Workshop 10:
Aging, the Central Nervous System, and Mobility in Older Adults: Intervention Strategies to Prevent and Improve Late Life Gait Decline

Sunday, June 28, 2015

Melia Sevilla Hotel
Seville, Spain

A pre-congress workshop in conjunction with the International Society for Posture and Gait Research

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Aging, the Central Nervous System, and Mobility in Older Adults
2012–2015

The aims of Aging, the Central Nervous System, and Mobility in Older Adults are to:
1. Examine existing evidence from basic, epidemiological, and clinical perspectives and enhance links from animal studies to human investigation of both normal aging and disease at the individual and population level.
2. Promote collaborations among basic, epidemiological, and clinical scientists of interrelated disciplines who might not otherwise have an opportunity to work together.
3. Identify knowledge gaps, barriers to progress, alternative strategies, and prospects for future inquiry through discussions of emerging research findings.
4. Emphasize cutting-edge methodologies for central nervous system (CNS) and mobility measures.
5. Support involvement from junior investigators, women, minorities, and other underrepresented groups.
6. Encourage discussions and exchanges of ideas from workshop participants by providing ample time for interactions and using multimedia presentation formats, including videos.
7. Disseminate findings, discussions, and recommendations to investigators, clinicians, and the public through symposia at The Gerontological Society of America Annual Scientific Meeting, as well as submit coordinated individual papers to a variety of related journals (e.g., Neurology, Gait & Posture, Behavioral and Brain Functions, Movement Disorders, The Journal of Gerontology: Medical Sciences, Frontiers in Aging Neuroscience) for publication.

The scientific focuses for the 3-year program are:
- 2012 Workshop: Establish the best evidence to date for a relationship between the CNS and mobility in the context of other contributors, and identify state-of-the-art technology to measure CNS plasticity and mobility in older adults.
- 2013 Workshop: Ascertain the mechanisms and causes of mobility impairment in older adults.
- 2014 Workshop: Discuss implications for clinical practice, as well as prevention and intervention studies, and recommend future studies on mobility impairments in older adults.
- 2015 Workshop: Identify and critically review intervention strategies to prevent and improve late life gait decline.
Aging, the Central Nervous System, and Mobility in Older Adults: Intervention Strategies to Prevent and Improve Late Life Gait Decline
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Workshop 10: Aging, Central Nervous System and Mobility
Intervention Strategies to Prevent and Improve Late Life Gait Decline
Sunday, June 28, 2015
Melia Sevilla Hotel, Seville, Spain
Speaker Roster and Bios

Caterina Rosano, MD, MPH
Co-Principal Investigator and Workshop Co-Chair
Caterina Rosano is Associate Professor and Director of the Neuroepidemiology Area of Concentration for the Department of Epidemiology in the Graduate School of Health at the University of Pittsburgh. She received her medical degree from the University of Palermo Medical School in Italy and later received her master’s degree in public health in epidemiology at the University of Pittsburgh. Her background includes training in geriatric neuroepidemiology and neuroscience. Dr. Rosano has extensive experience integrating brain imaging techniques into large clinical epidemiologic studies. The goal of her research is to investigate the interactions and synergisms between brain structure and function in relation to the aging process and to identify the modifiable factors underlying this relationship. Her work applies state-of-the-art neuroimaging methodologies, structural and functional magnetic resonance imaging, in large epidemiological studies to identify key brain structures that affect locomotion in elderly individuals. Collectively, Dr. Rosano’s studies constitute a unique and novel resource comprising large datasets of detailed brain and functional markers from several hundreds of individuals. It is expected that these data will augment our understanding of brain aging and will contribute to the discovery of new approaches to the promotion of disability-free survival. Additionally, Dr. Rosano is interested in the application and validation of advanced statistical modeling algorithms for data reduction and the study of the mechanisms underlying brain degeneration, specifically dysmetabolic processes.

Michelle Carlson, PhD
Michelle Carlson is Associate Professor at The Johns Hopkins School of Public Health and a core faculty member of The Johns Hopkins Center on Aging and Health. Dr. Carlson leads observational and randomized controlled trial research to evaluate environmental and biologic modifiers of neurocognitive aging, dementia risk, and the intersection of cognitive and physical frailty. She serves as Johns Hopkins site principal investigator (PI) of the national Cardiovascular Health Study. Dr. Carlson has 10 years of experience in leading large-scale clinical trials, having served as PI of the Johns Hopkins site of the Ginkgo Evaluation of Memory randomized controlled trial and as a project leader on the Baltimore Experience Corps Trial to evaluate the impact of high-intensity volunteer service on older adults’ cognitive, brain, and physical health. Within this trial, Dr. Carlson conducted a nested Brain Health Study to evaluate the mechanisms through which Experience Corps impacts older adults’ health using neuroimaging biomarkers and accelerometry. Dr. Carlson uses wearable devices to objectively link patterns of real-world activity to neurocognitive and functional health with the goal of defining how socially and cognitively enriching activity in daily life may help to simultaneously delay dementia and physical frailty.

Stephen Lord, PhD
Stephen Lord is a Senior Principal Research Fellow at Neuroscience Research Australia, in Sydney, Australia. He has published over 300 papers in the areas of balance, gait, and falls in older people and is acknowledged as a leading international researcher in his field. Dr. Lord’s research follows two main themes: (1) the identification of physiological risk factors for falls and (2) the development and evaluation of falls prevention strategies. Key aspects of this research have been the elucidation of sensorimotor factors that underpin balance and gait and the design, implementation, and evaluation of exercise programs for the general population of older people as well as for those identified as being at increased risk of falls, specifically people with Parkinson’s disease, stroke, dementia, and frailty. His methodology and approach to fall-risk assessment have been adopted by many researchers and clinicians across the world and he is actively engaged in initiatives aimed at implementing falls prevention evidence into policy and practice.
Manuel Montero-Odasso, MD, PhD, AGSF, FRCPC

