

Interplay Between Cognition and Mobility in Older Adults

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Mobility, the ability to move independently, is a critical function for a human being to live a normal life. Mobility impairment poses a major burden on the individual, family, and society as its prevalence increases worldwide with aging of the population. Gait has long been considered as an automatic motor task and this approach has been followed in clinical practice and in the research field. However, more recently studies have suggested that gait requires high-level cognitive function, leading to increased scientific interest in the association between gait and cognition. These findings have significant implications for the development of novel interventions to prevent mobility and cognitive decline among older adults. This article reviews the current literature on the interplay between gait and cognition and on how these findings should be applied for clinical evaluation and intervention to prevent functional decline in older adults.

Key Words: Mobility, Gait, Cognition, Aging, Older adults

INTRODUCTION

Cognitive and mobility impairment often coexist in older adults and both represent independent risk factors for falls. Decline in gait is one of the main features experienced by the aging population. Approximately 35% of community dwelling adults aged 70 years or older have abnormal gait¹⁾. Neurological gait abnormality comprises 41% of all gait abnormalities¹⁾. Gait abnormality is a powerful predictor for the risk of falls, disability, institutionalization, and death^{1,2)}. It has been reported that the prevalence and impact of gait abnormalities are greater among older individuals with cognitive impairment than among those without^{3,4)}. Executive function has been recognized as the main cognitive domain associated with gait and balance impairment among older adults^{5,6)}. In longitudinal studies, older adults with executive function deficits are more prone to falls and this prediction can be made almost 5 years prior to the occurrence of falls^{7,8)}. Based on these clinical observations, a range of neuroscientific investigations on the interplay between gait and cognitive function have been conducted using dual-task paradigm and neuroimaging. The clinical implications of these findings are: (1) the potential predictive value of gait performance for cognitive decline and, similarly, the ability of cognitive function to predict gait decline and risk of falls, and (2) the

development of novel interventions (i.e., cognitive remediation) for the prevention of functional decline in older adults. This article reviews the current literature on the interplay between cognition and mobility, focusing on these 2 clinical implications.

EXPERIMENTAL MODEL FOR COGNITIVE CONTRIBUTION TO GAIT

Twenty years ago, Lundin-Olsson et al.⁹⁾ described how the majority of older adults who stopped walking while talking experienced falls within 6 months, compared to those who were able to continue walking and talking. This clinical observation provided the platform to utilize the dual-task paradigm as an experimental model for the study of the role of cognition on gait in older adults. Participants in the experiments were asked to walk while simultaneously performing cognitive tasks (i.e., serial subtraction of numbers, reciting every other letter of the alphabet). Simultaneous performance of 2 tasks resulted in competition for attentional resources, and forced the brain to unconsciously decide which tasks were to be prioritized when no specific instructions were given. Even in healthy individuals, regardless of age, gait performance tends to decline under dual-task conditions. The specific gait changes during dual-tasking among older adults and individuals with cognitive impairment are summarized in Table 1. A major

change in gait under dual-tasking is the reduction in gait speed¹⁰⁻¹⁶. This finding has been consistently documented for all age groups, although the effect of dual-tasking on gait is significantly greater among older adults compared to the young individuals. During dual-tasking, older individuals also show less stable gait, demonstrated by quantitative gait assessment as increased gait variability¹⁷. Gait variability is typically measured as temporospatial variables (i.e., stride-to-stride length or stride-to-stride time variability)^{18,19}. Motor control theories suggest that a certain degree of variability is necessary for normal gait to accommodate unexpected situations. In fact, both low and high stride-to-stride variability are reported among fallers, implying the importance of optimal gait variability for normal ambulation¹⁹. The performance of cognitive tasks during walking increases temporospatial gait variability^{12,15,20}. It has been postulated that these findings are largely due to cognitive overload on motor performance, compromising the stability of gait during dual-

tasking^{12,15,20}. Other gait parameters are also reported to be affected by dual-tasking in older adults, although these changes are often associated with the simultaneous reduction in gait speed¹⁴. For example, reports indicate that arm swing and axial rotation are reduced during dual-tasking in older adults, and this is mediated by reduced gait speed¹⁴. Therefore, the changes in gait parameters, other than gait speed or variability, require careful interpretation, taking into account the simultaneous reduction in gait speed in these studies.

