Motor imagery of walking and walking while talking: a pilot randomized-controlled trial protocol for older adults

Helena M Blumen^{*,1} & Joe Verghese¹

¹Departments of Medicine & Neurology, Albert Einstein College of Medicine, Bronx, NY 10461, USA

* Author for correspondence: helena.blumen@einstein.yu.edu

Practice points

- Accelerated gait decline is common in older adults.
- Accelerated gait decline is associated with increased rates of morbidity, mortality and dementia.
- Motor imagery has been effectively used as a therapeutic tool for improving gait in Parkinson's disease and poststroke.
- This single-blind pilot randomized-controlled trial protocol aims to establish feasibility, and explore the efficacy of motor imagery for improving gait in relatively healthy elderly.
- A total of 24 healthy elderly will complete a 3-month (36 session) phone-based motor imagery intervention that involves imagined walking, imagined talking and imagined walking while talking.
- A total of 24 healthy elderly will complete a 3-month (36 session) active control/visual imagery intervention that involves imagining concrete objects (e.g., giraffe).
- Primary outcomes will be gait speed during actual walking and walking while talking.
- Secondary outcomes will include functional neuroplasticity during imagined walking and walking while talking, and cognitive performance during actual talking and walking while talking.

Over a third of community-residing elderly have clinical gait abnormalities, and gait impairment is associated with morbidity, mortality and dementia. Motor imagery – envisioning motor actions without actual execution – has been used to improve gait in Parkinson's disease and poststroke, but the efficacy of motor imagery in healthy elderly is unknown. This single-blind pilot randomized-controlled trial aims to establish feasibility and explore the efficacy of a 3-month, telephone-based motor imagery intervention – that involves imagined walking, imagined talking and imagined walking while talking for improving gait in 48 healthy elderly. The primary outcomes will be gait speed during actual walking and walking while talking. Secondary outcomes will include cognitive performance during actual talking and walking while talking, and functional neuroplasticity during imagined walking and walking while talking. This clinical trial has been registered on clinicaltrials.gov (identifier NCT02762604).

First draft submitted: 19 June 2017; Accepted for publication: 9 August 2017; Published online: 22 November 2017

Keywords: clinical trial protocol • executive function • gait speed

Accelerated gait decline is common among older adults; with more than a third of community-dwelling elders having clinically diagnosable gait abnormalities, such as parkinsonian, neuropathic or arthritic gait [1]. Accelerated gait decline is also associated with an increased risk for falls, morbidity, hospitalization, mortality, cognitive decline and dementia [2–6]. Physical exercise programs can improve gait in the elderly, but long-term adherence to physical exercise programs is low, and particularly difficult to implement in older adults [7–9]. Exploring novel alternatives to physical exercise programs that can be used to maintain or improve gait and mobility in older adults is therefore imperative.

Motor imagery involves envisioning motor actions without actually executing them [10], and offer a novel path for gait intervention that could and should be explored in older adults. Motor imagery has been successfully used by athletes to improve athletic performance for quite some time [11–14], and more recently in individuals

with Parkinson's disease [15–17] and poststroke patients [18–20] to improve gait, gait-related, and cognitive functions – including gait speed, stride length, tandem stance, timed up and go, clock drawing and Stroop interference. Motor imagery is considered an effective rehabilitative tool in athletes, Parkinson's disease, and poststroke because it engages the same or similar neural systems as the actual execution of motor actions [15–22]. The rehabilitative potential of motor imagery in the general elderly population, however, is unknown. Examining the rehabilitative potential of motor imagery in the healthy older adults could help us understand how to maintain gait and prevent mobility disability in aging, which are key to functional independence. Motor imagery also potentially could be used to safely initiate or complement physical exercise programs in physically frail or sedentary older adults with fairly intact cognition.

Dual-task gait conditions – or walking while performing a secondary cognitive task – are particularly sensitive to age-related changes in gait [23–30], and therefore particularly appropriate for exploring the efficacy of motor imagery for improving gait in healthy older adults. Dual-task gait conditions demand executive functions to properly allocate attention between two tasks, are typically localized to the prefrontal cortex, and are affected by aging [31–35]. We recently developed and validated a motor imagery of gait protocol against an actual gait protocol that involves an ecologically valid dual-task situation called the walking while talking (WWT) test – that is, walking while reciting alternate letters of the alphabet [30,36–37]. We chose to develop and validate an imagery version of the WWT test, rather than other dual-task gait conditions described in the literature [23,28–29,38], because it reliably predicts falls, frailty, disability and mortality in older adults [30,36,39]. This motor imagery of gait protocol involves imagined walking (iW), imagined talking (iT), and imagined walking while talking (iWWT). Using functional magnetic resonance imaging (fMRI) during motor imagery of gait, we also identified a network of brain regions that changed as a function of imagery task difficulty (iWWT > iT > iW), and was associated with actual WWT performance [37]. Brain activation increases during iWWT relative to iW and iT alone were primarily observed in cerebellar, precuneus, supplementary motor and prefrontal cortex regions. These early findings implied that this motor imagery of gait protocol engage similar neural systems as actual gait and executive function, and urged the translation of this protocol into an intervention for improving not only gait, but potentially also executive function, in older adults.

