



# Gait and Cognitive Declines in Dementia—Double or Nothing

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The aging of populations worldwide with an attendant increase in geriatric syndromes such as dementias has spurred interest in developing clinical approaches to identifying cognitive decline early in order to improve management of older adults presenting with cognitive concerns. While effective dementia therapies have not yet resulted, there has been a recent explosion of knowledge regarding the nature and clinical course of dementias that has led to the identification of noncognitive markers of dementia.<sup>1,2</sup> An extensive body of research demonstrates that gait performance is impaired early during dementia.<sup>1,2</sup> The study from Collyer and colleagues<sup>3</sup> in this issue highlights the clinical relevance of identifying gait markers of dementia in older individuals.

Collyer and colleagues report the associations between a dual decline in gait speed and cognition with risk of dementia in 16 885 participants from the ASPREE (ASpirin in Reducing Events in the Elderly) study, a double-masked, randomized, placebo-controlled trial of low-dose aspirin in older adults conducted in the US and Australia from 2010 to 2017.<sup>3</sup> Gait speed and multiple measures of cognition (global cognition, memory, processing speed, and verbal fluency) were assessed in all participants at baseline and annually until closeout. Participants were classified into 4 groups based on their pattern of decline on gait speed and cognitive tests over the study period: (1) dual decline in gait and cognition (dual decliners); (2) gait decline only; (3) cognitive decline only; and (4) nondecliners. Cognitive decline was defined as being in the worst tertile of annual change on the selected cognitive tests. Gait decline was defined as decline in gait speed of 0.05 m/s or more per year. Dementia status was adjudicated by an expert panel. The trial randomization group was not included in the analysis as aspirin did not reduce risk of dementia in the parent study. Compared with nondecliners, risk of dementia was higher in dual decliners. Furthermore, dual decliners had a higher risk of dementia than those with either gait or cognitive decline alone. These findings are in line with smaller cohort studies that have shown the dual decliner phenotype to be predictive of cognitive decline.<sup>1,2</sup>

What is the significance of the findings of the study by Collyer and colleagues? Gait speed has been termed a geriatric vital sign that predicts not only dementia but also other geriatric syndromes such as falls, frailty, and disability.<sup>1,4</sup> Gait speed measurement is simple, brief, and does not require elaborate equipment or training to administer. The Canadian Consensus Conference on Diagnosis and Treatment of Dementia (CCCDTD) has recommended testing gait speed in clinics in all patients with cognitive concerns if time and resources permit.<sup>2</sup> Despite the established predictive validity of gait assessments for geriatric syndromes,<sup>1,2,4</sup> an implementation barrier for routine gait assessment in clinics exists that needs to be addressed to improve care of older patients. Routine annual assessments of gait speed and cognition will need to be established in clinical settings to identify dual decliners. One possibility is that these assessments could be done during the Medicare Annual Wellness Visit, which has required cognitive and fall risk screening elements. Meanwhile, the dual decliner phenotype will be useful in future research studies to define populations at high risk for dementia. Other single time point assessments that combine cognitive and motoric elements can also be considered in clinical settings to detect high-risk older patients. For instance, the Motoric Cognitive Risk syndrome is a clinical prodementia phenotype combining self-reported cognitive complaints with slow gait that can be easily implemented in clinics and has been shown to predict dementia.<sup>5</sup> The CCCDTD panelists recommended the use of dual task walking tests (eg, walking while reciting alternate letters of the alphabet<sup>4</sup>) in memory clinics to identify among individuals with mild cognitive impairment syndrome (MCI) those at higher risk of converting to dementia.<sup>2</sup>

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Traditionally, gait dysfunction has not been considered an early clinical feature in patients with Alzheimer disease and is seen more as a marker of non-Alzheimer pathology.<sup>1</sup> However, systematic longitudinal studies and finer-grain analysis of gait performance in the context of cognitive decline is calling this view into question.<sup>1,2,5</sup> For instance, both neurological gait abnormalities and quantitative gait dysfunction were reported in older individuals with amnesic MCI, a precursor of Alzheimer disease.<sup>1</sup> Postmortem Alzheimer pathology in the brain stem in older adults with and without dementia was associated with presence of antemortem clinical gait abnormalities.<sup>6</sup> Among dual decliners in the current study,<sup>3</sup> risk of dementia was highest in the group with memory impairment (an early Alzheimer marker), although the risk of tautological redundancy was present given that cognitive tests being used in prediction were also used for diagnosis of dementia. Cognitive and gait dysfunction is also linked to vascular and Parkinsonian pathologies.<sup>1</sup> Hence, multiple pathologies may underlie dual declines in older adults and should be examined in clinico-pathological and biological studies.

Finally, are dual declines in gait and cognition the cause or consequence of dementia pathology? The evidence suggests that both explanations are likely. A causal role is suggested by observations that regular exercise to improve mobility reduces the risk of dementia in epidemiological studies, although the evidence from randomized clinical trials is not as clear cut.<sup>7</sup> Hence, another direction suggested by the current findings is in developing interventions to improve walking abilities in individuals with dual declines with the aim of reducing downstream risk of cognitive decline.

#### ARTICLE INFORMATION

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