Manuel Montero-Odasso is Associate Professor of Medicine, Epidemiology, and Biostatistics at the University of Western Ontario in Canada and Director of the Gait and Brain Lab at Parkwood Hospital in London, Ontario. Dr. Montero-Odasso received his medical and doctoral degrees from the University of Buenos Aires in Argentina and completed a postdoctoral fellowship at McGill University in Canada. He is an internist, geriatrician, and a clinician scientist who is aiming to understand the mechanisms and potential treatment of age-related mobility and cognitive decline. He focuses on gait performance research as methodology to early detect mobility and cognitive decline and future prevent the development of frailty, falls, and dementia. Dr. Montero-Odasso leads the Gait and Brain Study, a longitudinal study aimed to assess the role of gait disturbances in the absence of overt disease as early predictor of dementia and mobility decline. He is also conducting clinical trials using cognitive enhancers and physical and cognitive exercises to improve mobility. He leads of the Mobility, Exercise, and Cognition Team, as part of the Canadian Consortium in Neurodegeneration and Aging, which is delivering standardized terminology and protocols to integrate cognitive and mobility assessments and treatments across Canada. Dr. Montero-Odasso has established a successful research program on Gait and Brain Health while remaining an active clinician. His research has received peer-reviewed funding, and he has published in high-impact journals, established collaborations with expert colleagues worldwide, and received several research accolades including the American Geriatrics Society New Investigator Award (2009), the Schulich Clinician Scientist Award (2008–2011), and the New Investigator Award from the Canadian Institute of Health and Research (2012–2017). He serves as an editorial board member of aging journals including The Journal of Gerontology: Medical Sciences, Geriatrics, and Journal of Alzheimer’s Disease. He has been invited to give more than 40 international presentations.

Anat Mirelman, PhD

Anat Mirelman is Director of the Laboratory of Early Markers of Neurodegeneration (LEMON) and the Associate Director of the Center for the Study of Movement, Cognition, and Mobility (CMCM). Dr. Mirelman is affiliated with the Department of Neurology, Sackler Medical School, Tel Aviv University. She completed her doctoral degree in 2007, which focused on technology for the treatment of gait disorders. Her work focuses on motor and cognitive function in neurodegenerative disorders, the understanding of reserve capacity and predictive measures for neurodegeneration, and the development of innovative technology to enhance function. In addition, Dr. Mirelman heads a research team investigating genetics in Parkinson’s disease and biomarkers for disease.

Jacques Duysens, MD, PhD

Jacques Duysens is Emeritus Professor in Motor Control at the Catholic University (KU) Leuven in Belgium. In October 2012, Dr. Duysens retired with emeritus status with a mission to allow for continuing research activities. His main current interests are falls in elderly adults, obstacle avoidance, gait perturbations, and modulation of reflexes during gait in normal subjects and in various patients. He is currently an editorial board member on three international journals, namely Experimental Brain Research, Gait and Posture, and Motor Control (section editor). Among his publications, Dr. Duysens has 245 PUBMED listed articles as well as several books and articles in books. In 1972, he earned his medical degree, cum laude, in Leuven and the following year he achieved an MSC in psychology, cum laude, in Leuven. He also obtained an MSC in neurology and later a doctoral degree in physiology (cum laude, in 1976; “Reflex control of cat locomotion”; supervisor K.G. Pearson) at the University of Alberta in Canada. At the National Institutes of Health (Bethesda, Maryland, USA), he received a Fogarty Scholarship in 1978 to work with Dr. Loeb. He then returned to Europe as a research associate at the KU Leuven in 1979. In 1992, Dr. Duysens obtained a joint appointment as Associate Professor at the University of Hasselt (Belgium). He was appointed Assistant Professor in the Biophysics Department in Nijmegen (Netherlands) in 1987 and stayed until 2005. In 2000, he was appointed full Professor in Nijmegen with a joint appointment at an orthopedic clinic (the Sint Maartenskliniek; RD&E). From 2005 to 2007, Dr. Duysens was Professor in the Department of Rehabilitation and from 2007 to 2012 he was Professor in Motor Control at the KU Leuven.
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Workshop 10: Aging, the Central Nervous System, and Mobility in Older Adults: Intervention Strategies to Prevent and Improve Late Life Gait Decline
Melia Sevilla Hotel, Seville, Spain
Sunday, June 28, 2015

This workshop aims to move beyond discipline-specific and disease-based approaches to suggest priority topics and strategies to identify successful prevention and intervention strategies to improve gait in older adults. This workshop builds on a very successful conference series started in 2012-2014 and supported by the National Institute on Aging and The Gerontological Society of America that reviewed evidence in favor of an association between the central nervous system (CNS) and mobility in older adults who have no overt neurological conditions. Specific objectives are: (a) identify main components of a toolbox to assist clinicians to better manage gait problems in older adults; and (b) prepare a document to summarize the proceedings of the workshops, with specific attention to novel intervention strategies and suggestions of study designs to test the effectiveness of such interventions. The workshop will be divided into two main themes through a combination of presentations and roundtable discussions, with active participation of the attendees: (1) examine CNS plasticity as a potential mechanism to explain the high variability in gait decline that exists between older individuals and to explain the variable response to interventions; and (2) critically review existing cutting-edge intervention strategies that have shown promise in aging and other fields/conditions that also could be successful for older adults.

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Caterina Rosano, MD, MPH, Associate Professor of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pennsylvania
Stephanie A. Studenski, MD, MPH, Medical Officer (Clinical), Chief, Longitudinal Studies Section, Director, Baltimore Longitudinal Study of Aging, National Institute on Aging, Baltimore, Maryland

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As of June 15, 2015
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SUNDAY, JUNE 28, 2015

15:00–15:15 Opening Remarks and Overview of the Workshop
Caterina Rosano, MD, MPH†
Co-Principal Investigator and Workshop Co-Chair
Associate Professor of Epidemiology
Graduate School of Public Health
University of Pittsburgh, USA

15:15–15:30 Emerging questions to promote mobility in older adults
Michelle Carlson, PhD
Workshop Co-Chair
Associate Professor
Department of Mental Health
Department of Epidemiology
Core Faculty, Johns Hopkins Center on Aging and Health
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15:30–16:00 Sensorimotor and biomechanical aspects of gait in older adults: Observations and potential for intervention
Stephen Lord, PhD
Senior Principal Research Fellow
Falls and Balance Research Group
Neuroscience Research Australia
Sydney, Australia

15:50–16:00 Questions & Answers

16:00–16:30 Cutting-edge intervention strategies to improve gait and mobility: A critical review
Manuel Montero-Odasso, MD, PhD, AGSF, FRCPC
Director of the Gait and Brain Lab, Parkwood Hospital
Lawson Health Research Institute
Division of Geriatric Medicine, The University of Western Ontario, Canada

16:20–16:30 Questions & Answers

16:30–17:00 Compensatory mechanisms underlying changes in mobility in aging and neurodegeneration
Anat Mirelman, PhD
Associate Director of the Center for the Study of Movement, Cognition, and Mobility
Tel-Aviv Medical Center, Movement Disorders Unit, Department of Neurology
Tel-Aviv University, Israel

16:50–17:00 Questions & Answers
17:00-17:30  Discussion

*Jacques Duysens, MD, PhD*
Emeritus Professor of Motor Control, Catholic University of Leuven (KU Leuven)
Radboud University Nijmegen Medical Centre
Antwerp, Belgium

18:00  Closing Remarks and Adjournment

*Caterina Rosano, MD, MPH*

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As of June 15, 2015

*Program Committee Member*
Aging, the Central Nervous System, and Mobility in Older Adults

Three-year U13 cooperative conference grant 1 U13 AG041613-01 from the National Institute on Aging 2012-2015

Co-Chairs: Caterina Rosano, MD, MPH, and Jeff Kaye, MD

Universal scaling law in human behavioral organization. Nakamura et al. 2007

We do not need the brain to walk.

