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Review article

What can gait tell us about dementia? Review of epidemiological and neuropsychological evidence

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ABSTRACT

Background: Cognitive impairment and gait disorders in people over the age of 65 represent major public health issues because of their high frequency, their link to poor outcomes and high costs. Research has demonstrated that these two geriatric syndromes are closely related.

Methods and results: We aim to review the evidence supporting the relationship between gait and cognitive impairment, particularly focusing on epidemiological and neuropsychological studies in patients with Mild cognitive impairment, Alzheimer's disease and Vascular dementia. The review demonstrates that gait and cognition are closely related, but our knowledge of their interrelationship is limited. Emerging evidence shows that gait analysis has the potential to contribute to diagnosis and prognosis of cognitive impairment.

Conclusions: An integrated approach for evaluating these major geriatric syndromes, based on their close relationship, will not only increase our understanding of cognitive-motor interactions, but most importantly may be used to aid early diagnosis, prognosis and the development of new interventions.

1. Introduction

Cognitive impairment and gait disorders in people over the age of 65 represent major public health issues because of their high frequency, their link to poor outcomes and high costs [1].

Gait changes with ageing [2]. A gait disorder is present when the patient walks even more slowly than expected for age, or when there are qualitative abnormalities of locomotion, such as disturbances of the initiation of gait or balance [2]. Gait dysfunction and gait abnormality are terms describing deviation from normal walking, but not to the degree of a recognised gait disorder. Motor dysfunction is a broader term, including not only impairment in gait, but other motor skills as well.

We describe the evidence supporting the relationship between gait and cognition, possible shared pathomechanisms and the gait changes associated with Mild Cognitive Impairment (MCI) and Dementia. We review the evidence suggesting that gait performance is a predictor of adverse outcomes, particularly cognitive decline and conclude by outlining the role of interventions and future directions in this growing area of research.

2. Methods

We searched PubMed from 1970 to October 2016 for the following terms and keywords: 'gait'; 'walking'; 'gait analysis'; 'gait disorder'; 'gait variability'; 'gait measures'; 'mobility'; 'ageing'; 'cognition'; 'cognitive impairment'; 'dementia' and 'older adults'. 1203 titles and abstracts were screened and we then reviewed 171 full text papers. We included epidemiological and neuropsychological studies that investigated the relationship between gait and cognition in healthy older adults; as well as in people with MCI; Alzheimer's disease (AD) and Vascular dementia (VD); particularly when caused by small vessel disease (SVD). Studies in disorders associated with well-characterised motor symptoms were excluded; as these are beyond the scope of the review. We identified additional studies by hand-searching reference lists (Fig. 1).

3. Results

3.1. Relationship between gait and cognition

Human gait is considered a complex, non-linear process during which the locomotor system incorporates input from the cerebellum, the motor cortex, and the basal ganglia, as well as feedback from visual, vestibular and proprioceptive sensors [3]. Converging evidence suggest that gait also relies on a higher order cognitive control [4]. Because intact walking requires coordinated function

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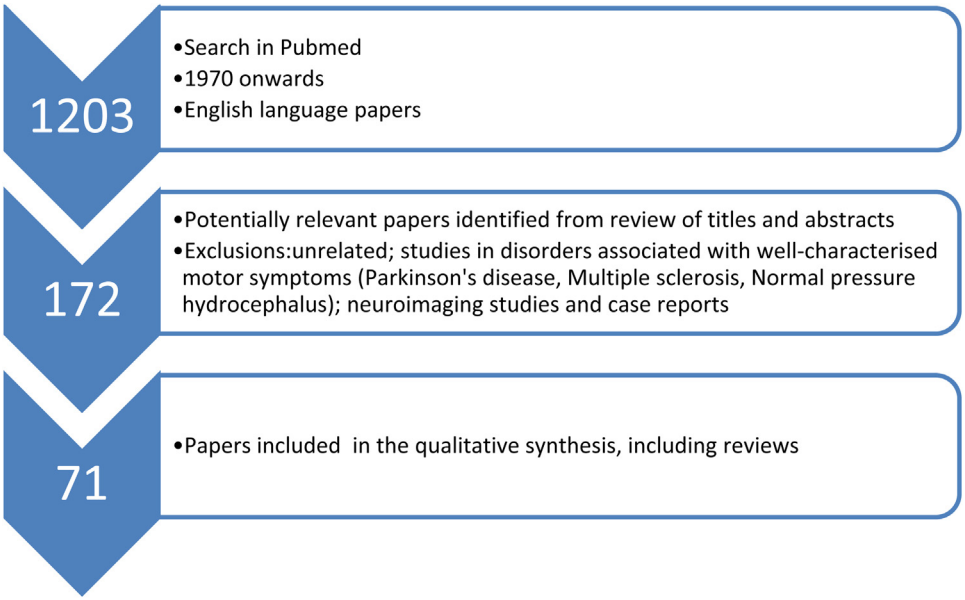

