

Falls in Cognitively Impaired Older Adults: Implications for Risk Assessment And Prevention

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OBJECTIVES: To provide an overview of the role of cognition in falls, with potential implications for managing and preventing falls in older adults.

DESIGN: Review.

SETTING: Observational and interventional studies addressing the role of cognition on falls.

PARTICIPANTS: Community-dwelling older adults (65 years and older).

MEASUREMENTS: The relationship between gait and cognition in aging and neurodegeneration was reviewed in the medical literature to highlight the role of brain motor control deficits in fall risk. The benefits of dual-task gait assessments as a marker of fall risk were reviewed. Therapeutic approaches for reducing falls by improving certain aspects of cognition were appraised.

RESULTS: Low performance in attention and executive function are associated with gait slowing, instability, and future falls. Drug-enhancement of cognition may reduce falls in Parkinson's disease, and cognitive training, dual-task training, and virtual reality modalities are promising to improve mobility in sedentary older adults and in those with cognitive impairment and dementia.

CONCLUSION: Falls remain common in older people, with higher prevalence and morbidity in those who are cognitively impaired. Disentangling the mechanism and contribution of cognitive deficits in fall risk may open new treatment approaches. Mounting evidence supports that cognitive therapies help reduce falls. *J Am Geriatr Soc* 2017.

Key words: falls; cognitive impairment; dementia; gait; dual-task; cognitive function

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Forty years ago, Bernard Isaacs postulated that attributing falls in older individuals to muscular-articular and sensory impairments and their effect on gait and balance was overly simplistic. Rather, a failure of our sophisticated system of brain motor control plays a capital role in triggering falls.^{1,2} Since his seminal article, clinical and research evidence has established that cognitive impairment and falls are related;³ dementia and falls often coexist in older adults, gait impairments and falls are more prevalent in individuals with dementia than in those with normal cognitive aging, and this prevalence increases with the severity of cognitive impairment.⁴

Falling, a common geriatric syndrome affecting approximately one-third of older adults each year, is a major cause of morbidity, with higher prevalence in those with moderate to severe cognitive impairment and reaching an annual incidence of approximately 70%, twice the rate in cognitively normal older adults.⁵ The consequences of falls in this group are serious; fallers with cognitive problems are approximately 5 times as likely to be admitted to institutional care as cognitively impaired people who do not fall.⁶ They are also at high risk of major fall-related injuries, including fractures and head injuries, and mortality. In addition to indirect costs and caregiver burden, the direct costs of emergency, acute, rehabilitation, and long-term care due to falls are substantial and challenge healthcare system sustainability.

As currently understood, cognition is a complex construct comprising several domains. Although the precise mechanisms underlying fall risk in cognitively impaired older adults have not been completely determined, it seems clear that impaired attentional resource allocation significantly compromises postural and gait stability.⁷ Specifically, executive function, a set of cognitive processes that includes attention, inhibitory control, working memory, and cognitive flexibility is essential for normal walking. Executive dysfunction is associated with greater fall risk, even in individuals deemed to be cognitively normal.⁸ Such findings challenge our definition of clinically significant cognitive impairment. For example, even in older adults with "normal" cognition, as assessed using the Mini-

Mental State Examination, low performance in executive function is prospectively associated with falls.⁹

Many early prospective cohort studies of falling in older adults systematically excluded those with moderate or severe cognitive impairment, which limited our ability to evaluate fall risk across the full cognitive spectrum. Consequently, until recently, falls and dementia were assessed in research studies separately, which may have led to a gap in our understanding of the cognitive-motor interactions that affect the pathways to future falls and fall-related disability. This gap may also explain why cognition has received little attention in fall prevention strategies. Mounting evidence reveals that these two geriatric syndromes, falls and cognitive impairment, are interrelated and associated with aging.³

COGNITION AND MOBILITY IN AGING

Although walking was long considered a primarily automatic motor task, it is now accepted that this view was too simplistic.¹⁰ Walking in the real world requires paying attention to various environmental features to avoid trips and slips and quickly recovering from postural perturbations to regain a stable base of support. Therefore, it is not surprising that deficits in attention and executive function processes are independently associated with risk of postural instability, impairment in activities of daily living, and future falls.⁸ Previous systematic reviews have found a relationship between executive dysfunction and falls, and a metaanalysis of 27 prospective cohort studies found that executive dysfunction doubled the risk of future falls and increased the risk of serious injury by 40% in community-dwelling older adults.¹¹

Recent studies have also shown that older adults with mild cognitive impairment (MCI), a transitional state between normal aging and early dementia, have a higher prevalence of gait impairment and higher risk of falling than cognitively normal older adults.¹²⁻¹⁵ Thus, older adults with MCI are a population at risk, not only for future dementia, but also for falls, and should perhaps be specifically targeted for interventions to reduce fall risk. One specific early change in gait performance seen in cognitively impaired older adults is a decrease in gait velocity.⁴ Quantitative spatiotemporal gait parameters are also impaired across the entire cognitive spectrum, and gait variability (variations in a given gait parameter from stride to stride) has emerged as a sensitive marker of high-level brain gait control.^{3,16} High gait variability represents gait instability and has been shown also to predict falls even after changes in gait velocity are taken into consideration.

Mechanistically, the relationship between cognitive deficits and gait disturbances has been attributed to specific brain regions such as the prefrontoparietal and cingulate cortical areas and striatal hippocampal networks. Neurodegeneration, brain small vessel disease, and aging can affect these areas, as demonstrated in brain imaging studies.¹⁷

COGNITIVE ASPECTS OF THE PATHOPHYSIOLOGY OF FALLS

The human upright position is naturally unstable, with a narrow base of support and a high center of body mass.