Move around plan, purpose
Major emerging questions:

• Studies adopting discipline-focused and disease-based approach have failed to produce models that substantially explain the variance of physical limitations in older adults living in the community.

• There is the need to explain not only why the relationship of exposure to risk factors or to neuromuscular impairment with disability is highly variable, but also why the response to rehabilitative intervention is quite different from individual to individual.

• To understand the variability of mobility impairment in community-dwelling older adults and identify effective interventions to ameliorate mobility problems, novel approaches that will cut across disciplines and go beyond conventional disease-based models are needed.

POTENTIAL EXPLANATIONS:

1. CNS plasticity may provide new insights and strategies for managing and treating mobility problems. The variance of mobility impairment in older adults may result from different degrees of brain plasticity that may buffer the disabling potential of other systems’ impairment.

2. Homeostasis of the system in its entirety.

1st Workshop—2012: Aims

OBJECTIVE: Establish the best evidence to date for a relationship between the CNS and mobility in the context of other contributors, and identify state-of-the-art technology to measure CNS plasticity and mobility in older adults.

1) Examine existing evidence from basic, epidemiological, and clinical perspectives and enhance links from animal studies to human investigation of both normal aging and disease at the individual and population level.

2) Discuss knowledge gaps, barriers to progress, alternative strategies, and prospects for future inquiry through discussions of emerging research findings.

3) Identify cutting-edge and state-of-the-art technology to measure CNS plasticity and mobility in older adults.

4) Promote collaborations between basic, epidemiological, and clinical scientists of interrelated disciplines who might not otherwise have an opportunity to work together.
1st Workshop—2012: Process

**OBJECTIVE:** Establish the best evidence to date for a relationship between the CNS and mobility in the context of other contributors, and identify state-of-the-art technology to measure CNS plasticity and mobility in older adults.

**MONDAY**
- Opening Session
- Networking Reception

**TUESDAY**
- Session 1: Evidence From Epidemiological and Clinical Studies
  - Panel presentation and focus-group discussion
- Session 2: Evidence From Basic Science Studies
  - Panel presentation and focus-group discussion
- Small group reports and feedback
- Session 3: Tools and Methods
  - Panel presentation and focus-group discussion
- Focus-group reports and feedback

**WEDNESDAY**
- Group Discussion

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**Session 1: The Evidence From Epidemiological and Clinical Studies, Moderator: R. Camicioli, MD**
- Evidence for a multisystem approach to mobility impairment in older adults living in the community, Jack M. Guralnik, MD, PhD, MPH
- Evidence from neuroimaging and neuroepidemiology: The artificial dichotomy of cognition vs. mobility, Caterina Rosano, MD, MPH, Joe Verghese, MBBS
- The evidence from epidemiological and clinical studies: Evidence from human disease-based models, David A. Bennett, MD

**Session 2: The Evidence From Basic Science Studies, Moderator: Wen G. Chen, PhD**
- Central nervous system control of locomotion, dual tasking, and automaticity, M. Hallett, MD
- Age-related changes in cortical gate propulsion control: Evidence from human data, O. Beauchet, MD, PhD
- Influences on brain plasticity: Implications for cognition and mobility control, Y. Stern, PhD
- Evidence from animal models: Effects of aging and lifestyle factors on motor synapses, Gregorio Valdez, PhD

**Session 3: Tools and Methods, Moderator: Howard Aizenstein, MD, PhD**
- Structure, neurochemistry, and function of CNS components related to mobility, Nicolaas I. Bohnen, MD, PhD
- Mobility measures in the laboratory and in the field using body-worn and fixed sensor systems, Jeffrey M. Hausdorff, PhD
- Using neuropsychological measures, dual-task paradigms and functional near infrared spectroscopy to determine cognitive and brain mechanisms of mobility, Roee Holtzer, PhD
- Statistical and mathematical modeling approaches to multisystem studies, Heather Allore, PhD
Focus on Key Points Offered by Moderator.

Suggested Format: N-GBS

N = New questions? New study design and/or additional methods/approaches?
G = Gaps in knowledge?
B = Barriers to address these gaps?
S = Strategies to address these barriers?

1st Workshop—2012: Results

Figure 1. Model of current gaps in knowledge of central nervous system (CNS) involvement in mobility of older adults: 1) what is the CNS contribution to mobility; 2) what are the mechanisms of brain reserve in mobility; 3) when do neurologic changes related to mobility decline occur; and 4) what aspects of CNS are modifiable and amenable to interventions?

Results. Evidence from basic, clinical, and epidemiological studies supports the CNS as an important contributor to mobility limitations in older adults without overt neurologic disease. Three main goals for future work that emerged were as follows: (a) develop models of mobility limitations in older adults that differentiate aging from disease-related processes and that fully integrate CNS with musculoskeletal contributors; (b) quantify the contribution of the CNS to mobility loss in older adults in the absence of overt neurologic diseases; (c) promote cross-disciplinary collaboration to generate new ideas and address current methodological issues and barriers, including real-world mobility measures and life-course approaches.

Conclusions. In addition to greater cross-disciplinary research, there is a need for new approaches to training clinicians and investigators, which integrate concepts and methodologies from individual disciplines, focus on emerging methodologies, and prepare investigators to assess complex, multisystem associations.
Explore potential models because they drive inquiry and frame the questions.