PRIORITY DURING DUAL-TASKING AND FALL PREDICTION

Both young and old individuals tend to give a higher priority to motor over cognitive tasks^{21,22}. Bloem et al.²¹ described that during dual-tasking, young adults committed more errors in cognitive tasks than the older adults, and conversely,

Table 1. Effect of dual-tasking on gait

| Study | Study population | Secondary cognitive task | Findings during dual-tasking compared to usual walking | Interpretation |
|--|--|--|--|--|
| Lindenberger et al. (2000) ¹⁰ | Healthy older adults | Memorizing | Reduced speed | Need for cognitive resource for gait during dual tasking involving memorization. |
| Li et al. (2001) ¹¹ | Healthy older adults | Memorizing | Reduced performance in memorization more pronounced than walking | Older adults may prioritize walking over memory. |
| Verghese et al. (2007) ²² | Community dwelling older adults | Reciting alternate letter of the alphabet | Reduced speed (more pronounced when focusing on talking than when focusing on both talking and walking) | Dual task cost may differ according to the explicit instruction of prioritization of single task. |
| Hausdorff et al. (2008) ¹² | Community-living older adults | Subtracting serial 7s | Reduced speed and swing time Increased swing time variability | Usual walking ability and cognitive function contribute to dual task effect on gait. |
| Montero-Odasso et al. (2012) ²⁷ | Subjects with mild cognitive impairment (MCI) | Naming animals, subtracting serial 7s | Reduced gait speed Increased gait variability (more pronounced than gait speed change) | Dual-task effect may help in the identification of fall risk in MCI population. |
| Oh-Park et al. (2013) ¹³ | Healthy older adults in senior housing | Holding a tray while walking | Reduced gait speed Relatively higher proportion of subjects sacrificed tray stability over gait | Older adults may compromise the task of upper limbs during motor dual tasking even when instructed to prioritize this task over gait. |
| Cedervall et al. (2014) ²⁵ | Subjects with Alzheimer disease | Naming names and animals | Reduced gait speed Reduced step length | May explain the increased risk of falls. |
| Mirelman et al. (2015) ¹⁴ | Healthy older adults | Serial subtracting 3s from a predefined 3 digit number | Reduced speed Reduced arm swing (mediated by gait speed) and trunk axial rotation, increased asymmetry of arm swing | Need to maintain dynamic balance during challenging tasks (dual tasks) may require decrease in degrees of freedom manifested in a decrease in the amplitude of arm and trunk with less jerky movement. |
| Hamacher et al. (2016) ¹⁵ | Healthy older adults | Auditory cues (metronome beats) | Increased stride time variability No change in foot clearance | Imposed focus of subjects negatively influences motor performance. |
| Smith et al. (2016) ¹⁶ | Systematic review, community dwelling older adults | Cognitive tasks | Reduced gait speed | Dual task walking may be added as a part of the standard clinical assessment of older adults. |

older adults committed more motor errors during dual tasking compared to the young. This finding suggests that young individuals may be more inclined to use a 'posture first' strategy than older individuals. This strategy is chosen particularly if the postural task is perceived as hazardous^{21,23,24}. The taxing effect of secondary tasks on mobility depends on the nature of cognitive and motor tasks, instructions of priority, and the baseline functional status of an individual. When regulation of gait is necessary, as with obstacles and changes in direction, supraspinal involvement is more required to perform movements adapted to the environment than usual walking in a controlled environment²³. Higher levels of attentional resources are required for walking than for standing or sitting in a chair²³. Reaction time when a person is in the single limb support phase is significantly longer than that in a person in double-limb support phase, suggesting that attentional demands are greater as the balance requirements for the task increase²³.

The extent of compromise in gait or postural stability during dual-tasking may vary, according to the baseline cognitive function of the individual. Dual-task effect on gait is greater among individuals with cognitive impairment^{25,26}. Montero-Odasso et al.²⁷ reported that individuals with mild cognitive impairment (MCI) showed a significant reduction in gait speed and an increase in gait variability during dual-tasking compared to the control group. Similar findings are shown in patients with Alzheimer disease, with reduced gait speed and short step length²⁵. The increased risk of falls may be due to the greater dual task effect on gait in the cognitively impaired population.