The first aim of this pilot randomized-controlled trial (RCT; clinicaltrials.gov: NCT02762604) is to establish the feasibility and explore the efficacy of this motor imagery of gait protocol for improving gait in older adults. We will conduct a single-blind pilot RCT of 48 healthy older adults who will be randomly assigned to a motor imagery of gait intervention or an active control (AC; nonmobility related visual imagery) intervention. The motor imagery of gait (or AC) intervention will be administered over the phone three-times a week for 3 months. Pre- and post-intervention change in gait velocity (cm/s) during actual W and WWT will be our primary outcome measures.

The second aim of this pilot RCT is to explore neuroplasticity changes in response to this motor imagery of gait intervention. To this end, participants will complete the imagined gait protocol (iW, iT and iWWT) during fMRI scanning at the pre- and post-intervention study visits, 3 months apart. We expect that our motor imagery of gait protocol will engage neural systems previously linked to actual gait and executive function, while the AC or visual imagery protocol will engage neural systems linked to visual processing and imagery in general. We further expect that the neural systems engaged during motor imagery of gait will be strengthened following our motor imagery of gait intervention.

Methods

Study design

We will recruit 48 community-dwelling older adults to participate in a single-blind RCT. Participants will be randomly assigned to a 12 week (three-times a week) phone-based motor imagery of gait or visual imagery (AC) intervention for 12 weeks (36 sessions).

Screening, recruitment & randomization

Older adults between 65 and 85 years old residing in the Bronx, Westchester, Manhattan, Brooklyn, and Queens counties will be recruited using public records such as voter registration lists and advertisements posted around local clinics and community organizations. Those expressing interest will be screened to exclude dementia over the phone using established cut scores on the memory impairment screen (MIS <5) and the ascertain dementia eight-item informant questionnaire (AD-8 >1) [40–43]. The MIS is a brief four-item dementia screen that can be

Box 1. Eligibility criteria.**Inclusion criteria**

- Adults between 65 and 85 years and older, residing in the community
- Able to speak English at a level sufficient to undergo study procedures
- Plan to be in the area for the next 3 months

Exclusion criteria

- Presence of dementia (telephone-based memory impairment screen <5 or AD-8 score >1)
- Presence of gait disorder diagnosed by clinician (e.g., neuropathy)
- Any medical condition or chronic medication use (e.g., neuroleptics) that will compromise safety or affect cognitive functioning
- Terminal illness with life expectancy <12 months
- Progressive, degenerative neurologic disease (e.g., Parkinson's disease, ALS)
- Major psychiatric disorders such as Schizophrenia
- Pacemaker or any permanent metal implants like hip prosthesis (other than tooth fillings) and claustrophobia
- Participation in other intervention trial or observational studies during the intervention period, or physical exercise program initiated within 2 weeks of the intervention period

ALS: Amyotrophic lateral sclerosis.

administered over the phone and has a sensitivity of 85%, and a specificity 86% [42,43]. The AD-8 is a brief informant questionnaire that can be administered over the phone and has a sensitivity of 74%, and a specificity 86% [40,41]. Those expressing interest will also be queried about their medical history to rule out a clinical diagnosis of a gait disorder, hearing problems, terminal illness with life expectancy <12 months, progressive neurodegenerative disease, and major psychiatric disorder. Participation in other intervention studies during the study period will be an exclusion criterion. Finally, those expressing interest will be screened for MRI safety and be queried about current participation in physical activities. Initiation of a physical exercise program within 2 weeks of the intervention period will be an exclusion criterion. **Box 1** includes a complete list of inclusion and exclusion criteria. Albert Einstein College of Medicine Institutional Review Board and a National Institute on Aging appointed Data and Safety Monitoring Board have approved all study procedures. Study staff and key personnel have also completed courses in responsible conduct of research from the Collaborative Institutional Training Initiative.

Study measures

A complete list of outcomes and other study measures are provided in **Table 1**, and primary outcomes are discussed below. These study measures will also serve to characterize participants at baseline, identify potential confounders to be considered in future studies, and determine the feasibility of this RCT. A number of different strategies will be used to reduce bias including concealing treatment allocation until participants have entered into trial [44], administering motor imagery and visual imagery interventions individually at home, instructing participants and study staff not to disclose assignment or details of interventions and using different study staff for the pre- and post-intervention assessments and the phone-based interventions. Pre- and post-intervention assessments are limited to 180 min over 1 day to avoid fatigue, if needed testing will be completed during an additional visit. Each phone-based interventions session will last for approximately 15 min.

Primary outcomes: gait speed during walking & walking while talking

Gait speed is a reliable, valid and sensitive functional outcome in clinical trials of older adults [48] and monitoring gait speed is a recommended strategy for identifying older adults at increased risk for a number of adverse health outcomes, including falls, frailty and disability [49–52]. Study staff will conduct gait evaluations using a computerized 4×14 foot Zeno electronic walkway using ProtoKinetics Movement Analysis Software (PKMAS; Zenometrics LLC; NY, USA). Participants will be asked to walk around this computerized walkway three-times at their normal pace (W). They will also be asked to walk around this computerized walkway three-times while reciting alternate letters of the alphabet (WWT), starting with the letter 'B'. During WWT they are further instructed to pay equal attention to both tasks to reduce task prioritization effects [30,36,53–55]. Finally, they will be asked to stand still on this walkway while reciting alternate letters of the alphabet for 30 s (T). Our primary outcome is gait speed (cm/s) during W and WWT, but additional gait parameters are obtained and available for analysis (see **Table 1**).