--- “Able to get where you want on your own”; walking is the core of human mobility; mobility is a broad continuum from complete immobility to very high levels

---- Ability to move through the environment and complete daily living successfully

---- Ability and will to safely move (walk) to do activities of daily living independently

---- Capacity to safely navigate through the environment and adapt to perturbations (subtypes: transfers, walking, stair climbing, wheelchair use)

--- Two levels definition:

**Conceptual:** mobility independence: ability to move easily and freely in environment

**Operational:** ambulation in life space, movement (walking, walker, wheelchair); upper extremity-manipulation; lower extremity – bADL

<table>
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<th>Box 1. Definitions of Mobility-Related Terms</th>
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<tr>
<td>Mobility</td>
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<td>Mobility limitation</td>
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<td>Gait</td>
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<td>Gait impairment</td>
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<td>Motor control</td>
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These networks are also related to information processing and mood. Therefore, these networks may represent a shared CNS resource for information processing- and for motor-related control.

3. Arterial stiffness, diabetes, physical activity, SBP are all related to worse mobility and to lower brain structural integrity. Since these factors are also known to be associated with mobility, the next line of inquiry should focus on:

a) Characterize these mechanisms (workshop 2)

b) Ask whether modification of these factors can improve mobility and whether such improvements have neurological correlates (workshop 3)
THANKS TO: J. Kaye, Co-Chair Workshop 1 and all workshop attendees

AG041613-01, NIA
Emerging Design Questions to Promote Mobility in Older Adults

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ISPGR Workshop 10: Aging, the CNS, and Mobility in Older Adults: Intervention Strategies to Prevent and Improve Late Life Gait Decline
June 28, 2015

Dynamic Interaction Between Motor and Cognitive Functions

• Gait abnormalities (e.g., slow and variable gait) → cognitive decline, MCI, and dementia
• Impaired cognition → mobility limitations, slow gait and falls
• Suggests interdependence
• Shared or common pathology (Hausdorff, 2013)
Targeting One Pathway: 
Motor to Improve Mobility

- Sensorimotor targets → Lord talk  
  - Balance and gait  
  - Exercise

- Motor enhancing drugs → Montero-Odasso talk  
  - Vitamin D

Targeting One Pathway: 
Cognition to Improve Mobility

- Cognitive targets → Montero-Odasso & Mirelman talks  
  - Executive function  
  - Dual-task training

- Cognitively enhancing drugs → Montero-Odasso talk  
  - Methylphenidate in community-dwelling older adults and Parkinson patients  
  - Donepezil (cholinesterase inhibitors)
Challenges of Physical Exercise, Cognitive Training, and Drug/Dietary Interventions

- **Exercise**
  - Spontaneous physical activity decreases with age in all organisms
  - Current Activity Guidelines not met by most older adults
  - Safe access to resources may be restricted

- **Cognitive Training**
  - You only get better at what you train on; no near or far transfer
  - Hard to sustain and enjoy in moderate to large doses

- **Drug/Dietary**
  - Potential adverse effects (e.g., blood thinning)
  - Effective dosing

Design Interventions to Target Both Simultaneously?

- **Could individual adhere to interventions?**
  - If adhering to 1 is difficult, how could we expect an older individual to adhere to 2?

- **Sustainable post intervention?**
  - Double the resources?

- **Scalable?**
  - Can we reach large numbers of older at-risk community and patient populations?
Maybe there are ways to make exercise, cognitive stimulation and dietary supplements easier to enjoy and sustain through combinations.

Lifestyle Physical Activity and Brain Health

Small Increases in Daily Step Activity Cross-sectionally Associated with Larger Hippocampal Volume

Even small increases in physical activity may matter

Varma, Chuang, Harris, Tan, & Carlson, 2014, *Hippocampus*
Physical and Cognitive Activity “in the wild”
Through Community Engagement: Experience Corps

- Serve as mentors in public elementary schools: K-3
- Cognitive “Training”: multiple roles to exercise executive function, memory
  - Reading literacy
  - Library support
  - Math support
  - Behavioral support
- 15 hours per week
- Travel to/from schools; walking within schools
- Sustained dose: full school year

Freedman & Fried, 1997; Fried et al., 2004; Carlson et al., 2008; Carlson et al., 2009; Fried et al., 2013; Carlson et al., 2015

Did We Increase Daily Physical Activity Following Program Participation? Step Activity (N=115)

- Women in Experience Corps maintained average steps/day over 24 months post-intervention while controls declined
- Men had significantly higher baseline levels of daily physical activity than women and maintained these levels

Women

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Varma et al., 2015 AJPM
Emerging Methods that Allow for Innovation in Intervention Design and Evaluation

- Virtual environment treadmill training → Mirelman & Hausdorff
- Accelerometers to assess falls and fall risk
- Real-world activity interventions that incorporate accelerometry/smartphones to directly target physical exercise and sensorimotor function and also target executive function

One Application: Identify Where the Greatest Amounts of Activity Occur in Daily Life and Build Interventions Around Them
Greatest Amount and Highest Intensity of Daily Step Activity Occurs Outdoors in Community Spaces

Carlson, Varma, Adam, Crainiceanu, & Zippunnikov, under review
Activity in Community Spaces Most Strongly Associated with Cognitive Health in Older Adults

Study sample: community dwelling older adults with CNS mediated mobility impairment

- Other systems
- Mobility
- Cognition

Intervention

Falls, dementia, mortality, hospitalization, quality of life
Sensorimotor & biomechanical aspects of gait in older adults: observations and potential for intervention

Professor Stephen Lord, PhD


Gait changes with age

- Slowed walking speed
- Shorter stride length
- Longer time in dual stance
- Wider stance
- Fewer steps/min (cadence)

- Reduced joint range of motion
- Reduced head control

- Reduced push-off power
- Increased gait variability
Muscles controlling gait

- Eccentric: dorsiflexors, plantarflexors, knee extensors
- Concentric: plantarflexors, hip extensors
- Control of swing: hip flexors, ankle dorsiflexors, knee flexors

Perturbations to gait

- Stepping around obstacle
  - Control lateral balance

- Stepping over obstacle
  - Longer period of time spent on one leg
  - Risk of the making contact with the obstacle

- Trips
  - Body moves forward over the BOS

- Slips
  - BOS moves under the body
Control of swing: Toe clearance

Big toe Ground Clearance (mm)

Big toe Horizontal Velocity (m/s)

% Stride

Tripping reactions

Reaction time [ms]

Peak moment [Nm·kg⁻¹]

Rate of moment generation [Nm·s⁻¹·kg⁻¹]

Pijnappels et al. Gait & Posture 2005
Physiological and Psychological Predictors of Walking Speed in Older Community-Dwelling People

Anne Tiedemann  Catherine Sherrington  Stephen R. Lord
Prince of Wales Medical Research Institute, UNSW, Randwick, Australia

668 community-dwelling people aged 75–98 years (mean age 80.1, SD = 4.4), 238 men