Fig. 1. Main search strategy.

of multiple regulatory circuits, deviation from the normal walking pattern is a sensitive marker of failure in any of the circuits.

The cortical involvement in gait control is highlighted by studies using the dual task paradigm, which is based on the hypothesis that two simultaneously-performed tasks interfere if relying on identical functional subsystems. The dual task effect, which represents the change in gait pattern between dual and single task performance or change in absolute performance under dual task conditions, is observed in healthy adults, but it increases with age and in subjects with cognitive impairment. The magnitude of the effect is directly related to the degree of cognitive impairment [5–8]. It has been postulated that impaired cognition results in reduced attentional resource allocation, which can compromises gait stability [9].

3.2. Possible shared pathomechanisms underlying the relationship between gait and cognition

3.2.1. Neurodegeneration

Neurodegeneration in multiple systems leading to coexisting motor and cognitive symptoms is a mechanism common to several neurological disorders [10]. Little is known about the underlying pathophysiology of the motor symptoms in early AD. Later, when the degenerative process spreads to the frontal areas of the brain, gait apraxia is a common finding [11]. Contrary to the original view of AD as involving mainly cortical degeneration, systematic pathological studies have found considerable involvement of brainstem nuclei, which by means of their widespread afferent projections can modulate disparate brain regions to generate integrated motor and cognitive responses [12]. Degeneration in multiple systems is thus likely to underlie the motor symptoms in AD.

3.2.2. Inflammation

Another pathological process, common to ageing and associated with decline in gait speed and memory impairment, is low-grade systemic inflammation characterised by increased proinflammatory markers [13]. Inflammation is present in most neurological diseases manifesting with impairment of mobility and cognition: it has been implicated in development and progression of AD. Elevated inflammatory markers and activated microglia are found in both disorders [13,14], as it is in vascular cognitive impairment [15]. Neuroinflammation, manifesting as microglial activation, may lead to increased oxidative stress, pathologic synaptic pruning and impaired neuroplasticity in key brain regions sub-serving cognition and motor function.

3.2.3. Vascular

Of particular importance is vascular burden [13,16]. While vascular damage is the main causal factor in VD, it also plays a key role in normal ageing and in the development and progression of cognitive, affective and motor symptoms associated with other disorders [16]. Vascular risk factors, including hypertension, diabetes, hypercholesterolemia and atrial fibrillation, among others, confer increased risk for developing of not only VD but also AD, with mixed pathologies present in a significant proportion of cases [17]. Vascular risk factors are associated with white matter changes, which are associated with gait slowing (defined as gait velocity <0.5 m/s) in cognitively healthy older adults [18].White matter changes also represent a marker for current and future cognitive and gait impairment [19,20].

A possible unifying underlying pathological mechanism could be the age-related diffuse micro-damage to small vessels, which compromises the integrity of the frontal-subcortical circuits involved in the cortical control of motor behaviour and in complex cognitive functions [16]. While there is an empirical association between vascular risk factors, cognitive and gait impairment, it remains difficult to identify the biological mechanisms linking these conditions.

3.3. Relationship between neuropsychological performance and gait

3.3.1. Cognitively healthy older people

In healthy older adults, there is evidence of a small positive association between gait and *global cognition* (12 studies, d = 0.12, 95% CI = 0.09–0.15, $p < 0.001$) [21]. In this *meta*-analysis, most studies used speed of gait as the outcome measure, while the most common test of global cognition was the MMSE (Mini Mental State Examination, with a score below 24 denoting cognitive impairment).

Neuropsychological studies have consistently demonstrated a positive association between *executive functions* and gait measures