To maintain this delicate equilibrium while walking or standing, the human body uses harmonious modulation and coordination of trunk, hip, and ankle flexibility. Impairments such as muscle weakness, joint problems, motor slowness, and poor coordination challenge this equilibrium. These challenges increase the risk of falling under physiological perturbations, such as body sway during standing or walking, or after an extrinsic destabilizing factors such as tripping. The rapid succession of strategies aimed at preserving postural stability after a perturbation includes first the “ankle strategy” for small perturbations and later the “hip strategy” for larger perturbations. The “ankle strategy” is a motor plan characterized by the relaxation of trunk muscles and stiffening of the ankle joint, whereas the “hip strategy” relaxes the hip muscles and stiffens the leg muscles, with the head moving out of phase and the hips moving to maintain the center of body mass over the base of support.¹⁸ When the perturbation is more severe and these strategies are insufficient, a third motor plan used to avoid falling is the “stepping strategy,” in which the ankle joint is released and the individual performs one or more steps to enlarge the base of support. Finally, if these motor acts fail to regain postural stability, the upper limbs perform rescue strategies, such as grabbing a support, or use protective reactions, such as extending the arms, to limit the traumatic consequence of falling.

Figure 1 schematizes a falls pathophysiological model, which helps to explain the link between trunk inflexibility (worsened by rigidity or fear of falling), instability during the “ankle strategy,” and the mechanistic link between gait disorders and falling during the “stepping strategy.” Cognitive resources, including attention and executive functions, play critical roles in modulating each of these strategies.¹⁹ An adequate flow of information through visual, vestibular, and somatosensory afferents is required (depicted as sensory input in Figure 1), paired with attentional and executive resources to adapt to the environment and the type of perturbation by rapidly switching from one strategy to the other. Older adults show an innate preference to maintain posture while attempting to simultaneously perform a cognitive task by prioritizing walking over a secondary cognitively demanding task.²⁰

In situations in which there is a risk of falling, cognitively normal older adults adopt a “posture first” strategy to prioritize the maintenance of balance over other tasks, but cognitively impaired older adults have limitations in enacting this strategy and may have inverse reactions, adopting a “posture second” strategy by prioritizing the cognitive task over walking, as has been described in individuals with Parkinson’s disease (PD).^{21,22} Executive function is also important for inhibitory control, for example by avoiding situations that may perturb balance. Lack of inhibitory control is more likely to occur in individuals who are farther along the cognitive decline spectrum and may cause failure to accurately appraise the risk of activities that were once safe for them (e.g., older individuals with physical impairments climbing on ladders or roofs). This in turn would explain higher incidence of severe injuries with increasing deterioration of executive function due to falling from greater heights or with greater impacts. In this line of thinking, investigations have shown that, although individuals with dementia appear to walk slowly,