Sensorimotor correlates of six metre walking speed

<table>
<thead>
<tr>
<th>Measures</th>
<th>Mean (SD)</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sensorimotor</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visual acuity – high contrast, logMAR</td>
<td>1.3 (1.2)</td>
<td>-0.15***</td>
</tr>
<tr>
<td>Visual acuity – low contrast, logMAR</td>
<td>2.6 (2.0)</td>
<td>-0.17***</td>
</tr>
<tr>
<td>Edge contrast sensitivity, dB</td>
<td>18.8 (2.5)</td>
<td>0.29***</td>
</tr>
<tr>
<td>Depth perception, cm error</td>
<td>2.8 (3.6)</td>
<td>-0.14***</td>
</tr>
<tr>
<td>Proprioception, cm error</td>
<td>2.1 (1.4)</td>
<td>-0.11**</td>
</tr>
<tr>
<td>Tactile sensitivity, log(_{10}) mg pressure</td>
<td>4.4 (0.5)</td>
<td>-0.08*</td>
</tr>
<tr>
<td>Vibration sense, µm</td>
<td>39.7 (26.6)</td>
<td>-0.10**</td>
</tr>
<tr>
<td>Ankle dorsiflexion strength, N</td>
<td>69.1 (34.9)</td>
<td>0.38***</td>
</tr>
<tr>
<td>Knee extension strength, N</td>
<td>266.5 (121.3)</td>
<td>0.43***</td>
</tr>
<tr>
<td>Knee flexion strength, N</td>
<td>150.1 (64.1)</td>
<td>0.47***</td>
</tr>
<tr>
<td>Composite strength measure, N/[(weight (kg) \times height (m))/2]</td>
<td>8.9 (3.1)</td>
<td>0.46***</td>
</tr>
<tr>
<td>Simple reaction time – hand, ms</td>
<td>274.3 (49.2)</td>
<td>-0.30***</td>
</tr>
<tr>
<td>Simple reaction time – foot, ms</td>
<td>352 (62.6)</td>
<td>-0.34***</td>
</tr>
</tbody>
</table>
### Balance and psychological correlates of six metre walking speed

<table>
<thead>
<tr>
<th>Measures</th>
<th>Mean (SD)</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sway eyes open-floor (area)³</td>
<td>460 (496)</td>
<td>-0.18**</td>
</tr>
<tr>
<td>Sway eyes closed-floor (area)⁴</td>
<td>598 (631)</td>
<td>-0.22***</td>
</tr>
<tr>
<td>Sway eyes open-foam (area)⁴</td>
<td>1,385 (1,009)</td>
<td>-0.31***</td>
</tr>
<tr>
<td>Sway eyes closed-foam (area)⁴</td>
<td>3,220 (2,242)</td>
<td>-0.27***</td>
</tr>
<tr>
<td>Coordinated stability (errors)</td>
<td>8.4 (8.4)</td>
<td>-0.42***</td>
</tr>
<tr>
<td>Psychological measures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bodily pain</td>
<td>1.61 (0.98)</td>
<td>-0.25***</td>
</tr>
<tr>
<td>Depression</td>
<td>5.26 (1.00)</td>
<td>0.09*</td>
</tr>
<tr>
<td>Anxiety</td>
<td>2.30 (1.05)</td>
<td>-0.04</td>
</tr>
<tr>
<td>Vitality</td>
<td>3.06 (1.41)</td>
<td>-0.37***</td>
</tr>
<tr>
<td>Fear of falling</td>
<td>1.99 (0.99)</td>
<td>-0.26***</td>
</tr>
</tbody>
</table>

³ Product of maximal anterior-posterior and lateral sway scores.
* p < 0.05, ** p < 0.01, *** p < 0.001.

### Association between lower limb strength and walking speed

![Graph showing association between lower limb strength and walking speed](image)
Hierarchical multiple regression of six-metre walking speed

<table>
<thead>
<tr>
<th>Predictor variables</th>
<th>Beta weights</th>
<th>p value</th>
<th>( r^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite strength measure</td>
<td>0.246</td>
<td>&lt;0.001</td>
<td>0.207***</td>
</tr>
<tr>
<td>Edge contrast sensitivity</td>
<td>0.104</td>
<td>0.002</td>
<td>0.335***</td>
</tr>
<tr>
<td>Reaction time – foot press</td>
<td>-0.123</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Sway eyes open – foam</td>
<td>-0.129</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Coordinated stability</td>
<td>-0.169</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Vitality</td>
<td>-0.185</td>
<td>&lt;0.001</td>
<td>0.382***</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>-0.095</td>
<td>0.004</td>
<td>0.368***</td>
</tr>
<tr>
<td>Age</td>
<td>-0.156</td>
<td>&lt;0.001</td>
<td>0.401***</td>
</tr>
</tbody>
</table>

*** p < 0.001.

6MWD and sit-to-stand predictors

Table 6: Predictor Variables of 6MWD and Their Unstandardized Coefficients and \( \beta \) Weights

<table>
<thead>
<tr>
<th>Predictor Variables</th>
<th>Unstandardized Coefficients (( \beta ))</th>
<th>Standardized Coefficients (( \beta ))</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balloon</td>
<td>2.94</td>
<td>0.083</td>
<td>0.027</td>
</tr>
<tr>
<td>Lower-limb strength</td>
<td>6.51</td>
<td>0.260</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Simple reaction time*</td>
<td>-120.567</td>
<td>-0.000</td>
<td>0.025</td>
</tr>
<tr>
<td>Balance</td>
<td>-41.96</td>
<td>-0.068</td>
<td>0.037</td>
</tr>
<tr>
<td>Maximal balance range</td>
<td>.49</td>
<td>.222</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cognition, pain, and mood</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SF-36 pain scale score</td>
<td>.75</td>
<td>.083</td>
<td>.049</td>
</tr>
<tr>
<td>PANS positive scale score</td>
<td>1.43</td>
<td>.088</td>
<td>.015</td>
</tr>
<tr>
<td>Health</td>
<td>1.90</td>
<td>.083</td>
<td>.016</td>
</tr>
<tr>
<td>SF-36 general health scale</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medications</td>
<td>-9.50</td>
<td>-0.177</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age</td>
<td>-4.31</td>
<td>-0.219</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Constant</td>
<td>799.43</td>
<td>-</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Note: 52.5% of variance explained