Table 1. Outcomes and other study measures.

Assessment	Preintervention	Intervention	Postintervention
Primary outcomes			
Gait speed (cm/s) during normal pace W	✓		✓
Gait speed (cm/s) during WWT	✓		✓
Secondary outcomes			
Cognitive performance (accuracy rate – correct-incorrect letters/time in seconds) during T	✓		✓
Cognitive performance (accuracy rate – correct-incorrect letters/time in seconds) during WWT	✓		✓
BOLD signal during imagined WWT	✓		✓
BOLD signal during imagined T	✓		✓
BOLD signal during imagined WWT	✓		✓
Quantitative gait measures other than speed = stride length, double support time, cadence, swing time, stance time, stride length variability and swing time variability	✓		✓
Trail making test (time, form B minus A)	✓		✓
Stroop interference test (time, color word trials minus color trials)	✓		✓
Flanker interference test (time, incongruent trials minus congruent trials)	✓		✓
Letter number sequencing (raw score)	✓		✓
Tertiary outcomes			
Free cued serial recall test (free recall)	✓		✓
Figure copy recall from RBANS [†]	✓		✓
Trail making test (time, Form A)	✓		✓
Semantic fluency	✓		✓
Digit symbol substitution test from WAIS [‡]	✓		✓
Short physical performance battery (range = 0–12)	✓		✓
Maze task (immediate, delayed, time and errors) [§]	✓		✓
Control oral word association test	✓		✓
Unipedal stance	✓		✓
Stair climbing	✓		✓
Grip strength	✓		✓
Falls history/questions	✓	✓	✓
Falls efficacy scale	✓		✓
Geriatric depression scale (30 item)	✓		✓
Beck anxiety inventory	✓		✓
Gray matter volume/cortical thickness	✓		✓
White matter integrity (fractional anisotropy)	✓		✓
White matter hyperintensities	✓		✓
Other study measures			
Demographic information	✓		
MIS	✓		
Ascertain dementia eight-item informant questionnaire (AD-8)	✓		
Medical history	✓		
Sensory screen	✓		
Medications	✓		
Height/weight/BMI	✓		✓
Blood pressure	✓		✓
WRAT	✓		
WTAR	✓		
Berg balance scale	✓		✓

[†]Repeatable battery for assessment of neuropsychological status [45].

[‡]Wechsler adult intelligence scale [46].

[§]Adult maze learning and recall task [47]

AD-8: Ascertain dementia 8-item informant questionnaire; BOLD: Blood–oxygen–level–dependent; CHAMPS: Community health activities model program for senior; MIS: Memory impairment screen; MOS: Medical outcomes study; RBANS: Repeatable battery for the assessment of neuropsychological status; T: Talk; W: Walk; WRAT: Wide range achievement test; WTAR: Wechsler test of adult reading; WWT: Walking while talking.

Table 1. Outcomes and other study measures (cont.).

Assessment	Preintervention	Intervention	Postintervention
Duke activity status index	✓		✓
General mobility questionnaire	✓		✓
Instrumental activities of daily living questionnaire	✓		✓
Activity balance confidence scale	✓		✓
12-item short form health survey (SF-12)	✓		✓
CHAMPS	✓	✓	✓
Social network index	✓		✓
MOS social support survey	✓		✓

[†]Repeatable battery for assessment of neuropsychological status [45].
[‡]Wechsler adult intelligence scale [46].
[§]Adult maze learning and recall task [47].
AD-8: Ascertain dementia 8-item informant questionnaire; BOLD: Blood-oxygen-level-dependent; CHAMPS: Community health activities model program for senior; MIS: Memory impairment screen; MOS: Medical outcomes study; RBANS: Repeatable battery for the assessment of neuropsychological status; T: Talk; W: Walk; WRAT: Wide range achievement test; WTAR: Wechsler test of adult reading; WWT: Walking while talking.

Secondary outcomes: accuracy & neuroplasticity

One secondary outcome is accuracy rate – correct-incorrect letters/time in seconds – during actual T and WWT. Another secondary outcome is neuroplasticity – or changes in the blood-oxygen-level dependent (BOLD) signal – during imagined Walking (iW) and imagined Walking While Talking (iWWT). Secondary outcomes also include quantitative gait parameters other than gait speed (see Table 1) and executive function assessed with the Trail Making Test [56], the Stroop Interference Test [57], a flanker interference task [58], and the letter number sequencing task from the Wechsler Adult Intelligence Scale-III [46]. Other secondary and tertiary outcomes are listed in Table 1.

