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LETTER

Sharpening the tools for the assessment of vascular cognitive impairment

TO THE EDITOR

For decades, cognitive neuroscientists have attempted to unveil brain pathology through studying cognitive dysfunction in specific cognitive domains. In their recent article, Salvadori et al. venture further down this path. They summarize the current literature to conclude that there is “incomplete evidence” that a single cognitive test could differentiate underlying cerebral small-vessel disease from other causes of cognitive impairment.¹ While we support the utility of clinical signs to indicate potential underlying disease etiology, for example, by differentiating types of primary progressive aphasia, we believe the diagnosis of vascular cognitive impairment warrants an approach that extends beyond cognitive testing.

In the vast majority of patients, cerebral small vessel disease is accompanied by other types of neurodegenerative pathology. The co-occurrence of pathology increases rapidly with age. At the time of death, 78% of community-dwelling individuals have multiple types of pathology present in their brains, at least one of which often is of a vascular nature.² As a consequence, distinguishable clinical phenotypes merge into a more generalized cognitive deficit in older individuals. Patients who seek health advice for memory complaints are generally well into their seventies or eighties, rendering an etiological diagnosis on the basis of clinical phenotypes in these patients challenging at the very least. This notion led to the concept of “vascular cognitive impairment” (VCI), which replaced the different monocausal classifications, diagnoses, and terminologies that were used prior to describe cognitive impairment due to cerebrovascular disease. Prior descriptions, such as “multi-infarct dementia,” “subcortical dementia,” or “vascular cognitive disorders,” had mainly focused on the most severe end of the spectrum (i.e., dementia), whereas VCI captures the full range of cognitive changes due to cerebrovascular disease.³ Moreover, the concept of VCI allows for concomitant contributions of other diseases, like Alzheimer's disease (AD), to the phenotype of an individual patient with vascular brain injury. This is especially relevant in light of the expanding evidence for a reciprocal interaction of cerebrovascular disease and neurodegeneration.⁴ Involvement of the neurovascular unit, the blood-brain barrier, and vascular clearance mechanisms are just three examples of mechanisms illustrating the broad interface between vascular and AD pathology.

In light of these developments, we believe that assigning monocausal etiological diagnoses does not serve a patient well if multiple different types of pathologies are contributing to their cognitive complaints in concert. For example, a 75-year-old patient with cognitive impairment that is due both to AD and cerebral small-vessel disease might inadvertently be withheld (symptomatic or disease-modifying) treatment against either cause, while targeting *both* may be crucial for optimal treatment. Indeed, consensus guidelines for diagnostic assessment of VCI stress that “the order of the descriptive phenotypic terms relevant to patients should attempt to reflect the relative contribution of phenotypes present” (e.g., cognitive impairment due to small vessel disease and AD).^{5,6} This requires specific and easily obtainable markers of the different types and manifestations of vascular brain injury (e.g., through brain imaging), accompanied ideally by reference values from unselected age-matched populations. This process can be facilitated by existing and new collaborations that make use of comprehensive data from well-characterized representative cohorts.⁷ Only when markers of vascular brain injury are appreciated in the context of other neuropathology can we come to the correct diagnosis and tailored management for the majority of patients.⁸

The challenge before us is not only to identify patients with VCI, but also to determine the extent to which their overall cognitive deficits are due to vascular pathology. This will require further studies to establish the contribution of small-vessel disease, relative to other pathologies within the same individual. Neuropsychological assessment will be an important part of this diagnostic process, but the review by Salvadori et al. shows us that cognitive assessment is unlikely to achieve this on its own.

CONFLICTS OF INTEREST

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