J Geront A(Med Sci) 2002;57:539-43

Arch Phys Med Rehabil 2002;83:907-11
Gait adaptability correlates

<table>
<thead>
<tr>
<th>Variables</th>
<th>Stroop score</th>
<th>TMT score</th>
<th>Reaction time</th>
<th>Postural sway</th>
<th>Lower limb strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gait speed</td>
<td>-.093</td>
<td>-.250</td>
<td>-.317*</td>
<td>-.515**</td>
<td>.433**</td>
</tr>
<tr>
<td>Green short</td>
<td>-.158</td>
<td>-.276</td>
<td>-.266</td>
<td>-.513**</td>
<td>.450**</td>
</tr>
<tr>
<td>Green long</td>
<td>-.234</td>
<td>-.332*</td>
<td>-.227</td>
<td>-.581**</td>
<td>.532**</td>
</tr>
<tr>
<td>Pink</td>
<td>-.218</td>
<td>-.368**</td>
<td>-.290*</td>
<td>-.631**</td>
<td>.476**</td>
</tr>
<tr>
<td>Target step length</td>
<td>-.120</td>
<td>-.242</td>
<td>-.399*</td>
<td>-.513**</td>
<td>.380**</td>
</tr>
<tr>
<td>Green short</td>
<td>-.125</td>
<td>-.080</td>
<td>-.241</td>
<td>-.243</td>
<td>.245</td>
</tr>
<tr>
<td>Green long</td>
<td>-.366**</td>
<td>-.341*</td>
<td>-.263</td>
<td>-.447**</td>
<td>.456**</td>
</tr>
<tr>
<td>Pink</td>
<td>-.352*</td>
<td>-.238</td>
<td>-.251</td>
<td>-.428**</td>
<td>.206</td>
</tr>
<tr>
<td>Double support</td>
<td>.021</td>
<td>.219</td>
<td>.155</td>
<td>.305*</td>
<td>-.209</td>
</tr>
<tr>
<td>Green short</td>
<td>.187</td>
<td>.196</td>
<td>.080</td>
<td>.398**</td>
<td>-.305*</td>
</tr>
<tr>
<td>Green long</td>
<td>.267</td>
<td>.236</td>
<td>.236</td>
<td>.382**</td>
<td>-.319*</td>
</tr>
<tr>
<td>Pink</td>
<td>.219</td>
<td>.206*</td>
<td>.079</td>
<td>.378**</td>
<td>-.255</td>
</tr>
</tbody>
</table>

Gait adaptability correlates with:
- 22-week randomized controlled trial of exercise
- 160 women aged 60-83 years (mean age 71.1, SD = 5.2)
- Exercisers and controls performed similarly in strength and gait parameters and well matched in terms of age and a number of health and lifestyle characteristics at baseline.
The exercise program

- One hour sessions, twice a week
- Warm up - 5 minutes
- Conditioning period - 35 minutes
  - Aerobic, strengthening, balance, flexibility, endurance and co-ordination activities
- Stretching - 15 minutes
- Relaxation - 5-10 minutes

Percentage change in fall risk factors

**Strength**

<table>
<thead>
<tr>
<th>Strength</th>
<th>Ankle</th>
<th>Knee Ext</th>
<th>Knee Flex</th>
<th>Hip Ext</th>
<th>Hip Flex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercisers</td>
<td><img src="image1.png" alt="Graph" /></td>
<td><img src="image2.png" alt="Graph" /></td>
<td><img src="image3.png" alt="Graph" /></td>
<td><img src="image4.png" alt="Graph" /></td>
<td><img src="image5.png" alt="Graph" /></td>
</tr>
</tbody>
</table>

**Reaction Time**

<table>
<thead>
<tr>
<th>Reaction Time</th>
<th>RT</th>
<th>Tapping speed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercisers</td>
<td><img src="image6.png" alt="Graph" /></td>
<td><img src="image7.png" alt="Graph" /></td>
</tr>
</tbody>
</table>

**Body Sway**

<table>
<thead>
<tr>
<th>Body Sway</th>
<th>E O</th>
<th>E C</th>
<th>E O</th>
<th>E C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Floor</td>
<td><img src="image8.png" alt="Graph" /></td>
<td><img src="image9.png" alt="Graph" /></td>
<td><img src="image10.png" alt="Graph" /></td>
<td><img src="image11.png" alt="Graph" /></td>
</tr>
<tr>
<td>Foam</td>
<td><img src="image12.png" alt="Graph" /></td>
<td><img src="image13.png" alt="Graph" /></td>
<td><img src="image14.png" alt="Graph" /></td>
<td><img src="image15.png" alt="Graph" /></td>
</tr>
</tbody>
</table>

**Walking Patterns**

<table>
<thead>
<tr>
<th>Walking Patterns</th>
<th>Velocity</th>
<th>Cadence</th>
<th>Stride length</th>
<th>Stride duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercisers</td>
<td><img src="image16.png" alt="Graph" /></td>
<td><img src="image17.png" alt="Graph" /></td>
<td><img src="image18.png" alt="Graph" /></td>
<td><img src="image19.png" alt="Graph" /></td>
</tr>
<tr>
<td>Controls</td>
<td><img src="image20.png" alt="Graph" /></td>
<td><img src="image21.png" alt="Graph" /></td>
<td><img src="image22.png" alt="Graph" /></td>
<td><img src="image23.png" alt="Graph" /></td>
</tr>
</tbody>
</table>
Main findings

- Exercise participants showed improved strength in five lower limb muscle groups, increased walking speed, cadence, stride length, and shorter stride times as indicated by both reduced swing and stance duration.
- Within the exercise group, increased cadence was associated with improved ankle dorsiflexion strength, and increased stride length was associated with improved hip extension strength.
- Within the exercise group, the degree of change in the tests of velocity, cadence and stance duration was significantly associated with number of sessions attended.
- Exercise participants with initial slow walking speed showed greater changes in velocity, stride length, cadence and stance duration than those with initial fast walking speed.

