Poststroke Cognition and the Fight Against the Hard Problem
Vascular Neurologists, Enter the Arena!

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n this issue of Stroke, Snaphaan and de Leeuw report on their results obtained from a systematic review on poststroke memory dysfunction.1 Of the 798 articles their search strategy identified, only 5 mentioned memory testing at different poststroke intervals, only 3 studies followed patients for at least 1 year, whereas the largest study contained only 196 patients. The results of the review allow at least 2 conclusions. One is drawn by the authors, in that memory dysfunction, a key element in the “diagnosis” of poststroke dementia, does not follow a linear time course after stroke. Leys et al came to a similar conclusion with regard to poststroke dementia, which was defined as any dementia after stroke.2 Short-term studies overdiagnose cognitive poststroke dysfunction. The finding warns us against making simple models of reality when it comes to poststroke cognitive impairment, and makes us aware that we should save our patients the embarrassment of early, false-positive predictions in this respect.

The second conclusion the review allows is that our current knowledge of poststroke cognitive impairment and its long-term development is rather poor, as illustrated by the review’s data on memory dysfunction, a key element in the diagnostic criteria for dementia. The poststroke dementia studies reviewed by Leys et al, although larger and with longer follow-up by some, did not provide any detail either except for the criteria that they used for the diagnosis.2 One may question the value of studying any cognitive details when we can already make diagnoses such as vascular dementia to characterize the condition. We, physicians, are keen on making a diagnosis because it will tell us something about disease cause, spectrum of clinical manifestation, progression, and hopefully also about treatment. Exactly for those reasons we should not be misled by the concepts of “vascular dementia” (VaD) or “poststroke dementia”; these are not diagnoses but concepts that have resulted from the procedure of medical consensus. The word diagnosis implies the “identification of the nature or cause of some phenomena”; it stems from the Greek dia, meaning ”through”, and gnosis, meaning “knowledge”.3 It is obvious that our “gnosis” about the relationship between the clinical syndrome defined as “dementia” and manifestations of cerebrovascular disease suffers too badly to allow the definition of a diagnosis. How can we reliably estimate a specific cause of a symptom complex if we don’t know the (time contingent?) spectrum of symptoms that follows from that specific cause? One might oppose that at least the syndrome of “subcortical ischemic vascular dementia” appears to be a homogeneous concept if not a diagnosis: cerebral small vessel disease causes lacunar infarcts and white matter hyperintensities, which are strongly associated with a homogeneous pattern of cognitive impairment.4 However, such brain lesions are also associated with the syndrome of Alzheimer disease, and the severity of dementia in subcortical ischemic vascular dementia is more strongly associated with the degree of hippocampal and cerebral atrophy than with the severity of white matter hyperintensities.4,5 So, even for this “specific” vascular type of dementia the difference between the sets of neuroimaging characteristics in use to differentiate between types of dementia is rather one of degree than of category. The same holds true for cardiovascular risk factors with respect to VaD and Alzheimer disease in general.6 Snaphaan and de Leeuw found prestroke medial temporal lobe atrophy, a predictor of Alzheimer disease, related to poststroke memory function.

The “diagnostic criteria” for VaD as defined in 1992 were “intended as a guide for case definition in neuroepidemiological studies . . . .”, but had not been validated.6 Now, almost 15 years on, they are still not validated, and the criteria were never revised. The need for uniform criteria at that time probably arose from the increasing number of studies in subjects with memory complaints, who visited an ever growing number of so-called memory clinics, and easy accessibility to CT scanning which allowed for specific causes of memory problems to be ruled out. Because most patients were older, vascular lesions were detected in varying kinds and degrees. This further increased after the wide introduction of MRI, and easy accessibility to CT scanning which allowed for specific causes of memory problems to be ruled out. Because most patients were older, vascular lesions were detected in varying kinds and degrees. This further increased after the wide introduction of MRI, and their strength as “independent risk factors” identified by statistical modeling. However, such procedures do not falsify the inappropriate a priori assumption about causality between these factors and cognitive impairment. Apart from the fact that we do not know the exact contribution of vascular lesions on CT or MRI to cognitive defects, we should be aware of possible relevant vascular factors causing functional rather than structural impairment, such as inadequate local cerebral blood flow, impaired cerebral autoregulation, metabolic disturbances, dysfunction on a cellular or molecular level, which may also influence cognition. Insight into the role of such factors in cognitive impairment.
is scarce. The current paucity of knowledge is a stumbling block in the formulation of valid hypotheses that should lead to rational therapeutic trials. If the clinical value of a diagnostic concept is measured by its facilitation of ultimate therapeutic potential, the concepts of VaD and poststroke dementia may be abandoned without regret. These concepts have grown into atavisms, they have outlived their relevance. Whether concepts such as vascular cognitive impairment or mild cognitive impairment will do the job is doubtful. Vascular cognitive impairment will probably fail because of absence of clarity because it contains in its definition the restriction of (undefined) degree of impairment. Although mild cognitive impairment may predict further cognitive decline, it is doubtful whether it is predictive of the cause of that decline.  