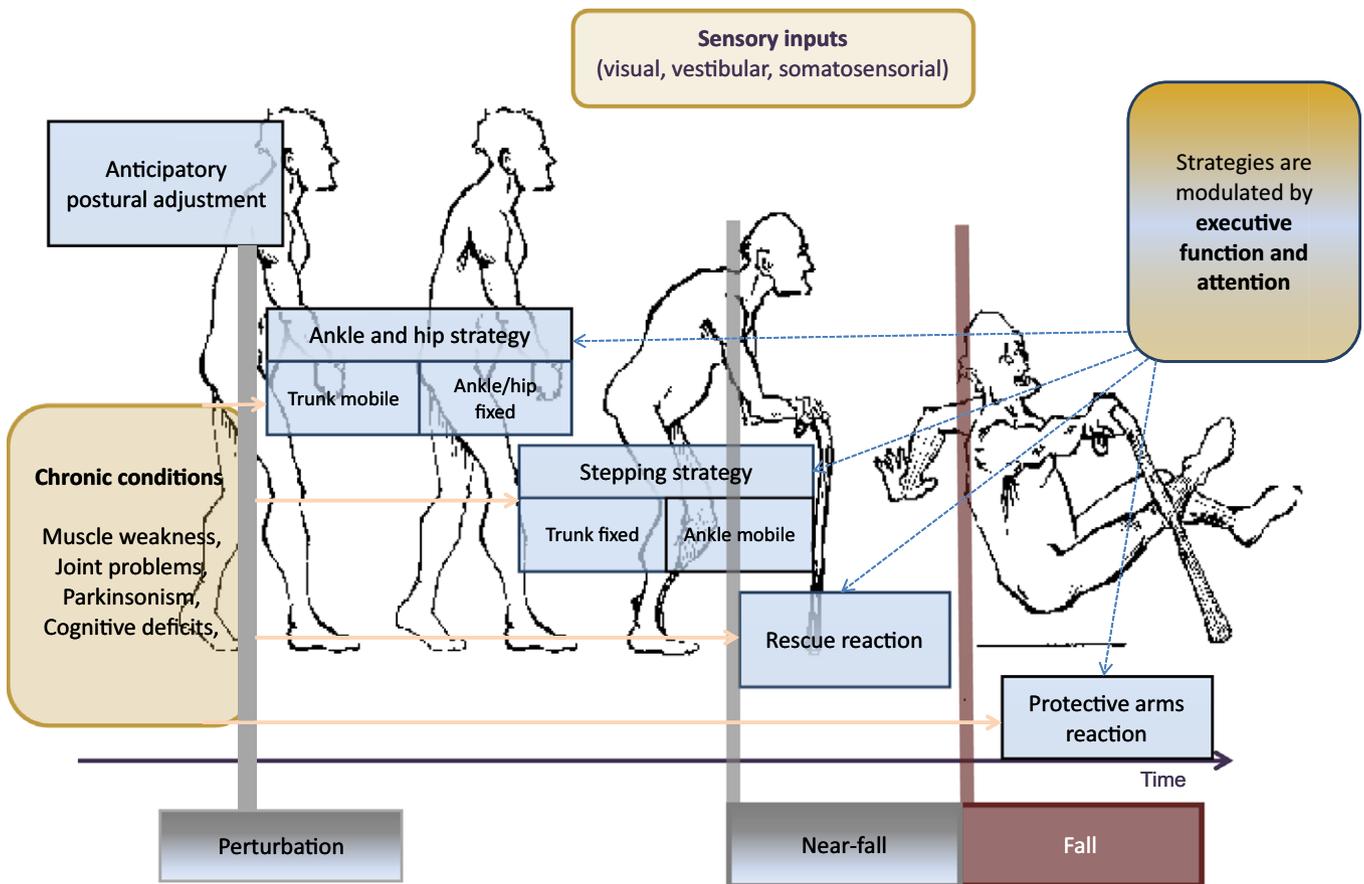


Figure 1. Schematization of rapid succession of strategies aimed at preserving body stability after a single perturbation. Note the role of cognitive processes modulating the three classic rescue strategies. Modified from Fasano et al.¹⁹

they walk faster than their motor and cognitive abilities allow, leading to greater risk of falling.²³ This may reflect an inability to appraise the hazard of walking fast due to their cognitive deficits. These multiple interactions demonstrate that improving cognitive functioning may have an essential role in the rehabilitation of gait disorders in older adults to restore “posture first” strategies.

Walking performance in real-life situations relies on cognition, as studies using the dual-task gait paradigm show (the effect on walking while performing a secondary cognitive task).^{3,24} Dual-task walk performance isolates the role of attention and executive function in the regulation of gait control.^{3,7,14,25} The underlying hypothesis is that two simultaneously performed tasks interfere with one another and compete for brain cortical resources.⁸ Recent evidence showed that activity levels in the prefrontal brain while performing a dual-task walk predicted falls in high-functioning older adults.²⁶ Therefore, a dual-task walk can act as a “brain stress test” to detect deficits of motor-gait control and fall risk, particularly in early stages of mobility decline, as shown in a recent systematic review.²⁷ Individuals with an overt neurological disease such as stroke, PD, MCI, and dementia have marked gait slowing during dual-tasking.^{14,16,25} This may explain why individuals with cognitive impairment and dementia syndromes are vulnerable to dual-task challenges. Activities of daily living involve many attention-demanding events, which explains the high

occurrence of falling in older adults while they are walking and performing an attentional demanding task. Even during standing, postural sway increases when a cognitive task is performed, suggesting that constant dynamic control of postural adjustments during standing also requires certain levels of cognitive attentional resources. The fact that central nervous system psychotropic and sedative drugs such as benzodiazepines negatively affect postural control, reaction times, and gait performance and increase risk of falls adds to the evidence of the role of cognition in postural and gait control and falls risk.

EMERGING STRATEGIES TO ENHANCE MOBILITY AND PREVENT FALLS BY TARGETING COGNITION

Fall prevention trials in cognitively normal older adults have demonstrated that multifactorial (e.g., review of medications, strength and balance training, visual and hearing corrections, environmental modifications) and single (e.g., resistance exercise, progressive balance training) interventions are effective in preventing falls. In contrast, fall prevention studies in cognitively impaired populations have been inconsistent or found only modest success.²⁸ Cognitively impaired older adults, although at high risk of falls, may be less responsive to the interventions.^{28,29} Potential explanations for this lack of benefit may include that

cognitively impaired individuals have limitations in learning, understanding, and following recommendations; that there is a different underlying mechanisms for falls in this population; and that the interventions fail to address cognitive deficits adequately. Regarding the role of cognitive deficits, we have postulated that improving certain aspects of cognition may help to prevent falls in older adults.^{2,3} To appraise this emerging evidence, we performed a systematic search in PubMed using the following search terms: “accidental falls”[Medical Subject Heading (MeSH) Terms] OR (“accidental”[All Fields] AND “falls”[All Fields]) OR “accidental falls”[All Fields] AND (“gait”[MeSH Terms] OR “gait”[All Fields]) AND “executive function” [All Fields] AND “cognition” [All Fields] without language, years, or age restrictions. One hundred thirty-one articles were found. After removing duplicates and selecting articles that were interventional studies and targeted older adults (aged ≥ 65), 19 studies were selected and appraised.

Nonpharmacological Approaches

Table 1 summarizes studies found in our PubMed search that specifically evaluated the effects of cognitive training and dual-task cognitive training interventions on balance, gait, and fall risk in older adults with and without cognitive impairment and dementia.

In a cognitively normal population, a pilot study conducted in sedentary older adults randomly assigned 20 participants to a computerized cognitive remediation intervention or a wait list.³⁰ Cognitive remediation improved gait velocity and dual-task gait velocity, indicating that a nonpharmacological cognitive intervention may improve gait performance, especially during dual-task walking. These results were replicated in a subsequent randomized controlled trial (RCT) in 51 community-dwelling older adults without cognitive impairment.³¹

Combining dual-task training with physical exercise has also been evaluated and found to improve cognition and, in turn, mobility and gait performance. A small but seminal pilot study that provided dual-task training to 21 cognitively normal older adults with balance and gait impairments showed that dual-task training with variable-priority instructions had sustained benefits in maintaining gait velocity after 12 weeks of intervention. These results suggested that varying focus of attention during training between the cognitive and motor tasks apparently had more benefits than focusing on both tasks.³² These results were replicated in a subsequent RCT involving 36 cognitively normal older adults.³³ A large, multicenter, parallel-group RCT performed in retirement homes randomly assigned 182 cognitively normal older adults to strength and balance (SB) or strength, balance, and cognitive (SBC) training. Participants in the SBC group had significant improvements in fast gait velocity, dual-task gait velocity, executive function, and fall rate.³⁴

