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Vascular cognitive impairment: Advances and trends

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ABSTRACT

The presence of vascular neurocognitive impairment (whatever the severity) is always associated with a functional impact and increased risk of dependency and institutionalization. However, vascular cognitive impairment remains underdiagnosed, and the mechanisms underlying post-stroke cognitive disorders are still poorly understood. However, the advent of new criteria and a standardized international neuropsychological battery is expected to lead to improved diagnosis and management, and the development of novel techniques (such as brain imaging and amyloid PET) should improve our understanding of the mechanisms underlying vascular cognitive impairment and help to identify potential targets for therapy.

1. Introduction

Vascular cognitive impairment (VCI) refers to a heterogeneous group of conditions in which vascular lesions cause or contribute to impaired cognitive function. In terms of severity, VCI ranges from mild neurocognitive disorder (mNCD) to dementia (now referred to as "major NCD"), and encompasses vascular dementia (VaD), mNCD and mixed dementia [1,2]. Even though VCI is potentially preventable, it is the second most prevalent cause of cognitive impairment, and yet, it remains underdiagnosed. Diagnosis of VCI may be challenging, as it is observed both post-stroke and during the etiological work-up for cognitive impairment, which involves two different settings: the stroke unit (or post-stroke outpatients clinic) [3] and the memory clinic [4], respectively. Two critical points have to be emphasized: (i) VCI may be observed in patients with no history of stroke (more frequently the case than post-stroke VCI); and (ii) post-stroke cognitive impairment is not always due to a pure vascular lesion, as a significant proportion of cases are related to other types of concomitant lesions (especially those caused by Alzheimer's disease). Yet, thanks to recent technical and normative progress, medical knowledge and patient management in this area are changing rapidly. The present review focuses on recent developments influencing the diagnosis of VCI.

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However, as patterns of impairment in the various cognitive domains have already recently been reviewed, they are not detailed here [5].

2. Prevalence of vascular cognitive impairment

Cognitive complaints and behavioral changes may reveal VCI even in the absence of acute symptoms leading to a diagnosis of stroke; in fact, this is probably by far the most frequent situation. The Rotterdam Scan Study [6] showed that incident infarcts on follow-up magnetic resonance imaging (MRI) were associated with a stroke episode in only 11 out of 86 cases (or around one stroke episode per seven incident infarcts). These so-called ''silent infarcts'' constitute a major cognitive risk factor. Thalamic silent infarcts are predominantly associated with impaired memory performance, and infarcts in other locations affect action speed [6]. To following on from the recent publication of epidemiological studies [7], here is a brief review of the prevalence of VCI in both post-stroke settings and non-stroke patients assessed for cognitive complaints.

2.1. *Post-stroke cognitive impairment*

Post-stroke neurocognitive impairment has been documented by a large number of studies, most of which were focused on major post-stroke NCD (post-stroke dementia). Systematic review and meta-analysis [8,9] have shown that the prevalence of major post-stroke NCD ranges from 7% to 67.3%, depending on the study setting (hospital- or population-based studies), stroke type (ischemic or hemorrhagic), frequency of pre-stroke dementia, frequency of recurrent stroke and the post-stroke interval [9]. The presence of post-stroke NCD (regardless of severity) constitutes an independent risk factor for dependency and institutionalization [10,11], with more than half of all stroke survivors experiencing post-stroke NCD (mild in two-thirds of cases and major in one-third) [12]. The marked interstudy heterogeneity is mainly due to the different thresholds used for performance impairment and, to a lesser extent, the differences in rates of recurrent stroke and age profiles [12].

2.2. *Etiological work-up of cognitive impairment*

VaD is the second most common cause of dementia, with a prevalence of around 1.5% in community-dwelling over-65s [11,13,14] and a frequency ranging from 15% to 25% in autopsy studies [15]. Mixed lesions (vascular lesions combined with Alzheimer's lesions and, to a lesser extent, Lewy bodies) have a prevalence of around 40% in systematic autopsy studies [16–22], whereas vascular mNCD has a prevalence of 2.6%, which is around twice that of VaD observed in the Canadian Study of Health and Aging [11]. Importantly, a diagnosis of mNCD exposes the patient to an increased risk of dependency and death [11,23]. Yet, the prevalence of VaD contrasts with the low reported rates of the diagnoses in memory clinics (according to the French National Alzheimer's Disease Plan) [24] and even in studies of patients with early-onset dementia [25]. Thus, these findings suggest that VCI is underdiagnosed. Moreover, the underdiagnosis of mNCD is probably even more marked.

3. Toward a harmonized diagnosis of VCI

As the above-mentioned considerations suggest that VCI is significantly underdiagnosed in both post-stroke and memory clinic settings, to improve the characterization of VCI and refine its diagnostic criteria, an international group convened by the US National Institute of Neurological Disorders and Stroke (NINDS) and Canadian Stroke Network (CSN) [26] has elaborated a new, standardized reference battery of clinical, cognitive, behavioral and neuroimaging data. One major challenge in the assessment of VCI is the development of reliable, accurate (both sensitive and specific) instruments that reflect the presence and severity of cognitive and functional impairments due to vascular brain lesions. A large proportion of the reference protocol concerns neuropsychological assessments, which require linguistic and cultural adaptation and harmonization with the tests commonly used in each country. Several groups around the world are now using the NINDS–CSN battery to examine the characteristics and determinants of VCI. Indeed, the Groupe d'évaluation cognitive de la pathologie vasculaire (GRECOGVASC) Study Group adapted and normalized the NINDS–CSN battery for French-speaking subjects in 2007 [27,28], and is now examining the prevalence and determinants of post-stroke cognitive impairment in a clinical study [NCT01339195]. In parallel, several methodological issues have been examined, including the analysis and interpretation of cognitive scores [29], and the sensitivity of screening tests [30,31]. The International Society of Vascular Behavioural and Cognitive Disorders (VasCog) recently proposed a new set of diagnostic criteria for VCI [32] (see below for more details).

3.1. *Cognitive assessment: the standardized international battery and additional assessments*

The GRECOGVASC battery [27] comprises 19 tests and questionnaires (Table 1), and explores five cognitive domains: instrumental abilities (language, visuospatial and visuoconstructive skills); episodic memory (verbal and visual); executive function and speed; assessment of behavioral changes; and anxiety and depressive symptoms. There are also tests for cognitive impairment and disability. Two tests were added to the original battery: a test of reaction time; and a questionnaire exploring behavioral dysexecutive disorders. The reaction time test comes from a previously validated protocol based on the observation that action-slowing is frequently seen after a stroke and is related to outcomes [43]. The test explores action-slowing independently of hemiplegia and determines the origin of the slowing (attentional deficit vs. sensorimotor slowing). The Behavioral Dysexecutive Syndrome Inventory included in the GRECOGVASC battery is an adaptation of the Inventaire du syndrome dysexécutif comportemental (ISDC) [44], which was added because pure executive behavioral disorders with no executive function deficit are observed in about 10% of stroke patients [40]. It should be noted that this questionnaire has validated