We were unable to confirm a useful predictive value of mild cognitive impairment subclassification in the distinction between the development of either Alzheimer disease or VaD.  

However, the use of this concept has its value in underlining the magnitude of the problem regarding cognitive dysfunction after stroke. We recently found that even after a first lacunar stroke ≈70% of patients had mild cognitive impairment at 3 months and 2 years (Rasquin SM, et al, unpublished data, 2006).  

So, where does that currently leave us? On applying the notion that when phenomena succeed each other in time they are more likely to be causally related than when found together in varying degrees at a certain moment, we should evaluate the influence of cerebrovascular disease on the development of cognitive impairment. Pragmatically, we should start by studying patients with proven disease, as is the case when they experience a first stroke. Extensive “cognitive profiling” should be done at regular time points taking various cognitive domains of disability into account, including tests for executive functions, accompanied by structural brain evaluation using various MRI modalities, and, whenever possible, tests for brain function, and molecular markers of disease activity. The extent of cognitive testing should not be limited by predefined but insufficiently validated criteria sets which are supposed to be more or less predictive of preassumed types of underlying disease. Follow-up should be long enough not to allow detection of time-related fluctuations, a possibility illustrated by the review of Snaphaan and deLeeuw, but also because patients expect counseling regarding the chance and degree of eventual cognitive consequences of their stroke not to be restricted to a few months. Poststroke prognosis in terms of survival, recurrent stroke, and overall functioning after stroke depends on a number of factors, an important one of which is stroke subtype. If eventual stroke subtypes can be characterized not only by their clinical manifestation but also by patterns of disturbances at a cell-biological level, it would not come as a surprise that this type of pathology may also predict cerebral dysfunction leading to a certain pattern of cognitive dysfunction, in which case we would be allowed to speak of a diagnosis. Over time, different clinical phenotypes within the often-used subtypes of cardioembolic, large vessel and small vessel infarcts may be identified. Within the small vessel subtype, for example, we can already distinguish between patients with a first, single, symptomatic lacunar infarct from those with concomitant silent lacunar lesions which is often accompanied by white matter hyperintensities. These types differ in prognosis, and probably have a different type of underlying small vessel pathology.  

It is obvious that long-term studies on cognition should be large enough to allow reliable estimates for various stroke subtypes, the more so because the more distinct the clinical phenotype, the lower its incidence will probably be. This would not make such studies an easy objective, but this “splitting” policy will without doubt bring us closer to our aim than the so far failed “lumping” concepts such as VaD and multi-infarct dementia. Funding bodies need to be convinced of the importance to fund such projects beyond the usual limit of 3 or 4 years. Not only observational studies but also future secondary stroke prevention trials should include cognitive evaluation as an outcome measure, as was suggested before in this journal.  

So far, most neurologists have considered cognitive impairment as a soft end point which remained below their threshold of interest. However, for stroke victims and their families it often constitutes the “hard problem” in daily life after a stroke.  

Now it is time for vascular neurologists to enter the arena in the fight against cognitive impairment. Studies as indicated above may eventually clarify the role of vascular factors in cognitive decline, which may pave the way for a more rational therapeutic approach to the problem. Until then, the review of Snaphaan and deLeeuw serves to remind us of the need of vascular neurologists’ participation in this fight.

Disclosures

None.

References


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