Motor & visual imagery training

During motor imagery training, participants will be asked to iW, iT and walking while reciting alternate letters of the alphabet iWWT. They will be instructed to close their eyes during imagery, use both visual and kinesthetic imagery, and pay equal attention to both tasks in the iWWT condition. Seated at a desk, they will then complete two trials of imagery training in 16-s blocks for approximately 15 min. During trial 1, each movement will be imagined once and during trial 2 each movement will be imagined twice, in a randomly generated order. Imagery instructions will be presented visually and auditorily, and the beginning and the end of a block will be initiated with a tone. During the first trial, instructions will be detailed (i.e., “*Imagine walking: at the start of the next tone, close your eyes and imagine or envision yourself walking on the mat. At the start of the following tone, stop, and wait for further instructions*”), but during the second trial they will simply prompted to begin at the start of the tone (e.g., “*imagine walking*”). Following each trial, participants will be asked to evaluate the quality of their visual and kinesthetic images on a validated scale from 1 (no image; no sensation) to 5 (image as clear as seeing; as intense as executing the action) [59,60]. Participants will also be queried about whether they were able to pay equal attention to both task during the iWWT condition, and if not, be encouraged to do so. During visual imagery training, participants will be trained to imagine a set of concrete objects (e.g., giraffe) from a standardized set of pictures [61] that have been normed for name agreement, image agreement and visual complexity. Again, they will be instructed to close their eyes during imagery and will complete two trials of imagery training for approximately 15 min. During trial 1, each object will be imagined once, and during trial 2 each objects will imagined twice, in a randomly generated order. Imagery instructions will be presented visually and auditorily and the beginning and the end of a block will be initiated with a tone. Following each trial participants will be asked to evaluate the quality of their visual images on a scale from 1 to 5.

Motor imagery & visual imagery during fMRI scanning

During the motor imagery of gait fMRI protocol, imagery prompts (e.g., imagine walking) will be presented visually and auditorily and volume will be adjusted to ensure instructions can be heard clearly in the presence of scanning noise. Imagery will occur in 16-s blocks (eyes closed). A tone will indicate the beginning and the end of a block, and each block will be repeated six-times. During the visual imagery of concrete objects fMRI protocol, imagery prompts (e.g., imagine a giraffe) will be presented visually auditorily and volume adjusted to ensure instructions could be heard clearly in the presence of scanning noise. Again, imagery will occur in 16-s blocks (eyes closed). A

tone will indicate the beginning and the end of a block, and each block will be repeated six-times. Following each imagery task, participants will again be asked to evaluate the overall quality of their kinesthetic and or visual images on a 1–5 scale.

MRI scanning will be performed with a Philips 3T Achieva Quasar TX multinuclear MRI/MRS system. All BOLD (T2*-weighted) images [62,63] will be acquired with echo planar imaging (EPI) using a whole brain gradient over a 240 mm field of view on a 128×128 acquisition matrix, 3 mm slice thickness (no gap); TE = 30 ms, TR = 2000 ms, flip angle = 90 degrees and 42 trans-axial slices per volume. T1-weighted whole head structural images will also be acquired using axial 3D-MP-RAGE parameters over a 240 mm field of view and 1.0 mm isotropic resolution, TE = 4.6 ms, TR = 9.9 ms, $\alpha = 8^\circ$, with SENSE factor 2.5. Our motor imagery and visual imagery during fMRI protocols are written in E-Prime 2.0 (Psychology Software Tools Inc.) and will be presented with an *In Vivo* Eloquence fMRI system. A neuroradiologist will review each MRI scan to confirm that there are no clinically significant findings for any of the participants. Any participant with potentially clinically significant findings are contacted and encouraged to follow-up with their physician. The results of the neuroradiologist review can also be shared with their physician if requested. Additional MRI images and secondary outcomes will also be examined and recorded for consideration as potential covariates in upcoming full-scale RCTs, including diffusion-weighted imaging (see Table 1).

Study interventions: motor imagery & visual imagery phone-based intervention

During the imagined gait intervention, participants will be called by the experimenter three-times a week and be asked to iW, iT and iWWT in the same manner as during their study visit. They will also be asked to rate their visual and kinesthetic qualities of their images on a 1–5 scale [59,60] following each trial. During the visual imagery intervention, participants will be called three-times a week by the experimenter and be asked to imagine concrete objects following the same protocol as during their study visit. They will also be asked to rate their visual qualities of their images on a 1–5 scale.

Study interventions: performance monitoring, frequency, duration & feasibility

The motor imagery of gait and visual imagery interventions will be administered by designated study staff under controlled conditions to protect internal validity of the study, and to ensure compliance with protocol. Participants will be instructed to take a seat and turn-down any distracting noise (such as the radio or TV) before beginning each session. Following each 15-min session, the visual and kinesthetic qualities of the images will be tracked to ensure that participants are fully engaged during each session. Tracking imagery performance in this manner will be used to establish feasibility, to assess the presence of a dose response effect, and will help in the design of future studies. Participants will be contacted over the phone on Monday, Wednesday and Friday mornings (before 12 noon), unless other times or days are preferred. If a participant is unavailable at the scheduled time, we will try to reach them later in the day, but if we are still unsuccessful, we will skip that particular session and wait until the next scheduled session. Any unexpected distractions or missed sessions will be carefully recorded, and examined to inform the development of full-scale RCT

Our first criteria for feasibility will be that the average visual and kinesthetic imagery ratings for completed imagery sessions will be above 2, which corresponds to more than a blurred image and a mildly intense sensation, respectively. A total of 36 sessions of phone-based motor imagery or visual imagery sessions will be administered over 12 weeks. Each training session takes 15 min to complete and the total training time over 12 weeks is 540 min. Any unexpected distractions or missed sessions will be carefully recorded, and examined for feasibility and to inform the development of future full-scale RCTs. Our second criteria for feasibility will be that on average at least 75% of imagery sessions are completed, which corresponds to at least 27 sessions.