Whether dual-task mobility training can reduce falls has also been tested in cognitively impaired populations. An RCT evaluating the efficacy of a 12-week dual-task mobility training program was conducted in 49 participants with mild to moderate dementia. The intervention group that received progressive dual-task training

performed significantly better in a complex dual-task gait condition than the control group that received low intensity exercises.³⁵

The effect of treadmill training enhanced with virtual reality (TTVR) on falls in older adults with PD has been evaluated. The enhanced virtual reality consisted of a screen in front of the treadmill displaying a path with obstacles and targets that was designed to expose participants to similar real-life situations that would make them prone to falls. Preliminary findings demonstrated that TTVR improved motor-cognitive performance assessed as dual-task gait velocity more effectively than treadmill walking alone.³⁶ A larger multisite RCT that the same group conducted in a heterogeneous sample of 300 adults with normal cognition, MCI, or PD showed a significant reduction in the fall incidence rate for TTVR 6 months after the end of training from their fall incidence before the training and a significantly lower fall incidence rate than in the treadmill alone group.³⁷ Treadmill training with enhanced visual stimuli was also compared with conventional treadmill training in 90 older adults during rehabilitation from fall-related hip fractures for improving walking ability, reducing fear of falling, and fall incidence.³⁸ This parallel-group RCT showed that visually enhanced treadmill training modestly improved walking adaptability and fear of falling only in older adults with executive dysfunction, suggesting that this modality was superior to conventional treadmill training in this subgroup of older adults.³⁸

Although the effects on gait and falls risk of cognitive-based therapies to mitigate fall risk are promising, only three of the studies assessed examined falls as a primary outcome. Although definitive trials are needed before this approach can be widely recommended, it appears that cognitive training with or without physical exercise can improve gait performance. The results of dual-task training in individuals with cognitive impairment and TTVR in those with PD are promising; both interventions reduced falls in the appraised RCTs.

Pharmacological Approaches

Table 2 summarizes studies found in our search that specifically evaluated the effects of cognitive pharmacological interventions on gait and fall risk in older adults.

Methylphenidate

Methylphenidate, an attention-enhancing drug, has been tested to determine whether it improves motor function in older adults. In a pilot study conducted in 21 participants with PD, a single dose of methylphenidate significantly increased attention, executive function, gait velocity, and Timed Up and Go Test scores and reduced stride time variability.³⁹ Another pilot RCT that tested 26 community-living older adults without dementia showed that methylphenidate improved executive function and gait velocity and reduced gait variability.⁴⁰ Similarly, a RCT showed that a single dose of methylphenidate improved gait and postural stability in 30 healthy older adults and reduced the number of step errors and step error rate on gait in single and dual tasks.⁴¹ Despite barriers to using methylphenidate in older adults (short half-life, unsafe

Table 1. Nonpharmacological Cognitive Interventions for Gait, Balance, and Fall Risk

Study (Year)	Design	Type of Intervention and Control	Duration	Participants	Summary of Findings
Cognitively normal					
You et al. (2009) ⁵⁰	RCT	Dual-task cognitive-gait intervention: simultaneous motor (walking 30 m) and cognitive (memory recall) tasks (n = 8); control group (n = 5) walked while listening to music	18 sessions, 30 minutes per session, over 6 weeks	13 participants aged 68.3 ± 6.5, with history of falls	Working memory under dual-task condition improved ($P < .05$); no significant changes in gait velocity and variability found
Silsupadol et al. (2009) ³²	RCT	Participants randomly assigned to 1 of 3 interventions: single-task training (n = 7), dual-task training with fixed-priority instructions (n = 8), dual-task training with variable-priority instructions (n = 6)	12 sessions, 45-minute individualized sessions, 3 times/wk for 4 weeks	21 participants aged ≥65, with balance impairment	All groups improved balance and gait velocity; only group with dual-task training with variable-priority instructions demonstrated dual-task training effect at the second week and remained at 12-week follow-up
Vergheze et al. (2010) ³⁰	RCT	Computerized "Mindfit" program vs wait-list control; each training session included mix of 21 visual, auditory, and cross-modality tasks	24 sessions; 45–60 min/session, 3 times/week for 8 weeks	20 sedentary older adults aged 77.4 ± 7.0 at training, and wait-list (aged 79.9 ± 7.5)	Gait velocity ($P < .05$) and dual-task gait velocity ($P = .002$) improved in intervention group; processing cognitive speed improved in intervention group ($P = .03$)
Van het Reve et al. (2014) ³⁴	RCT	Participants randomly assigned to strength-balance (n = 98) or strength-balance-cognitive (n = 84) training	2 times/wk; 40-minute strength-balance. Strength-balance-cognitive received cognitive training, 3 times/wk for 12 weeks	182 participants aged ≥65 living in autonomous residences for elderly adults	Participants in strength-balance-cognitive group had significant improvements in fast gait velocity ($P = .04$), dual-task gait cost ($P = .03$), executive function (Trail-Making Test Part B, $P = .001$), and fall rate ($P = .001$)
PD and MCI					
Yogev-Seligmann et al. (2012) ⁵¹	Open-label, pilot	4-week program of one-on-one training included walking while performing several distinct cognitive tasks	12 sessions; 3 per week for 4 weeks	7 participants with PD aged 63.8 ± 8.4	Gait velocity and gait variability during dual task significantly improved. Untrained dual task also improved and was retained 1 month after end of training
Mirelman et al. (2011) ³⁶	Repeated-measures design	TT with virtual obstacles; VR simulation required obstacle negotiation while continuing to walk on treadmill; comparison made to historical control group that followed similar protocol of TT without VR	18 sessions (3 per week for 6 weeks)	20 participants with PD aged 67.1 ± 6.5 able to walk unassisted for at least 5 minutes	Dual task, gait velocity ($P = .003$), and stride length ($P < .001$) improved significantly more with TTVR than TT alone; dual-task gait variability decreased, and Trail-Making Test improved after TTVR training
Mirelman et al. (2016) ³⁷	RCT	TT with nonimmersive VR; participants walked on treadmill while watching large screen that projected path with obstacles, multiple pathways, and distracters; control group consisted of TT alone with no VR	18 sessions (3 per week for 6 weeks)	300 participants with normal cognition, MCI, and PD aged 60–90 with history of ≥2 falls	After 6 months of training, incident rate of falls was lower in TTVR group than before training ($P < .001$) and than in TT alone group ($P = .03$)