Resistance training

  - a moderate to large effect for getting out of a chair (11 trials, 384 participants, SMD -0.94, 95% CI -1.49 to -0.38)
  - a modest improvement in gait speed (24 trials, 1179 participants, MD 0.08 m/s, 95% CI 0.04 to 0.12)
Balance and functional task training


Summary

- Many gait changes with increasing age, including:
  - Slower pace
  - Shorter steps
  - Reduced joint motion
  - Wider stance
  - Poorer control
  - Reduced push-off power
- Main muscle groups driving forward gait:
  - Ankle plantarflexors
  - Ankle dorsiflexors
  - Hip flexors
  - Hip extensors
- Sensorimotor, balance and psychological factors underpin gait speed
  - Both for regular gait and for obstacle avoidance
- Exercise interventions can improve spatiotemporal gait parameters
  - Partly mediated through increased muscle strength
Acknowledgements

- Joana Caetano
- Daina Sturnieks
- NHMRC
Aging, the Central Nervous System, and Mobility in Older Adults: Intervention Strategies to Prevent and Improve Late Life Gait Decline
Seville, Spain – June 28, 2015

Cutting-edge intervention strategies to improve gait and mobility: A critical review

Manuel Montero-Odasso MD, PhD, AGSF, FRCPC
Associate Professor of Medicine, Epidemiology and Biostatistics
Director, Gait and Brain Lab, Parkwood Institute
Division of Geriatric Medicine, The University of Western Ontario
Scientist, Lawson Health Research Institute, London ON

Disclosures:
• No financial interest related to this presentation

Objectives:
• To review the role of subtle cognitive deficits in mobility impairment and falls risk
• To explore the role of non-pharmacological and pharmacological therapies for gait improvement and reducing risk of falls in older adults with cognitive impairment
• To postulate that cognitive treatment should be considered as a complementary option to improve gait and reduce risk of fall
ARE FALLS A MANIFESTATION OF BRAIN FAILURE?

B. Issacs

The probability that members of this audience will reach the age of eighty is about one in three. The probability that, having done so, they will suffer a damaging fall is about the same. Self-interest alone therefore dictates an active thrust towards fall prevention. Yet is the ability to prevent falls in old age a realistic research objective for the physician or for the pharmacologist? Can anything practical be done other than the avoidance of external hazards and unsuitable drugs?

In the hope of answering these questions I propose to review briefly some aspects of falls in old people; to put forward a classification of falls based on mechanical principles; to discuss the research implications of this classification; and to speculate on a possible pharmacological approach to fall prevention.

Falls Are Prevalent

25% of elderly people have at least 1 fall per year
75% of fallers will fall again in the same year

<table>
<thead>
<tr>
<th>Community Non-disabled</th>
<th>Community Disabled</th>
<th>In Hospital</th>
<th>Nursing Home</th>
</tr>
</thead>
<tbody>
<tr>
<td>15%</td>
<td>30%</td>
<td>40%</td>
<td>60%</td>
</tr>
</tbody>
</table>

Falls in the Cognitively Impaired

- Falls are two-fold in people with dementia\textsuperscript{1,2}
  - Fallers with cognitive problems have:
    \begin{itemize}
    \item↑ risk of injuries, falls & fractures
    \item↓ functional outcomes
    \item↓ access to rehabilitation
    \item↑ institutionalization
    \item↑ mortality
  \end{itemize}
- Multifactorial fall prevention programs not successful in those with MMSE < 20\textsuperscript{3}

Questions

- Why are falls so common in the cognitively impaired?
- Why does fall prevention not work in this population?
- Are we missing a treatment component?
- What does the evidence show?
- Are we assuming facts from the evidence?
- What can we learn from proven interventions in cognitive healthy seniors?

Evidence and Assumptions in Fall Prevention

- Evidence 1
  Falls are multifactorial

- Assumption 1
  Walking is almost automatic and it is affected by cognition only when you have cognitive deficits
Gait and Cognition: Is There a Relationship?

Dogma:
- Gait is an automatic task
- Not related to the cognitive systems
Gait and Cognition: Is There a Relationship?

- Gait is an automatic process (CPG)
- Adults can talk, walk, chew gum at the same time
- Decerebrate cats can walk, why not humans?

BUT…..
“Stops walking when talking” as a predictor of falls in elderly people

Lillanor Lundin-Olsson, Lars Nyberg, Yingwa Gustafsson

THE LANCET Vol 349 • March 1, 1997

Kaplan-Meier curves for falls during 6 months

Positive predictive value: 83%
Specificity: 95%

The most common diagnoses (some had more than one) were dementia (n=28), depression (25), and previous stroke (20). The median score (particular mean) of the Mini-Mental State Examination was 21.5 (18–26).

Gait and Cognition: Is There a Relationship?

YES!

• Patients often explain that they fall when they become distracted

• When they are performing more than one task (kitchen, bathroom, etc.)
**Dual-Task Paradigm: Why Is It Relevant?**

Dual-task paradigm
- Observing gait/balance while performing a secondary task
- “Walking while talking”

Relevant
- Daily activities involve the simultaneous performance of two or more cognitive/motor tasks
- Represents real life situations where falls are likely to occur

**Single-Task Gait Example**

Gait velocity: 1.46 m/sec
Gait variability: 2.83% CoV
Dual-Task Gait Example (Serial 7s)

Gait velocity: 1.03 m/sec
Gait variability: 13.06% CoV

Gait Variability: Single Case Examples

Elderly Control

Elderly MCI

Gait variability = (stride time variability) under single-task and dual-task in a normal control and in a participant with MCI.

Gait Variability in the Cognitive Spectrum

Gait variability in older adults with normal cognition (n=30), mild cognitive impairment (n=45) and very mild Alzheimer’s disease (n=34) while usual walking and with two dual-task walking conditions.


Evidence and Assumptions in Fall Prevention

• Evidence 1
  Falls are multifactorial

• Assumption 1
  Walking is almost automatic and it is affected by cognition only when you have cognitive deficits

• Emerging view 1
  Walking is NOT always automatic and relies on cognition
Evidence and Assumptions in Fall Prevention

• Evidence 2
  Cognitive impairment is a risk factor for falls

• Assumption 2
  Falls are not related to cognitive problems when a normal MMSE/MoCA is present

Cognitive Impairment and Fall Risk

• What do we mean by “cognitive impairment”?
  • Disease-specific diagnosis?
  • Deficits on measures of global cognitive function?
  • Deficits in specific cognitive domains?
Key points:
1-Cognitive impairment (MMSE<26) confers high risk of serious injury from a fall OR=2.33
2- Executive dysfunction increases fall risk OR=1.44
3- Executive dysfunction can be present despite normality in "global cognition"
4- EF assessment should be part of a falls risk evaluation

Evidence and Assumptions in Fall Prevention

- **Evidence 2**
  Cognitive impairment is a risk factor for falls

- **Assumption 2**
  Falls are not related to cognitive problems when a normal MMSE/MoCA is present

- **Emerging view 2**
  Executive dysfunction, even in “cognitively normal,” is associated with higher risk of falls (OR=1.32) and injury due to falls (OR=2.33)