Statistical plan: behavioral efficacy analyses

Behavioral efficacy analyses will examine change in performance from baseline (preintervention) to the end of the 3-month training period (postintervention). Our primary outcome measures will be gait speed (cm/s) during actual W and WWT. We will use linear mixed effects models that include time of test (pre and post), and trial type (W or WWT) as within subjects factors, and imagery condition (imagined gait or AC) as the between-subjects factor. Consideration of these analyses will focus on the interactions between time of test, trial type and imagery condition. Parallel analyses will be used for our secondary outcomes: Cognitive performance during actual T and WWT, the trail making test, the letter number sequencing test, the stroop color and word test and the flanker

interference task. All analyses will be performed with the intention to treat such that all randomized participants, regardless of adherence, whether the intervention was received and subsequently withdrawn or deviated from the protocol, are considered in the analyses. All behavioral analyses will be corrected for multiple comparisons, using the Bonferroni correction.

Statistical plan: neuroplasticity analyses

Preprocessing will be performed with statistical parametric mapping (SPM12). Each participant's EPI dataset will be realigned to the first volume to correct for motion, temporally shifted to correct for the order of slice acquisition, co-registered to the T1-weighted image, and spatially normalized [64] into Montreal Neurologic Institute space using an older adult brain template supplied by the clinical toolbox [65]. Finally, images will be spatially smoothed with an isotropic Gaussian kernel, full-width at half-maximum = 6 mm. In the first-level general linear model, the EPI time series will be modeled with regressors that represent the expected BOLD response (implicitly relative to blanks) for each trial type (iT, iW and iWWT). Each block will be convolved with a canonical model of the hemodynamic response function supplied with SPM12. The contrast maps for each imagery trial generated in our first-level analyses will then be used in the second-level group covariance analyses. We will use a whole-brain multivariate ordinal trend covariance analysis in the PCA suite [66] to analyze the motor imagery of gait protocol [67,68]. This is because we are interested in determining how the use of the entire locomotion and executive function systems change as a function of our imagined gait versus the active control condition. This is also because changes in neural activation are often masked by between-subject variability, an issue that is particularly important to consider in aging [69,70]. More specifically, ordinal trend covariance analysis will be used to identify covariance patterns in the BOLD signal as a function of trial type (iT, iW and iWWT) at each study visit (pre and postintervention) for each imagery condition (imagined gait or AC). Note also that these multivariate analyses involve data reduction, and therefore do not involve multiple comparisons.

Power: behavioral

We recognize that this is the first RCT of motor imagery in healthy older adults, and therefore reliable power estimates are difficult to obtain. Setting an α level of 0.05, power of 0.80 and a medium effect size of defined as $f = 0.25$, however, the necessary sample size for detecting an interaction between time of test (pre and post), trial type (W or WWT) and imagery condition (Imagined gait or AC) is $n = 34$. Thus, our study completion goal of $n = 48$ is sufficient to detect a medium effect size and account for the 18% attrition rate expected during the study period, as observed in our previous studies [71].

Power: fMRI

To detect a signal change at the individual subject level (i.e., first-level time-series modeling using SPM) at $p < 0.001$, a percent signal change of 0.34% is required using a published method and estimate of noise at a magnet strength of 3.0 Tesla [72]. Based on this estimation, to detect a difference in contrast values between groups (i.e., second-level analyses using SPM) at $p < 0.001$ and a power of at least 0.80, where the mean of one group's signal change is 50% of the other, 16 subjects per group are required. Thus, our study completion goal of $n = 48$ (24 in each condition) is sufficient to detect a 0.34% change in BOLD signal between imagery conditions (imagined gait vs AC), and leave room for the detection of interactions.

Data management & quality control

Trained study staff will collect and enter behavioral data in a secure REDcap [73] database at each study visit, and during the phone-based interventions. REDcap databases not only provide central storage and back-up of your data and export functions into different statistical software, but also real-time data validation and integrity checks. Neuroimaging data will be stored, preprocessed, and analyzed in a secure Linux server environment. Only trained study staff will be assigned data viewing and entry or login privileges in these databases. Data monitoring reports and analyses will performed for the Data Safety Monitoring Board (DSMB) meetings on a biannual basis.

Discussion

This pilot RCT is the first to establish feasibility and explore the therapeutic potential of motor imagery for improving gait and executive control in healthy older individuals. Our motor imagery of gait intervention builds upon previous studies in athletes, individuals with Parkinson's disease [15–17] and poststroke [18–19,74–76], which

suggest that motor imagery can improve gait, gait-related motor actions and cognitive functions. Given the high rates of mobility disability among US seniors, even in seniors without neurological diseases, this is a highly relevant public health issue. Investigating the rehabilitative potential of motor imagery in healthy older adults could inform us about how to maintain gait and mobility in older adults, and thereby increasing functional independence.

This pilot RCT will utilize a novel, but recently validated imagined gait protocol that involves an ecologically valid dual-task situation that is particularly challenging to older adults and predicts falls, frailty, disability and mortality in older adults [30,36]. If successful, this motor imagery of gait intervention could offer a noninvasive, cost-efficient new path to intervention that overcomes the challenges associated with physical exercise interventions, such as low long-term adherence, limiting medical conditions and limited access to physical exercise programs and facilities. Motor imagery also potentially could precede, supplement or complement physical exercise programs in older adults. The knowledge gained from this pilot RCT will set the foundation for future full-scale RCTs in healthy older adult and other aging populations. If successful, the results will be generalizable and sustainable in community-dwelling elderly populations. Moreover, these findings will provide the foundation to extend this intervention to vulnerable elderly populations such as those with physical frailty.