(Continued)

Table 1 (Contd.)

Study (Year)	Design	Type of Intervention and Control	Duration	Participants	Summary of Findings
Mild dementia					
Schwenk et al. (2010) ³⁵	RCT	Intervention group (n = 20) underwent dual-task-based exercise training (motor: throwing or catching ball; cognitive: arithmetic tasks, repeating names of animals); control group (n = 29) performed low-intensity exercise	24 sessions over 12 weeks, 1 hour twice a week	49 participants aged 81.9 ± 7.5 with mild to moderate dementia (Mini-Mental State Examination score 21.4 ± 2.9)	Dual-task training improved gait velocity under dual task ($P < .001$), cadence ($P = .007$), stride length ($P = .001$), single support ($P = .003$) under complex three-step backward calculation conditions more than in controls

Modified from Montero-Odasso et al.³

MCI = mild cognitive impairment; PD = Parkinson's disease; RCT = randomized controlled trial; TT = treadmill training; VR = virtual reality.

adverse event profile), these findings support the role of drugs designed to enhance attention as a therapeutic option for reducing fall risk.

Cholinesterase Inhibitors

Cognitive function, gait regulation, and brain motor control share a number of neurotransmitters that have been targeted to improve motor performance, specifically gait, and to reduce fall risk. Central cholinergic neurotransmission controls selective attention and memory and regulates gait motor control and balance.⁴² Cholinergic brain neurons are found in the hippocampus, nucleus basalis of Meynert, basal ganglia, thalamus, and pedunculopontine nucleus. Thalamic cholinergic activity, which derives mainly from terminals of pedunculopontine nucleus neurons, controls the generation of movement patterns during gait performance. Central acetylcholine denervation is associated with slow gait and falls in aging (independent of cognitive status) and in PD.⁴³ Thus, correcting the cholinergic loss seen in aging and neurodegeneration may improve motor function and reduce fall risk through cognitive and noncognitive mechanisms.⁴²

Cholinesterase inhibitors (e.g., donepezil, galantamine, rivastigmine) are used for symptomatic treatment of mild to moderate AD and vascular dementia. We postulated that cholinesterase inhibitors might improve cortical gait control by enhancing executive function and attention by increasing cortical and hippocampal acetylcholine and improve stride-to-stride variability through a motor enhancement that increases the cholinergic activity of pedunculopontine nucleus neurons.⁴²

Two small pilot studies indicated the potential effects of galantamine⁴⁴ and donepezil⁴² on gait performance in older adults with mild AD. A subsequent open-label trial in 43 individuals with mild AD found significant improvements in gait velocity and dual-task gait velocity after 4 months of treatment with donepezil.⁴⁵ Changes in stride-time variability were in the expected direction, although they were not statistically significant. Participants also experienced significant improvements in executive function, supporting the premise that gait improvement can be cognitively mediated. The effect of

cholinesterase inhibitors has also been tested in older adults with PD. A randomized cross-over study conducted in 23 older adults with PD observed a 50% lower fall frequency in participants given donepezil than in those given placebo.⁴⁶ A larger well-designed RCT randomly assigned 130 older adults with PD to rivastigmine (3–12 mg/d) or placebo.⁴⁷ After 8 months of treatment, the rivastigmine group improved step time variability during normal and dual-task walking and reduced their fall rate. Similarly, a cognitive enhancer that reduces glutamate neurotransmission, memantine, decreased stride time variability in older adults with AD followed in an open-label memory clinic study.⁴⁸

In summary, pharmacological cognitive enhancement in individuals with MCI and AD is a promising avenue to improve gait, but these preliminary studies need to be treated with caution because of their small samples, proof-of-principle nature, and lack of proper randomization. Definitive RCTs are still needed, but as preliminary in nature as studies in MCI and AD are, larger, well-constructed, controlled, randomized trials have shown that pharmacological cognitive enhancement in older adults with PD improves gait parameters and decreases fall rates.