Shumway-Cook et al.²⁴ observed that the taxing effect of added cognitive task on gait was greater among relatively healthy older adults with a history of falls compared to non-fallers. Conversely, among older individuals with cognitive impairment, there were no significant differences in the dual task effect on gait between fallers and nonfallers²⁸. A recent systematic review examining the association of dual-task testing and the future fall risk concluded that changes in gait under dual-task testing are associated with fall risk and this association is stronger than single-task conditions²⁹. Lack of clear recommendations for dual-task based gait testing remains a challenge for implementation of this finding in the clinical practice for fall risk stratification.

PREDICTIVE VALUE OF GAIT FOR COGNITIVE IMPAIRMENT AND DEMENTIA

The increase in age-associated dementia is worldwide with a prevalence of 5% to 7% in most world regions^{30,31}. Taking into account that there is no known cure for dementia and that the pathophysiological processes of dementia precede

diagnosis by several years or more, identifying markers that predict dementia is a major research interest³². Gait is now recognized as a complex task involving higher brain functions, including attention, planning, and execution. Furthermore, there is a plethora of evidence examining the overlap between the brain area involved in controlling gait and cognition. Therefore, it has been an attractive hypothesis that gait dysfunction predicts cognitive decline, which was supported by longitudinal studies³²⁻³⁴.

Older individuals with a clinically abnormal gait, particularly neurological gait, showed a twofold risk of developing non-Alzheimer dementia compared to those without gait abnormalities³³. Kikkert et al.³² conducted a recent systematic review of 20 longitudinal studies on walking ability to predict future cognitive decline in older adults. The majority of the longitudinal studies used gait speed as a proxy for walking ability, with an average follow-up of 4.5 years. Gait slowing preceded cognitive decline and the presence of dementia syndromes; mean baseline gait speed was 0.8 m/sec and 0.91 m/sec in subjects who developed dementia and MCI, respectively³². Mean baseline gait speed of participants who remained free from significant cognitive decline at follow-up was 1.11 m/sec³². This indicates that gait assessment may serve as an additional marker to predict cognitive decline, although gait speed measurement alone may lack specificity and other measures should be included in the prediction process. Verghese et al.³⁵ recently described Motoric Cognitive Risk Syndrome (MCR) in older individuals with (1) cognitive complaints, (2) slow gait speed (1 standard deviation or more below age- and sex-appropriate mean value established in the relevant cohort), (3) preserved activities of daily living, and (4) absence of dementia^{35,36}. Individuals with MCR have more than a threefold increase in the risk of developing dementia and the risk is considerably higher (adjusted hazard ratio of 12.8) for vascular dementia.

Gait abnormalities may be associated with different types or severity of cognitive impairment. However, these findings have not been consistently reported. Further research is required for gait assessment to serve as a surrogate marker for improving the subtyping of cognitive impairment. A recent report from the GOOD (Gait, cOgnitiOn, and Decline) initiative including aging cohorts of 7 countries showed that there are differences in gait abnormalities from the earliest to the later stages of dementia and among the different subtypes of dementia³⁷. Gait parameters were more disturbed among individuals with nonamnestic MCI compared to those with amnestic MCI. Conversely, the findings from the "Gait and Brain Study" showed that individuals with amnestic MCI, and in particular, those with episodic memory impairment, had poor gait performance³⁸. Patients with non-Alzheimer dementia had worse gait performance than those with Alzheimer dementia³⁷.

NEUROIMAGING FINDINGS SUPPORTING THE LINK BETWEEN GAIT AND COGNITION

Over the last 2 decades, there have been many studies examining the association among gait, cognition, and neuroimaging findings. The majority of these studies used morphological findings (i.e., volume change of whole brain and, in specific regions of the brain, white-matter hyperintensity [WMH]). Several studies reported the association between brain atrophy and reduced gait speed³⁹⁻⁴¹. Smaller volumes of prefrontal area have been associated with slower gait in nondemented older adults living in the community⁴². This association, however, was no longer significant after taking into account the information processing speed⁴². These findings support the hypothesis that as prefrontal area volume decreases, an overall slowing in processing may result in both information process and mobility⁴².

