

## MCI SERIES—INTRODUCTION

# Advancing the science of vascular cognitive impairment: How can we catalyze progress?

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It is not generally appreciated that Alzheimer did not think his case descriptions of Auguste and Johann represented his best work (see Libon, Price, Heilman, & Grossman, 2006, for a review). Many also do not recognize that Alzheimer wrote many more papers on vascular dementia (VaD) than pre-senile dementia, adeptly anticipating many of the current distinctions between “cortical” and “subcortical” dementia (see Libon et al., 2009, for a discussion). Despite this, and because of a variety of scientific, as well as sociopolitical events, VaD has historically received considerably less attention than Alzheimer’s disease (AD) in the clinical literature.

In the 1990s, Hachinski and colleagues (Bowler, Munoz, Merskey, & Hachinski, 1998; Bowler & Hachinski, 1995; Hachinski, 1990, 1991, 1992, 1994, 1997; Hachinski & Munoz, 1997; Hachinski & Norris, 1994) spearheaded an important movement towards a better understanding of the links between vascular disease, brain health, and cognition. This group of researchers has fervently argued against the “Alzheimerization” of the dementia diagnosis as a whole, and, accordingly, has called for greater international attention focusing on how best to define, diagnose, and identify early stages of vascular-related cognitive impairment, with the overarching goal of optimizing prevention and treatment.

There is now a growing awareness of the exceptionally high incidence and increasing prevalence of vascular risk and disease in the global aging population. In parallel with this greater recognition, research focusing on the relationships between vascular disease and concomitant cognitive impairment has burgeoned at an unprecedented pace. In fact, alarming statistics demonstrate that one in three older adults in the United States will sustain a stroke, become demented, or both (Seshadri et al., 2006). There is also increasing recognition that vascular disease plays a role in the majority

of cases of cognitive impairment and dementia (Schneider, Arvanitakis, Bang, & Bennett, 2007). Importantly, findings in the literature have demonstrated that the presence of vascular risk factors (e.g., hypertension, diabetes), as well as subclinical ischemic events, such as silent strokes and subtle changes in the white matter, can lead to accelerated cognitive impairment across the aging spectrum (see Black, Gao, & Bilbao, 2009, for a review).

Given the critical need for enhanced detection of early, milder forms of cognitive impairment when prevention and treatment can be most effectively initiated, a primary focus has been to gain a better understanding of vascular cognitive impairment (VCI). Although no formal criteria have yet been delineated, VCI is a clinically useful and relevant clinical concept that encompasses the spectrum of impairment and disability in the context of vascular disease, ranging from mild cognitive impairment to VaD. In this context VCI seeks to identify “brains-at-risk” (Bowler & Hachinski, 1995; Hachinski & Bowler, 1993).

Work investigating VCI has evolved considerably over the past few years, with VCI increasingly recognized as a highly prevalent syndrome in the context of aging (see Bowler & Gorelick, 2009, for a review). Currently, research regarding VCI is centered on several primary themes, most especially (1) how best to operationally define VCI and (2) the investigation of the interaction between cerebrovascular disease and other causes of cognitive impairment, particularly the gray matter alterations that typify AD (Bowler & Gorelick, 2009). Indeed, it is increasingly recognized that ischemia and vascular disease can predispose, potentiate, and perpetuate AD-related degenerative neuropathophysiology (de la Torre, 2002; Girouard & Iadecola, 2006).

Despite the increased interest in VCI, many issues regarding the brain–behavior relationships that underlie VCI remain poorly understood. The challenges associated with VCI are particularly important in the context of an increasingly aging population that is growing at an exponentially fast

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pace. Perhaps the largest challenge is the frequently disconnected manner in which VCI research has been conducted and disseminated. Indeed, recently, Hachinski (2007) argued that work in VCI has occurred in “disciplinary isolation,” and he has called for a new approach wherein researchers must “successfully confront the looming epidemic of cerebrovascular disease” (p. 1396), as well as its far-reaching and often disastrous implications. To this end, Hachinski has formulated and put forth the “Triple T Approach” which calls for *transdisciplinary*, *translational*, and *transactional* research in order to enhance our awareness and conception of the natural history of VCI, as well as associated underlying biological and neurological mechanisms.

In the spirit of Hachinski’s Triple T Approach to understanding and characterizing VCI, coupled with his recent call for a “new breed of leaders” to skillfully and successfully meet the challenges of this important endeavor, this special issue of *JINS* features multidisciplinary work by a collaborative, international group of scientists who, as a primary focus of their research, are investigating important issues related to vascular contributions to cognitive impairment. Collectively, these studies speak to the challenges inherent in understanding VCI, and they underscore the need for future pioneering efforts to elucidate and clarify the complex role that vascular risk and disease play in cognitive impairment. Ultimately, advancing the science of VCI research will have tremendous clinical implications by providing us with a better opportunity to recognize, prevent, and treat vascular risk factors, which will, in turn, dramatically decrease the risk for adverse outcomes.

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