IMPLICATIONS FOR PRACTICE AND RESEARCH

Cognitive deficits, as a fall risk factor, should be considered on a continuum from normal aging to advanced dementia, and executive function and attention should be evaluated during routine fall risk assessments. Specific groups, such as older adults with MCI, are at high risk of falls and should be prioritized for fall prevention interventions. Gait assessment under dual-tasking can be used to evaluate the effect of cognitive deficits on motor and gait regulations and to predict falls, particularly in older adults with relatively normal gait velocity.²⁷ Therapeutically, improving attention and executive function performance can have the added benefit of treating gait motor control deficits and preventing falls. This may be critical to reducing the fall risk of cognitively impaired individuals. It is unclear whether pharmacological and cognitive-exercise training approaches would have a synergistic effect if

Table 2. Pharmacological Cognitive Interventions for Gait and Balance and Fall Risk

Study (Year)	Study Design	Type of Intervention	Duration	Participants	Summary of Findings
Cognitively normal					
Ben-Itzhak et al. (2008) ⁴⁰	RCT, double-blind, placebo-controlled	Before and 2 hours after taking 20 mg MPH or a placebo	2 hours	26 participants without dementia with subjective memory complaints aged 73.8 ± 1.2, MMSE score 27.8 ± 1.4	MPH improved Timed Up and Go ($P = .004$), stride time variability ($P = .03$), and EF ($P = .03$); effects not observed after treatment with placebo
Shorer et al. (2008) ⁴¹	RCT, double-blind, placebo-controlled	Before and 2 hours after taking 20 mg MPH or a placebo	2 hours	26 participants without dementia with subjective memory complaints aged 73.8 ± 1.2, MMSE score 27.8 ± 1.4	MPH improved Timed Up and Go ($P = .004$), stride time variability ($P = .03$), and EF ($P = .03$); effects not observed after treatment with placebo
MCI and AD					
Assal et al. (2008) ⁴⁴	Before-after design	Galantamine mean dose 17.8 ± 3.5 mg/d	6 months	9 participants with mild to moderate AD aged 77.9 ± 2.1; mean MMSE score 26.4 ± 5.2 compared with 18 no-treatment control subjects without dementia aged 78.1 ± 1.0; mean MMSE score 29.4 ± 0.8	Stride time was shorter under dual tasking after treatment ($P = .01$); no change in controls
Montero-Odasso et al. (2009) ⁴²	Open-label study with controls	5 mg/d donepezil for 1 month; 10 mg/d for another 3 months; MCI group with no treatment	4 months	6 participants with mild AD aged 79.9 ± 4.8, MMSE score 22.3 ± 1.2 MoCA score 15 ± 1.4 compared with 8 participants with MCI aged 75.6 ± 6.2, MMSE score 27.9 ± 1.7; MoCA score 22.9 ± 1.7	Participants with AD increased gait velocity ($P = .04$) and dual-task gait velocity ($P = .047$) after 1 month; stride time variability decreased during follow-up; control group decreased in gait velocity and increased variability
Beauchet et al. (2011) ⁴⁸	Before-after design	Memantine mean dose 20 mg/d titrated in 5-mg increments over 4 weeks	4.4 to 8 months	17 participants with AD aged 83.8 ± 5.8, 52.9% female MMSE score 14.5 ± 4.2; 32 age- and sex-matched controls with AD without any anti-dementia drug aged 0.0 ± 6.6, MMSE score 23.2 ± 5.3	Stride time variability decreased during follow-up in memantine group (6.3 ± 6.1 vs 3.6 ± 1.3, $P = .04$)
Montero-Odasso et al. (2015) ⁴⁵	Before-after design	5 mg/d donepezil for 1 month, 10 mg/d for 5 months	5 months	43 participants with mild AD aged 76.9 ± 8, MMSE score 24.63 ± 2, MoCA score 18.5 ± 4	Gait velocity improved from 108.4 ± 18.6 to 113.3 ± 19.5 cm/s ($P = .01$); dual-task gait velocity from 80.6 ± 23.0 to 85.3 ± 22.3 cm/s ($P = .03$). Trail-Making Test Part A ($P = .03$), B ($P = .001$) and Part B-A ($P = .04$) improved after intervention
PD					
Auriel et al. (2006) ³⁹	Open-label, before-after design	Before and 2 hours after single dose of 20 mg MPH	2 h	21 participants with PD who receive L-Dopa aged 70.2 ± 9.2 years, MMSE score 28.8 ± 1.7	Improvement in attention ($P = .02$), EF Index ($P = .09$). Improvements in Timed Up and Go ($P = .001$), gait velocity ($P = .005$) and stride time variability ($P = .01$)

(Continued)

Table 2 (Contd.)

Study (Year)	Study Design	Type of Intervention	Duration	Participants	Summary of Findings
Chung et al. (2010) ⁴⁶	Randomized, crossover, double-blind	Donepezil vs placebo. 5 mg/d donepezil or placebo for 3 weeks, increase to 10 mg/d for remaining 3 weeks	6 weeks, 3 weeks washout, 6 weeks placebo	23 participants with PD who reported falling or nearly falling aged 68.3 ± 10.8, MMSE score 27.6 ± 4.5	Fewer falls with donepezil than placebo ($P = .049$). Subjects with most falls at baseline tended to have largest improvements. No differences in Activities of Balance Confidence Scale, Berg Balance Scale, Unified Parkinson's Disease Rating Scale III or MMSE scores
Henderson et al. (2016) ⁴⁷	RCT, phase II	Rivastigmine titrated from 3 mg/d (or placebo); incremented every 4 weeks to maximum of 12 mg/d from week 13 onwards	8 months	130 participants with mild PD aged 71.9 ± 4.8, MoCA score 25 ± 1.4; half in intervention groups and half in placebo group	Intervention improved gait velocity (greatest effect) and dual-task gait velocity. Stride time variability decreased but not significantly. Falls rate (secondary outcome) significantly lower in intervention group

Modified from Montero-Odasso et al.³

AD = Alzheimer's disease; EF = executive function; MCI = mild cognitive impairment; MMSE = Mini-Mental State Examination; MoCA = Montreal Cognitive Assessment; MPH = methylphenidate; PD = Parkinson's disease.

combined or if one would replace the other; large, controlled trials designed to test this interaction are needed.