A number of studies have investigated the association between hippocampal volume and gait parameters, specifically gait variability. The findings from these studies vary depending on the population studied and the degrees of the variance among the study sample. Gait variability greater than normal is typically considered negative as it predicts falls and mobility decline in older adults^{17,18,43}. Based on this finding, it is hypothesized that greater gait variability may be associated with low hippocampal volume. A number of studies in patients with MCI⁴⁴ and healthy older adults^{45,46} support this hypothesis. However, Beauchet et al. reported that an unexpected positive association existed between a greater (i.e., better morphological structure) hippocampal volume and a greater (i.e., worse) stride time variability among healthy older adults, but not in patients with MCI⁴⁷. This finding was interpreted as a compensatory mechanism used to maintain a physiologic control of gait, specifically the rhythmic stepping mechanism during normal aging, but not during pathological aging⁴⁷.

WMH is independently associated with gait dysfunction and cognitive impairment^{48,49}. The location of WMH may be an important factor in association with reduced gait speed⁵⁰. The presence of WMH in the periventricular area and brainstem appears to have a greater effect on reduced gait speed relative to the presence of WMH in the subcortical area⁵⁰. In addition to gait speed, a greater variability of step length was found to be independently associated with a greater burden of subclinical brain vascular abnormalities, including WMH and infarct⁴⁰. In longitudinal studies, the presence of WMH predicted faster decline in gait speed compared to cases with no magnetic resonance imaging (MRI) abnormalities among high-functional older adults⁴¹. Functional MRI has also been used to study the brain substrate involved in mobility, using mental imagery of gait. In healthy indivi-

duals, activity of the mesencephalic locomotor region (pedunculo-pontine nucleus and adjacent cuneiform nucleus) was modulated by the speed of imagined gait⁵¹.

Compared to the musculoskeletal and biomechanical systems, an understanding of the underlying neuronal processes for stable gait is still lacking. The main challenge for the research in this area is the difficulty in assessing neuronal processes during movement. Recent technical developments, including functional near infrared spectroscopy and electroencephalogram enable researchers to deduce neuronal activity during gait⁵². Gait activates several brain regions, including prefrontal, parietal, and parahippocampal regions, which are often associated with executive functions, spatial navigation, and memory⁵². Specifically, running increases the activities in the prefrontal cortex more than low-speed walking, indicating the higher cognitive demands for the high-speed locomotion⁵³.

CHOLINERGIC SYSTEM FOR COGNITION AND GAIT

It has been hypothesized that impairment of the cholinergic system plays an important role in the age-related cognitive and motor decline^{54,55}. In the brain, acetylcholine (ACh) is supplied via 3 main sources: intrinsic striatal neurons; nucleus basalis of Meynert in the basal forebrain, both supplying the majority of cholinergic input to the cerebral cortex; and pedunculo-pontine nucleus, supplying ACh to the thalamus⁵⁶. The cholinergic system is involved in arousal, sustained attention, executive function, and synaptic plasticity, affecting both cognition and mobility^{57,58}. In a positron emission tomography study of patients with Parkinson disease, a greater reduction in cortical cholinergic activity was found in fallers compared to nonfallers⁵⁹. Moreover, thalamic acetylcholinesterase, a surrogate marker for cholinergic activity, was significantly lower in fallers compared with nonfallers^{58,59}. The incidence of dementia in patients suffering from Parkinson disease is 6 times higher than that in the control group, with attentional deficit as the most remarkable feature⁵⁶.

A recent study reported that individuals with cholinergic dysfunction also showed a larger decrease in gait speed during dual tasking⁶⁰.

IMPLICATIONS FOR DEVELOPING INTERVENTIONS TO IMPROVE GAIT AND COGNITION

The interventions to improve mobility and to reduce functional decline among older adults have traditionally focused on the physical domain. Since the landmark trial, ACTIVE (Advanced Cognitive Training for Independent and Vital Elderly)⁶¹ demonstrated that cognitive interventions reduced

the functional decline among community living older adults, studies of small sample sizes have reported a promising role of cognitive training on gait (i.e., increasing gait speed⁶²) and balance⁶³ (Table 2). A single-blinded randomized control trial examining the computerized cognitive remediation in a large group of community dwelling older adults is currently ongoing⁶⁴. Considering the low adherence to physical exercise programs, cognitive remediation may be an attractive alternative or a complimentary intervention to the traditional approach, although further research on this topic is required.

Several studies have investigated the effect of pharmacologic agents traditionally used for cognitive enhancement (i.e., amantadine⁶⁵, donepezil^{66,67}) on gait function among elderly persons with cognitive impairment⁶⁸. To date, the re-

sults of these studies are also promising. However, the findings are preliminary due to small sample size and the fact that outcome measures are quantitative gait parameters (i.e., gait variability, double support time), rather than clinical measures^{65,67}.

