patients drawn from the Northern Manhattan Study. Similar to the findings reported by Libon and colleagues (this issue) and Price et al,12 a threshold effect for MRI-leukoaraiosis was demonstrated in that a specific volume of MRI-leukoaraiosis involvement was necessary to produce executive and psychomotor deficits. Also, compared to infarcts found in other
areas of the brain, frontal lobe infarcts were specifically associated with worse performance on tests of executive control. In sum, the pattern of findings linking neuroanatomical abnormalities as measured in vivo using MRI and concomitant neuropsychological impairment appears to be similar across individuals with mild dementia, MCI, or stroke.

Finally, Stopa and colleagues investigated a possible link between a breach in the blood-brain barrier and the presence of amyloid in patients with AD. These researchers studied frontal lobe arterioles (Brodman area 10) in AD and nondemented brains. Strong associations suggesting atrophy involving the smooth muscle contractile apparatus, increased vessel wall and lumen thickness, and the accumulation of vascular β-amyloid were found. These alterations were independent of Braak staging. These data suggest the intriguing possibility of a vascular route or mechanism leading to amyloid deposition in AD. Indeed, animal studies have demonstrated that elevated cholesterol intake increases the deposition of β-amyloid in the brains of transgenic mice expressing human amyloid precursor protein. Some have argued that an accumulation of β-amyloid may be both the cause and the consequence of cerebrovascular impairment.

Like a character from a Bronte novel, for many years VaD had been consigned to the orphanage of neglected neurological illnesses. The introduction of MRI technology, which first focused our attention on the presence of white matter disease in the brains of dementia patients, was the impetus for the eventual re-examination of assumptions about dementia, in general, and AD, in particular. It is our hope that these articles will add to the dialogue and generate new hypotheses aimed at understanding the specific brain-behavior relations associated with vascular disease in patients with dementia and patients at risk for developing cognitive impairment.

References


KEY WORDS: dementia vascular dementia
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Stroke. 2008;39:783-784; originally published online February 7, 2008;
doi: 10.1161/STROKEAHA.108.515569

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://stroke.ahajournals.org/content/39/3/783

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