Financial & competing interests disclosure

This research is supported by the NIH: National Institute on Aging (1K01AG049829-01A1). The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

References

Papers of special note have been highlighted as: • of interest

- Verghese J, Levalley A, Hall CB, Katz MJ, Ambrose AF, Lipton RB. Epidemiology of gait disorders in community-residing older adults. *J. Am. Geriatr. Soc.* 54(2), 255–261 (2006).
- **Characterizes the epidemiology of gait disorders in community-dwelling elderly.**
- Newman AB, Simonsick EM, Naydeck BL *et al.* Association of long-distance corridor walk performance with mortality, cardiovascular disease, mobility limitation, and disability. *JAMA* 295(17), 2018–2026 (2006).
- Verghese J, Wang C, Lipton RB, Holtzer R, Xue X. Quantitative gait dysfunction and risk of cognitive decline and dementia. *J. Neurol. Neurosurg. Psychiatry* 78(9), 929–935 (2007).
- Marquis S, Moore MM, Howieson DB *et al.* Independent predictors of cognitive decline in healthy elderly persons. *Arch. Neurol.* 59(4), 601–606 (2002).
- Waite LM, Grayson DA, Piguet O, Creasey H, Bennett HP, Broe GA. Gait slowing as a predictor of incident dementia: 6-year longitudinal data from the Sydney Older Persons Study. *J. Neurol. Sci.* 230, 89–93 (2005).
- Wang L, Larson EB, Bowen JD, Van Belle G. Performance-based physical function and future dementia in older people. *Arch. Intern. Med.* 166(10), 1115–1120 (2006).
- Singh MA. Exercise comes of age: rationale and recommendations for a geriatric exercise prescription. *J. Gerontol. A. Biol. Sci. Med. Sci.* 57(5), M262–M282 (2002).
- Elsawy B, Higgins K. Physical activity guidelines for older adults. *Am. Fam. Physician* 81(1), 55–59 (2010).
- Dishman RK, Sallis JF, Orenstein DR. The determinants of physical activity and exercise. *Public Health Rep.* (1974-) 100(2), 158–171 (1985).
- Jeannerod M. The representing brain: neural correlates of motor intention and imagery. *Behav. Brain Sci.* 17(02), 187–202 (1994).
- Martin KA, Moritz SE, Hall CR. Imagery use in sport: a literature review and applied model. *Sport Psychol.* 13(3), 245–268 (1999).
- Murphy SM. Models of imagery in sport psychology: a review. *J. Mental Imagery* 14(3–4), 153–172 (1990).
- Guillot A, Collet C. Construction of the Motor Imagery Integrative Model in Sport: a review and theoretical investigation of motor imagery use. *Int. Rev. Sport Exercise Psychol.* 1(1), 31–44 (2008).
- Feltz DL, Landers DM. The effects of mental practice on motor skill learning and performance: a meta-analysis. *J. Sport Psychol.* 5(1), 25–57 (1983).
- Tamir R, Dickstein R, Huberman M. Integration of motor imagery and physical practice in group treatment applied to subjects with Parkinson's disease. *Neurorehab. Neural Rep.* 21(1), 68–75 (2007).
- Heremans E, Feys P, Nieuwboer A *et al.* Motor imagery ability in patients with early- and mid-stage Parkinson disease. *Neurorehab. Neural Rep.* 25(2), 168–177 (2011).

