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Review article

The brain map of gait variability in aging, cognitive impairment and dementia—A systematic review

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ABSTRACT

While gait variability may reflect subtle changes due to aging or cognitive impairment (CI), associated brain characteristics remain unclear. We summarize structural and functional neuroimaging findings associated with gait variability in older adults with and without CI and dementia.

We identified 17 eligible studies; all were cross-sectional; few examined multiple brain areas. In older adults, temporal gait variability was associated with structural differences in medial areas important for lower limb coordination and balance. Both temporal and spatial gait variability were associated with structural and functional differences in hippocampus and primary sensorimotor cortex and structural differences in anterior cingulate cortex, basal ganglia, association tracts, and posterior thalamic radiation. In CI or dementia, some associations were found in primary motor cortex, hippocampus, prefrontal cortex and basal ganglia.

In older adults, gait variability may be associated with areas important for sensorimotor integration and coordination. To comprehend the neural basis of gait variability with aging and CI, longitudinal studies of multiple brain areas are needed.

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1. Introduction

While mean performance has been used to study the effects of age on movement and cognition (Beauchet et al., 2016), subtle aspects of development and aging are thought to be better captured by measures of intra-individual variability (Nesselroade, 1991). Performance tends to become increasingly consistent through childhood and adolescence, but then becomes more inconsistent with aging (Williams et al., 2005). In aging, intra-individual variability in speed-related performance, especially during neuropsychological tasks, is a known strong predictor of cognitive decline, brain aging and risk of neurodegenerative disease (MacDonald et al., 2006; Bielak et al., 2010).

Mean performance during mobility and gait-related tasks is strongly associated with cognitive decline and predicts cognitive impairment and Alzheimer's disease (Beauchet et al., 2016). Step-to-step gait variability, measured as fluctuations in the timing (i.e. temporal gait variability) and spacing (i.e. spatial gait variability) of steps, is a major predictor of fall risk and an indicator of impaired executive function and movement control (Hausdorff et al., 2009). As gait variability seems to reflect subclinical changes relevant to aging, cognitive decline and impairment, exploring the structural and functional alterations in the brain that are associated with gait variability might provide clinical and mechanistic insights. However, no systematic review has addressed the relationships between neuroimaging aspects of brain structure and function with gait variability, in usual aging, cognitive impairment or dementia.

Our goal is to review original research examining the relationship between neuroimaging indicators of brain health and gait variability in older adults with and without cognitive impairment and dementia, and to summarize prominent relationships for specific brain regions. While reviewing the literature, we identified gaps in knowledge and challenges in study design, neuroimaging approaches and gait variability assessment that should be addressed in future research.

2. Methods

2.1. Literature search

We searched existing literature through November 2016 using PubMed and PsycINFO databases, as well as references from published manuscripts. Studies were considered eligible if they were based on 1) original data on the relationship between neuroimaging measures of brain structure and function and gait variability, 2) included adults aged 50 and older, and 3) were written in English. Search terms included 1) older adults OR older persons OR older individuals OR elderly OR senior OR aged OR 50 years and older; 2) brain structure OR brain activity OR brain function OR brain metabolism OR neuroimaging marker OR cerebral perfusion OR cerebral blood flow OR amyloid OR gray matter OR white matter OR infarct OR leukoaraiosis OR default mode network OR functional connectivity OR magnetic resonance imaging OR diffusion tensor imaging OR near-infrared spectroscopy OR brain stimulation OR magnetoencephalography OR magnetic resonance spectroscopy; 3) gait variability OR spatiotemporal variability OR step length variability OR stride length variability OR step width variability OR stride width variability OR step time variability OR stride time variability OR stance time variability OR swing time variability OR single support time variability OR double support time variability OR step to step variability OR lap time variation. Studies were initially screened by title and abstract. All sources were merged to form a final listing.

2.2. Selection of studies

One author (QT) performed the initial search and two authors (QT and SAS) evaluated all articles based on title and abstract. All articles in which the two authors agreed on eligibility were included. There were five articles, all in persons with Parkinson disease, that used brain stimulation as an experimental maneuver to assess effects on gait variability (Hausdorff et al., 2009; Fasano et al., 2010; Thevathasan et al., 2012; Kaski et al., 2013; Vallabhajosula et al., 2015). After discussion, these studies were felt to deserve a separate evaluation and discussion due to the unique pathology and gait characteristics of the disease. In order to focus on older adults without diagnosed neurological conditions and those with cognitive impairment, we also excluded a study of peripheral neuropathy. Overall, of 571 studies initially identified, 555 were excluded by title and abstract because the study (1) did not focus on older adults, (2) lacked brain imaging data, (3) lacked information on gait variability, (4) was not original, or (5) did not assess the relationship between neuroimaging measures and gait variability. The remaining 17 met eligibility criteria and were included in this review (Fig. 1).

2.3. Analysis

For each study, the following data was abstracted (Tables 1 and 2); sample characteristics, type of gait variability assessment, type of neuroimaging assessment, covariate adjustment, analytic approach, and a summary of findings. We did not perform statistical analyses or pool data for meta-analyses because the neuroimaging and gait variability methods were quite heterogeneous.

3. Results

The 17 studies are presented in two groups; 1) those focusing on older adults without diagnosed neurological disease and 2) studies of persons with cognitive impairment and dementia (Tables 1 and 2). In four studies, cognitive status was not explic-

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