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Review

Walking ability to predict future cognitive decline in old adults: A scoping review

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ABSTRACT

Early identification of individuals at risk for cognitive decline may facilitate the selection of those who benefit most from interventions. Current models predicting cognitive decline include neuropsychological and/or biological markers. Additional markers based on walking ability might improve accuracy and specificity of these models because motor and cognitive functions share neuroanatomical structures and psychological processes. We reviewed the relationship between walking ability at one point of (mid) life and cognitive decline at follow-up. A systematic literature search identified 20 longitudinal studies. The average follow-up time was 4.5 years. Gait speed quantified walking ability in most studies ($n = 18$). Additional gait measures ($n = 4$) were step frequency, variability and step-length. Despite methodological weaknesses, results revealed that gait slowing (0.68–1.1 m/sec) preceded cognitive decline and the presence of dementia syndromes (maximal odds and hazard ratios of 10.4 and 11.1, respectively). The results indicate that measures of walking ability could serve as additional markers to predict cognitive decline. However, gait speed alone might lack specificity. We recommend gait analysis, including dynamic gait parameters, in clinical evaluations of patients with suspected cognitive decline. Future studies should focus on examining the specificity and accuracy of various gait characteristics to predict future cognitive decline.

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1. Introduction

1.1. Rationale

The increase in the number of old adults nearly parallels the incidence of age-associated dementia worldwide (Ferri et al., 2005; Prince et al., 2013). Data suggest that the pathophysiological processes of dementia may start several years or even decades before the eventual diagnosis (Sperling et al., 2013; Morris et al., 2012). Patients progress from a preclinical phase during which the disease might have already started in the brain without overt clinical symptoms, followed by a period characterized by the presence of Mild Cognitive Impairments (MCI), culminating in a diagnosis of dementia (DeCarli et al., 2012). In the absence of a cure, key strategies of disease management include early diagnosis, delaying disease onset, and a slowing of disease progression (de la Torre, 2010; Imtiaz et al., 2014). Therefore, identifying markers that predict dementia is a major subject of current interest (Li and Zhang, 2015; Panza et al., 2015).

Prediction of dementia is often studied in the context of MCI (Petersen et al., 2001), which is a transitional state between a cognitively intact condition and dementia (DeCarli, 2003). Patients with MCI have cognitive dysfunctions beyond those expected as a result of normal aging, yet the level of impairment is not severe enough to compromise the ability to perform activities of daily living (Petersen et al., 1999). Even though the published values vary, a recent review analyzing population data (>300 participants) estimated the prevalence of MCI to range from 16 to 20% in patients over age 60. Approximately 10 to 15% of these patients develop dementia annually (Roberts, 2013). This conversion rate is high, making it important to differentiate between patients who will develop dementia and those who will remain cognitively fit. Early identification of patients at risk for dementia might help to select those individuals who would benefit most from future interventions to delay disease onset and slow the progression of neurodegeneration (Friedrich, 2014).

1.2. Biomarkers in prediction models for dementia

Biomarkers are used to identify pre-dementia symptoms and can be broadly classified as (1) cognitive markers (test scores measuring cognitive functioning such as memory and executive function) and (2) biological markers (such as measures derived from cerebrospinal fluid and brain imaging). The most accurate predictors are memory tasks measuring long-delay free recall (Gomar et al., 2011; Schmand et al., 2010; Landau et al., 2010; Fleisher et al., 2008; Gallagher et al., 2010), the cerebrospinal fluid (CSF) markers Aβ1−42/t-tau ratio (Gomar et al., 2011; Vos et al., 2012; Hansson et al., 2006; Mattsson et al., 2009), and volumes of the hippocampal and entorhinal cortices (Gomar et al., 2011; Devanand et al., 2007; Vos et al., 2012; Prestia et al., 2013; Ewers et al., 2012). However, single predictors seem to be insufficiently sensitive to predict conversion from MCI to dementia. Therefore, prediction models ultimately employ a combination of markers (Shaffer et al., 2013). Nevertheless, such predictions are far from perfect, as age, duration of follow-up, subtype of MCI diagnosis, degree of cognitive decline (early versus late stage of MCI), and outcome (e.g., AD, mixed dementia) all seem to affect conversion rates (Schmand et al., 2010; Egli et al., 2015; Espinosa et al., 2013). For example, a recent study showed that both neuropsychological assessment and MRI variables can predict conversion to AD with 63–67% classification accuracy in patients with MCI both younger and older than 75, while CSF biomarkers reached this rate only in patients younger than 75 years old (Schmand et al., 2010). A systematic review about risk prediction models for dementia concluded that sensitivity and specificity values vary broadly between studies, (Area Under the Curve ranging from AUC = 50 to AUC = 87). In particular, specificity is low in numerous prediction models (Stephan et al., 2010), complicating the clinical use of such models.

Taken together, these observations show that it remains a persistent challenge and should be a research priority to develop dementia prediction models that ultimately employ a combination of markers to differentiate between old adults who will and who will not develop dementia. Current prediction models show low to moderate predictive ability with large variability, making it necessary to explore new markers. A possible candidate is motor function, in which walking ability may serve as a potential marker in the prediction of cognitive decline (Ambrose et al., 2010; Montero-Odasso et al., 2012b; Verghese et al., 2002).

1.3. Walking ability as a predictor of cognitive decline

The original observation of a correlation between motor and cognitive impairments was reported nearly two decades ago. The data suggested that motor slowing (e.g., low walking speed) precedes cognitive decline in healthy older adults (Camicioli et al., 1998), a finding substantiated by the relationship between reductions in gait function and the development of dementia (Richards et al., 1993). Numerous cross-sectional and longitudinal studies have recently confirmed these initial findings (Callisaya et al., 2015; Gale et al., 2014; Ijmker and Lamoth, 2012; Scherder et al., 2007; Verghese et al., 2013).

Viewing walking as a complex task could increase its validity to serve as a marker for early cognitive decline. Indeed, imaging and brain stimulation studies suggest that higher brain centers are involved in the planning and execution of normal human locomotion (Christensen et al., 1998) and balance (Taube et al., 2015; Papegaaij et al., 2014). The widespread network of brain areas that control walking involves regions responsible for attentional, executive and visuospatial functions as well as areas needed to per-