Although the current state of the knowledge precludes formulating evidence-based recommendations to manage falls in cognitively impaired older adults by targeting cognition, some specific practical suggestions can be made to complement established fall prevention recommendations.⁴⁹ Older adults with MCI and with executive dysfunction are at higher risk of falls, and exercise interventions combined with cognitive and dual-task training can improve their gait performance and balance and reduce their falls risk. Exercise interventions, including dual-task training, are feasible in older adults with mild AD, although their effect on reducing falls is not established. Mounting evidence supports that pharmacological interventions may reduce falls in PD populations, and thus, a trial treatment with cholinergic inhibitors can be used in individuals with PD with recurrent falls as a fall reduction strategy.

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Conflict of Interest: Dr. Montero-Odasso is member of the Board of the Canadian Geriatrics Society, Associate Editor of the *Journal of Alzheimer's Disease*, and Editorial

Board Member of the *Journal of Gerontology Medical Sciences*, and *Geriatrics*.

Author Contributions: MMO has full access to the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analyses.

Study concept and design, analysis and interpretation of data, preparation and critical review of manuscript: MMO, MS. Acquisition of subjects and data, obtained funding, statistical expertise: MS. Study supervision: MMO.

Sponsor's Role: None.

REFERENCES

1. Isaacs B. Are falls a manifestation of brain failure? *Age Ageing* 1978; Suppl:97-111.
2. Montero-Odasso M, Bherer L, Studenski S et al. Mobility and cognition in seniors. Report from the 2008 Institute of Aging (CIHR) Mobility and Cognition Workshop. *Can Geriatr J* 2015;18:159-167.
3. Montero-Odasso M, Verghese J, Beauchet O et al. Gait and cognition: A complementary approach to understanding brain function and the risk of falling. *J Am Geriatr Soc* 2012;60:2127-2136.
4. van Iersel MB, Hoefsloot W, Munneke M et al. Systematic review of quantitative clinical gait analysis in patients with dementia. *Z Gerontol Geriatr* 2004;37:27-32.
5. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. *N Engl J Med* 1988;319:1701-1707.
6. Morris JC, Rubin EH, Morris EJ et al. Senile dementia of the Alzheimer's type: An important risk factor for serious falls. *J Gerontol* 1987;42:412-417.
7. Woollacott M, Shumway-Cook A. Attention and the control of posture and gait: A review of an emerging area of research. *Gait Posture* 2002;16:1-14.
8. Yogeve-Seligmann G, Hausdorff JM, Giladi N. The role of executive function and attention in gait. *Mov Disord* 2008;23:329-342.
9. Herman T, Mirelman A, Giladi N et al. Executive control deficits as a prodrome to falls in healthy older adults: A prospective study linking thinking, walking, and falling. *J Gerontol A Biol Sci Med Sci* 2010;65:1086-1092.
10. Hausdorff JM, Yogeve G, Springer S et al. Walking is more like catching than tapping: Gait in the elderly as a complex cognitive task. *Exp Brain Res* 2005;164:541-548.
11. Muir SW, Gopaul K, Montero Odasso MM. The role of cognitive impairment in fall risk among older adults: A systematic review and meta-analysis. *Age Ageing* 2012;41:299-308.