17. Schlesinger I, Benyakov O, Erikh I, Nassar M. Relaxation guided imagery reduces motor fluctuations in Parkinson's disease. *J. Parkinsons Dis.* 4(3), 431–436 (2014).
18. Dunskey A, Dickstein R, Marcovitz E, Levy S, Deutsch JE. Home-based motor imagery training for gait rehabilitation of people with chronic poststroke hemiparesis. *Arch. Phys. Med. Rehabil.* 89(8), 1580–1588 (2008).
19. Dunskey A, Dickstein R, Ariav C, Deutsch J, Marcovitz E. Motor imagery practice in gait rehabilitation of chronic post-stroke hemiparesis: four case studies. *Int. J. Rehabil. Res.* 29(4), 351–356 (2006).
20. Dickstein R, Deutsch JE, Yoeli Y *et al.* Effects of integrated motor imagery practice on gait of individuals with chronic stroke: a half-crossover randomized study. *Arch. Phys. Med. Rehabil.* 94(11), 2119–2125 (2013).
21. Jeannerod M. Neural simulation of action: a unifying mechanism for motor cognition. *NeuroImage* 14(1), S103–S109 (2001).
22. Anderson WS, Lenz FA. Review of motor and phantom-related imagery. *Neuroreport* 22(17), 939–942 (2011).
23. Beurskens R, Bock O. Age-related deficits of dual-task walking: a review. *Neural Plast.* 2012, 131608 (2012).
24. Buracchio T, Dodge HH, Howieson D, Wasserman D, Kaye J. The trajectory of gait speed preceding mild cognitive impairment. *Arch. Neurol.* 67(8), 980–986 (2010).
25. Holtzer R, Verghese J, Xue X, Lipton RB. Cognitive processes related to gait velocity: results from the Einstein Aging Study. *Neuropsychology* 20(2), 215–223 (2006).
26. Holtzer R, Mahoney JR, Izzetoglu M, Izzetoglu K, Onaral B, Verghese J. fNIRS study of walking and walking while talking in young and old individuals. *J. Gerontol. A. Biol. Sci. Med. Sci.* 66(8), 879–887 (2011).
27. Holtzer R, Wang C, Lipton R, Verghese J. The protective effects of executive functions and episodic memory on gait speed decline in aging defined in the context of cognitive reserve. *J. Am. Geriatr. Soc.* 60(11), 2093–2098 (2012).
28. Lindenberger U, Marsiske M, Baltes PB. Memorizing while walking: increase in dual-task costs from young adulthood to old age. *Psychol. Aging* 15(3), 417–436 (2000).
29. Neider MB, Gaspar JG, Mccarley JS, Crowell JA, Kaczmariski H, Kramer AF. Walking and talking: dual-task effects on street crossing behavior in older adults. *Psychol. Aging* 26(2), 260–268 (2011).
30. Verghese J, Buschke H, Viola L *et al.* Validity of divided attention tasks in predicting falls in older individuals: a preliminary study. *J. Am. Geriatr. Soc.* 50(9), 1572–1576 (2002).
- **Early study of the validity of the walking while talking task adapted for motor imagery use, and extended into the motor imagery intervention described in this manuscript.**
31. Alvarez JA, Emory E. Executive function and the frontal lobes: a meta-analytic review. *Neuropsychol. Rev.* 16(1), 17–42 (2006).
32. Elderkin-Thompson V, Ballmaier M, Hellemann G, Pham D, Kumar A. Executive function and MRI prefrontal volumes among healthy older adults. *Neuropsychology* 22(5), 626–637 (2008).
33. Koechlin E, Ody C, Kouneiher F. The architecture of cognitive control in the human prefrontal cortex. *Science* 302(5648), 1181–1185 (2003).
34. Miller EK, Cohen JD. An integrative theory of prefrontal cortex function. *Ann. Rev. Neurosci.* 24(1), 167–202 (2001).
35. Holtzer R, Mahoney JR, Izzetoglu M, Izzetoglu K, Onaral B, Verghese J. fNIRS study of walking and walking while talking in young and old individuals. *J. Gerontol. A. Biol. Sci. Med. Sci.* 66(8), 879–887 (2011).
36. Verghese J, Holtzer R, Lipton RB, Wang C. Mobility stress test approach to predicting frailty, disability, and mortality in high-functioning older adults. *J. Am. Geriatr. Soc.* 60(10), 1901–1905 (2012).
37. Blumen HM, Holtzer R, Brown LL, Gazes Y, Verghese J. Behavioral and neural correlates of imagined walking and walking while talking in the elderly. *Hum. Brain Mapp.* 35(8), 4090–4104 (2014).
- **Describes the development of the motor imagery protocol extended into the motor imagery intervention described in this manuscript.**
38. Li KZ, Lindenberger U, Freund AM, Baltes PB. Walking while memorizing: age-related differences in compensatory behavior. *Psychol. Sci.* 12(3), 230–237 (2001).
39. Lundin-Olsson L, Nyberg L, Gustafson Y. "Stops walking when talking" as a predictor of falls in elderly people. *Lancet* 349(9052), 617 (1997).
40. Galvin JE, Roe CM, Powlishta KK *et al.* The AD8: a brief informant interview to detect dementia. *Neurology* 65(4), 559–564 (2005).
41. Galvin JE, Roe CM, Xiong C, Morris JC. Validity and reliability of the AD8 informant interview in dementia. *Neurology* 67(11), 1942–1948 (2006).
42. Lipton RB, Katz MJ, Kuslansky G *et al.* Screening for dementia by telephone using the memory impairment screen. *J. Am. Geriatr. Soc.* 51(10), 1382–1390 (2003).
43. Verghese J, Noone ML, Johnson B *et al.* Picture-based memory impairment screen for dementia. *J. Am. Geriatr. Soc.* 60(11), 2116–2120 (2012).
44. Day SJ, Altman DG. Blinding in clinical trials and other studies. *BMJ* 321(7259), 504 (2000).