The cognitive benefit of exercise may be not only due to cardiovascular conditioning but also due to engaging a highly complex behavior involving domains related to both motor and cognitive functions⁶⁹. The epidemiologic evidence supports the benefits of exercise and physical activity on cognition. However, RCTs, including the LIFE (Lifestyle Interventions and Independence for Elders) Study involving more than 1,500 participants from 8 centers in the United States, did not show a significant benefit of physical activity on

Table 2. Summary of intervention studies based on the association between cognition and mobility

| Study | Study population (n) | Interventions | Outcome variables | Main findings |
|---|--|---|--|--|
| Willis et al. (2006) ⁶¹ ACTIVE STUDY | Healthy older adults living in a community, 5-year follow-up of randomized control trial (total n=2,832) | Ten-sessions training for memory, reasoning, processing speed, 4-session booster at 11 and 35 months after initial training (optional) | Self-reported IADL (meal preparation, house-work, finances, health maintenance, telephone use, shopping) & performance based measures of daily function. | Training group reported less difficulty in IADL compared to control group (statistically significant effect size seen only for the group with reasoning training) No effect on performance based measure of daily function |
| Vergheze et al. (2010) ⁶² | Sedentary older adults (exercise <1/wk, gait velocity <1 m/sec) (n=10 for intervention group, n=3 for control group) | 8-Week computerized cognitive remediation, using a computer based program | Gait velocity of preferred pace. Gait velocity during talking (walking while talking) | Improvement in gait velocity of preferred pace by 8.2 cm/sec compared to control. Six out of 10 improved gait velocity while talking. |
| Smith-Ray et al. (2016) ⁶³ | Cognitively impaired older adults (n=20) | Cognitive intervention (×2/wk for 10 weeks) using online brain exercise program | Balance measured by timed up and go, side-by-side stand, partial and full tandem stand | Improved balance after the intervention (not reaching statistical significance) |
| Baezner et al. (2001) ⁶⁵ | Older adults with subcortical vascular encephalopathy (total n=40) Double-blind placebo-controlled trial | Amantadine (500 mg intravenous infusion) vs. placebo (×5 days) | Quantitative gait parameters (cadence, variability of double-support phase) | Patients in both the amantadine and placebo group improved, with no significant difference in improvement between the 2 groups. A greater number of gait parameters improved in the amantadine group compared to the control group. |
| Montero-Odasso et al. (2015) ⁶⁷ | Patients newly diagnosed with Alzheimer disease (n=43) | Donepezil of 4-month intake | Gait velocity of preferred pace Gait velocity during dual tasking | Improved from 108.4 cm/sec to 113.3 cm/sec (single task gait velocity) Dual tasking gait velocity also improved. |
| Sink et al. (2015) ⁷⁰ LIFE randomized trial | Community-living older adults (n=818 for intervention group, n=817 for control group) | Structured moderate-intensity physical activity program over 24 months for the intervention group; health education for the control group | Cognitive function measured by digit symbol coding task and Hopkins Verbal Learning Test-Revised scores | No difference in cognitive scores between the intervention and the control group |

Only relevant outcomes reflecting the interplay between cognition and mobility were listed. IADL, instrumental activities of daily living.

cognitive function compared to health education⁷⁰. The conflicting results of earlier studies may be explained by the insufficient amount of physical activity used as an intervention in RCTs, the dissipation of short term (i.e., months) cognitive benefit in pilot studies over a longer period of follow-up (i.e., years) of the RCTs, and low risk of cognitive decline in the high functioning older adults in RCT sample⁷⁰.

CONCLUSION

Human locomotion is a highly complex behavior requiring a wide spectrum of cognitive functions, particularly executive function, in addition to motor control. Cognitive impairment and gait abnormalities both increase with aging. Cognitive impairment plays a role in predicting gait decline and falls, and gait dysfunction may predict cognitive decline. These findings indicate that the evaluation of both cognition and gait should be included for risk stratification for functional decline among older adults. Recent studies reporting on cognitive intervention benefiting gait are promising; however, further studies are required to define the role of cognitive remediation as an alternative or as a complimentary intervention for mobility.

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