12. Liu-Ambrose TY, Ashe MC, Graf P et al. Increased risk of falling in older community-dwelling women with mild cognitive impairment. *Phys Ther* 2008;88:1482–1491.
13. Verghese J, Robbins M, Holtzer R et al. Gait dysfunction in mild cognitive impairment syndromes. *J Am Geriatr Soc* 2008;56:1244–1251.
14. Montero-Odasso M, Bergman H, Phillips NA et al. Dual-tasking and gait in people with mild cognitive impairment. The effect of working memory. *BMC Geriatr* 2009;9:41.
15. Delbaere K, Kochan NA, Close JC et al. Mild cognitive impairment as a predictor of falls in community-dwelling older people. *Am J Geriatr Psychiatry* 2012;20:845–853.
16. Muir SW, Speechley M, Wells J et al. Gait assessment in mild cognitive impairment and Alzheimer's disease: The effect of dual-task challenges across the cognitive spectrum. *Gait Posture* 2011;35:96–100.
17. Holtzer R, Epstein N, Mahoney JR et al. Neuroimaging of mobility in aging: A targeted review. *J Gerontol A Biol Sci Med Sci* 2014;69A:1375–1388.
18. Maki BE, McIlroy WE. Postural control in the older adult. *Clin Geriatr Med* 1996;12:635–658.
19. Fasano A, Plotnik M, Bove F et al. The neurobiology of falls. *Neurol Sci* 2012;33:1215–1223.
20. Holtzer R, Wang C, Verghese J. Performance variance on walking while talking tasks: Theory, findings, and clinical implications. *Age (Dordr)* 2014;36:373–381.
21. Bloem BR, Grimbergen YA, van Dijk JG et al. The “posture second” strategy: A review of wrong priorities in Parkinson's disease. *J Neurol Sci* 2006;248:196–204.
22. Holtzer R, Verghese J, Allali G et al. Neurological gait abnormalities moderate the functional brain signature of the posture first hypothesis. *Brain Topogr* 2016;29:334–343.
23. van Iersel MB, Verbeek AL, Bloem BR et al. Frail elderly patients with dementia go too fast. *J Neurol Neurosurg Psychiatry* 2006;77:874–876.
24. Lundin-Olsson L, Nyberg L, Gustafson Y. “Stops walking when talking” as a predictor of falls in elderly people. *Lancet* 1997;349:617.
25. Montero-Odasso M, Muir SW, Speechley M. Dual-task complexity affects gait in people with mild cognitive impairment: The interplay between gait variability, dual tasking, and risk of falls. *Arch Phys Med Rehabil* 2012;93:293–299.
26. Verghese J, Wang C, Ayers E et al. Brain activation in high-functioning older adults and falls: Prospective cohort study. *Neurology* 2017;88:191–197.
27. Muir-Hunter SW, Wittwer JE. Dual-task testing to predict falls in community-dwelling older adults: A systematic review. *Physiotherapy* 2016;102:29–40.
28. Oliver D, Connelly JB, Victor CR et al. Strategies to prevent falls and fractures in hospitals and care homes and effect of cognitive impairment: Systematic review and meta-analyses. *BMJ* 2007;334:82.
29. Hauer K, Becker C, Lindemann U et al. Effectiveness of physical training on motor performance and fall prevention in cognitively impaired older persons: A systematic review. *Am J Phys Med Rehabil* 2006;85:847–857.
30. Verghese J, Mahoney J, Ambrose AF et al. Effect of cognitive remediation on gait in sedentary seniors. *J Gerontol A Biol Sci Med Sci* 2010;65A:1338–1343.
31. Smith-Ray RL, Hughes SL, Prohaska TR et al. Impact of cognitive training on balance and gait in older adults. *J Gerontol B Psychol Sci Soc Sci* 2015;70B:357–366.
32. Silsupadol P, Shumway-Cook A, Lugade V et al. Effects of single-task versus dual-task training on balance performance in older adults: A double-blind, randomized controlled trial. *Arch Phys Med Rehabil* 2009;90:381–387.
33. Falbo S, Condello G, Capranica L et al. Effects of physical-cognitive dual task training on executive function and gait performance in older adults: A randomized controlled trial. *Biomed Res Int* 2016;2016:5812092.
34. van het Reve E, de Bruin ED. Strength-balance supplemented with computerized cognitive training to improve dual task gait and divided attention in older adults: A multicenter randomized-controlled trial. *BMC Geriatr* 2014;14:134.
35. Schwenk M, Zieschang T, Oster P et al. Dual-task performances can be improved in patients with dementia: A randomized controlled trial. *Neurology* 2010;74:1961–1968.
36. Mirelman A, Maidan I, Herman T et al. Virtual reality for gait training: Can it induce motor learning to enhance complex walking and reduce fall risk in patients with Parkinson's disease? *J Gerontol A Biol Sci Med Sci* 2011;66A:234–240.
37. Mirelman A, Rochester L, Maidan I et al. Addition of a non-immersive virtual reality component to treadmill training to reduce fall risk in older adults (V-TIME): A randomised controlled trial. *Lancet* 2016;388:1170–1182.
38. van Ooijen MW, Roerdink M, Trekop M et al. The efficacy of treadmill training with and without projected visual context for improving walking ability and reducing fall incidence and fear of falling in older adults with fall-related hip fracture: A randomized controlled trial. *BMC Geriatr* 2016;16:215.
39. Auriel E, Hausdorff JM, Herman T et al. Effects of methylphenidate on cognitive function and gait in patients with Parkinson's disease: A pilot study. *Clin Neuropharmacol* 2006;29:15–17.
40. Ben Itzhak R, Giladi N, Gruendlinger L et al. Can methylphenidate reduce fall risk in community-living older adults? A double-blind, single-dose cross-over study. *J Am Geriatr Soc* 2008;56:695–700.
41. Shorer Z, Bachner Y, Guy T et al. Effect of single dose methylphenidate on walking and postural stability under single- and dual-task conditions in older adults—a double-blind randomized control trial. *J Gerontol A Biol Sci Med Sci* 2013;68A:1271–1280.
42. Montero-Odasso M, Wells J, Borrie M. Can cognitive enhancers reduce the risk of falls in people with dementia? An open-label study with controls. *J Am Geriatr Soc* 2009;57:359–360.
43. Pelosin E, Ogliastrro C, Lagravinese G et al. Attentional control of gait and falls: Is cholinergic dysfunction a common substrate in the elderly and Parkinson's disease? *Front Aging Neurosci* 2016;8:104.
44. Assal F, Allali G, Kressig RW et al. Galantamine improves gait performance in patients with Alzheimer's disease. *J Am Geriatr Soc* 2008;56:946–947.
45. Montero-Odasso M, Muir-Hunter SW, Oteng-Amoako A et al. Donepezil improves gait performance in older adults with mild Alzheimer's disease: A phase II clinical trial. *J Alzheimers Dis* 2015;43:193–199.
46. Chung KA, Lobb BM, Nutt JG et al. Effects of a central cholinesterase inhibitor on reducing falls in Parkinson disease. *Neurology* 2010;75:1263–1269.
47. Henderson EJ, Lord SR, Brodie MA et al. Rivastigmine for gait stability in patients with Parkinson's disease (ReSPonD): A randomised, double-blind, placebo-controlled, phase 2 trial. *Lancet Neurol* 2016;15:249–258.
48. Beauchet O, Launay C, Fantino B et al. Does memantine improve the gait of individuals with Alzheimer's disease? *J Am Geriatr Soc* 2011;59:2181–2182.
49. Panel on Prevention of Falls in Older Persons, American Geriatrics Society and British Geriatrics Society. Summary of the updated American Geriatrics Society/British Geriatrics Society clinical practice guideline for prevention of falls in older persons. *J Am Geriatr Soc* 2011;59:148–157.
50. You JH, Shetty A, Jones T et al. Effects of dual-task cognitive-gait intervention on memory and gait dynamics in older adults with a history of falls: A preliminary investigation. *NeuroRehabilitation* 2009;24:193–198.
51. Yogev-Seligmann G, Giladi N, Brozgov M et al. A training program to improve gait while dual tasking in patients with Parkinson's disease: A pilot study. *Arch Phys Med Rehabil* 2012;93:176–181.