45. Randolph C, Tierney MC, Mohr E, Chase TN. The repeatable battery for the assessment of neuropsychological status (RBANS): preliminary clinical validity. *J. Clin. Exp. Neuropsychol.* 20(3), 310–319 (1998).
46. Wechsler D. *Wechsler Adult Intelligence Scale – III*. Psychological Corporation, San Antonio, TX, USA (1997).
47. Sanders AE, Holtzer R, Lipton RB, Hall C, Verghese J. Egocentric and exocentric navigation skills in older adults. *J. Gerontol. A. Biol. Sci. Med. Sci.* 63(12), 1356–1363 (2008).
48. Trials WGOFOMFC. Indications, labeling, and outcomes assessment for drugs aimed at improving functional status in older persons: a conversation between aging researchers and FDA regulators. *J. Gerontol. A. Biol. Sci. Med. Sci.* 64(4), 487–491 (2009).
49. Cummings SR, Studenski S, Ferrucci L. A diagnosis of dismobility – giving mobility clinical visibility: a Mobility Working Group recommendation. *JAMA* 311(20), 2061–2062 (2014).
50. Panel on Prevention of Falls in Older Persons AGS, British Geriatrics S. Summary of the updated American Geriatrics Society/British Geriatrics Society clinical practice guideline for prevention of falls in older persons. *J. Am. Geriatr. Soc.* 59(1), 148–157 (2011).
51. Society AG, Society G, Of AA, On Falls Prevention OSP. Guideline for the prevention of falls in older persons. *J. Am. Geriatr. Soc.* 49(5), 664–672 (2001).
52. Turner G, Clegg A. Best practice guidelines for the management of frailty: a British Geriatrics Society, age UK and Royal College of General Practitioners report. *Age Ageing* 43(6), 744–747 (2014).
53. Verghese J, Kuslansky G, Holtzer R *et al.* Walking while talking: effect of task prioritization in the elderly. *Arch. Phys. Med. Rehabil.* 88(1), 50–53 (2007).
54. Yogev-Seligmann G, Rotem-Galili Y, Mirelman A, Dickstein R, Giladi N, Hausdorff JM. How does explicit prioritization alter walking during dual-task performance? Effects of age and sex on gait speed and variability. *Phys. Ther.* 90(2), 177–186 (2010).
55. Oh-Park M, Holtzer R, Mahoney J, Wang C, Raghavan P, Verghese J. Motor dual-task effect on gait and task of upper limbs in older adults under specific task prioritization: pilot study. *Aging Clin. Exp. Res.* 25(1), 99–106 (2013).
56. Reitan R. *Manual for Administration of Neuropsychological Test Batteries for Adults and Children*. Reitan Neuropsychology Laboratories, Tucson, AZ, USA (1978).
57. Golden C. *Stroop Color and Word Test*. Stoltz, Chicago, IL, USA (1978).
58. Fan J, McClelland BD, Sommer T, Raz A, Posner MI. Testing the efficiency and independence of attentional networks. *J. Cog. Neurosci.* 14(3), 340–347 (2002).
59. Marks DF. Visual imagery differences in the recall of pictures. *Brit. J. Psychol.* 64(1), 17–24 (1973).
60. Marks DF. New directions for mental imagery research. *J. Mental Imagery* 19(3–4), 153–167 (1995).
61. Snodgrass JG, Vanderwart M. A standardized set of 260 pictures: norms for name agreement, image agreement, familiarity, and visual complexity. *J. Exp. Psychol. Hum. Learn.* 6(2), 174–215 (1980).
62. Ogawa S, Menon RS, Tank DW *et al.* Functional brain mapping by blood oxygenation level-dependent contrast magnetic resonance imaging. A comparison of signal characteristics with a biophysical model. *Biophys. J.* 64(3), 803–812 (1993).
63. Kwong KK, Belliveau JW, Chesler DA *et al.* Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation. *Proc. Natl Acad. Sci. USA* 89(12), 5675–5679 (1992).
64. Friston KJ, Ashburner J, Frith CD, Poline JB, Heather JD, Frackowiak RSJ. Spatial registration and normalization of images. *Hum. Brain Mapp.* 3(3), 165–189 (1995).
65. Rorden C, Bonilha L, Fridriksson J, Bender B, Karnath HO. Age-specific CT and MRI templates for spatial normalization. *NeuroImage* 61(4), 957–965 (2012).
66. NITRC: Generalized Covariance Analysis (gCVA). www.nitrc.org/projects/gcva_pca
67. Habeck C, Rakitin BC, Moeller J *et al.* An event-related fMRI study of the neural networks underlying the encoding, maintenance, and retrieval phase in a delayed-match-to-sample task. *Brain Res. Cogn. Brain Res.* 23(2–3), 207–220 (2005).
68. Habeck C, Stern Y. Neural network approaches and their reproducibility in the study of verbal working memory and Alzheimer's disease. *Clin. Neurosci. Res.* 6(6), 381–390 (2007).
69. Cabeza R, Anderson ND, Locantore JK, McIntosh AR. Aging gracefully: compensatory brain activity in high-performing older adults. *NeuroImage* 17(3), 1394–1402 (2002).
70. Colcombe SJ, Kramer AF, Erickson KI, Scalf P. The implications of cortical recruitment and brain morphology for individual differences in inhibitory function in aging humans. *Psychol. Aging* 20(3), 363–375 (2005).
71. Verghese J, Holtzer R. Walking the walk while talking: cognitive therapy for mobility in dementia? *Neurology* 74(24), 1938–1939 (2010).
72. Smith S, Jenkinson M, Beckmann C, Miller K, Woolrich M. Meaningful design and contrast estimability in fMRI. *Neuroimage* 34(1), 127–136 (2007).
73. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap) – a metadata-driven methodology and workflow process for providing translational research informatics support. *J. Biomed. Inform.* 42(2), 377–381 (2009).

74. Kim JS, Oh DW, Kim SY, Choi JD. Visual and kinesthetic locomotor imagery training integrated with auditory step rhythm for walking performance of patients with chronic stroke. *Clin. Rehab.* 25(2), 134–145 (2011).
75. Verma R, Arya KN, Garg RK, Singh T. Task-oriented circuit class training program with motor imagery for gait rehabilitation in poststroke patients: a randomized-controlled trial. *Top. Stroke Rehabil.* 18(Suppl. 1), 620–632 (2011).
76. Cho H-Y, Kim J-S, Lee G-C. Effects of motor imagery training on balance and gait abilities in post-stroke patients: a randomized-controlled trial. *Clin. Rehab.* 27(8), 675–680 (2013).