Evidence and Assumptions in Fall Prevention

- **Evidence 3**
  Exercise reduces falls

- **Assumption 3**
  Exercise reduces fall due to a physical effect
### Results: Exercise Programs to Reduce Falls

<table>
<thead>
<tr>
<th>Intervention</th>
<th>No. of trials</th>
<th>No. of participants</th>
<th>Rate ratio (95% CI)</th>
<th>Reduction in falls (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group classes</td>
<td>16</td>
<td>3622</td>
<td>0.71 (0.63 to 0.82)</td>
<td>29%</td>
</tr>
<tr>
<td>Home based</td>
<td>7</td>
<td>951</td>
<td>0.68 (0.58 to 0.80)</td>
<td>32%</td>
</tr>
<tr>
<td>Tai Chi classes</td>
<td>5</td>
<td>1563</td>
<td>0.72 (0.52 to 1.00)</td>
<td>28%</td>
</tr>
<tr>
<td>Tai Chi classes, not at high risk of falls</td>
<td>3</td>
<td>1008</td>
<td>0.59 (0.45 to 0.76)</td>
<td>41%</td>
</tr>
</tbody>
</table>


---

### Multi-component Exercise Programs Reduce Falls

By 32%

By 28%

Meta-analyses on Exercise to Improve Cognition


The impact of exercise on the cognitive functioning of healthy older adults: A systematic review and meta-analysis


*The NRE Programme, Institute of Neuroscience, Trinity College Dublin, Dublin 2, Ireland
**Department of Statistics, Trinity College Dublin, Dublin 2, Ireland


![Colcombe & Kramer (2003)](image)
Pilot RCT found that the OEP reduced falls by 47% in the absence of significant improvement in physical function (i.e., balance and muscle strength).

Attention and conflict resolution improved in the OEP group as compared with the usual care.

Evidence and Assumptions in Fall Prevention

- **Evidence 3**
  Exercise reduces falls

- **Assumption 3**
  Exercise reduces fall due to a physical effect

- **Emerging view 3**
  Exercise also has an effect on brain function

  Studies evaluating brain and muscle function together show improvement in brain related functions.
Evidence and Assumptions in Fall Prevention

• Evidence 4
  Vitamin D supplementation may reduce falls by 20%

• Assumption 4
  This effect is mediated by a “muscle effect”

Effect of Vitamin D on Falls
A Meta-analysis

• Meta-analysis identified 5 RCTs with 1237 subjects looking at the effect of vitamin D on falling
• Three on Vitamin D3, two on metabolite 1,25(OH)2D3. Vitamin D3 dose was 800IU for two studies, 400IU for one
• Found a 22% reduction in falling risk
• In LTC the falling rate correlates with vitamin D levels

## Vitamin D Supplements

<table>
<thead>
<tr>
<th></th>
<th>No. of trials</th>
<th>No. of participants</th>
<th>Rate ratio (95% CI)</th>
<th>Falls reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>All trials community living</td>
<td>7</td>
<td>9324</td>
<td>1.00 (0.90 to 1.11)</td>
<td>0%</td>
</tr>
<tr>
<td>Selected for low levels</td>
<td>2</td>
<td>260</td>
<td>0.57 (0.37 to 0.89)</td>
<td>43%</td>
</tr>
<tr>
<td>Not selected for low levels</td>
<td>5</td>
<td>9064</td>
<td>1.02 (0.93 to 1.13)</td>
<td>(+2%)</td>
</tr>
<tr>
<td>Aged care residents</td>
<td>5</td>
<td>4603</td>
<td>0.63 (0.46 to 0.86)</td>
<td>37%</td>
</tr>
</tbody>
</table>


No need for a blood test. Assume low level of vitamin D if housebound, requires support services, resident in aged care, or frail.

## Vitamin D and Muscle Function

Vitamin D status predicts physical performance. J Clin Endocrinol Metab 2007;92:2058-20659

LASA Study  
1008 older adults  
3y follow-up  
Baseline lower Vitamin D levels and higher PTH levels predict poor muscle outcomes

J Clin Endocrinol Metab. 2003;88:5766-5772

2015 International Society for Posture & Gait Research  
World Congress Workshop 10  
June 28, 2015
Vitamin D and Brain Function

Meta-Analysis of Memory and Executive Dysfunctions in Relation to Vitamin D

Cecile Armstrong1,2,*, Manuel Montero-Odasso1, David J. Llewellyn3, Yolande Richard-Ducrcey1, Géza Pataki1 and Olivier Benchetrit1

1Department of Neurosciences, Bishop’s University, Lennoxville, Quebec, Canada
2Department of Medicine, University of机器n, Montréal, QC, Canada
3Department of Neurology, University of Western Ontario, London, ON, Canada

Objectives: To systematically review and quantitatively synthesize the effect of vitamin D supplementation on muscle strength, gait, and balance in older adults.

Design: Systematic review and meta-analysis.

Setting: MEDLINE, EMBASE, Cochrane Library, bibliographies of selected articles, and previous systematic reviews were searched between January 1980 and November 2010 for eligible articles.

Results: Vitamin D supplementation demonstrated a statistically significant effect on muscle strength, gait, and balance in older adults. Further evaluation is recommended.

Key words: vitamin D; aged; systematic review; randomized controlled trials; muscle strength; balance; gait

JAGS 2011;59: 2291-2300
**Forest Plot for Balance Sway**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Vitamin D supplementation</th>
<th>Control</th>
<th>Std. Mean Difference (IV, Fixed, 95% CI)</th>
<th>Std. Mean Difference (IV, Fixed, 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bunau 2008</td>
<td>11.98</td>
<td>13.64</td>
<td>13.47</td>
<td>12.84</td>
</tr>
<tr>
<td>Chen 2004</td>
<td>0.009</td>
<td>0.040</td>
<td>0.009</td>
<td>0.051</td>
</tr>
<tr>
<td>Pfeifer 2007</td>
<td>0.81</td>
<td>1.12</td>
<td>0.86</td>
<td>1.18</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>207</td>
<td>286</td>
<td>100.0%</td>
<td>0.29</td>
</tr>
</tbody>
</table>

**Timed Up & Go Test**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Vitamin D supplementation</th>
<th>Control</th>
<th>Std. Mean Difference (IV, Fixed, 95% CI)</th>
<th>Std. Mean Difference (IV, Fixed, 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bunau 2008</td>
<td>13.8</td>
<td>15.2</td>
<td>15.7</td>
<td>15.1</td>
</tr>
<tr>
<td>Pfeifer 2008</td>
<td>7.5</td>
<td>8.3</td>
<td>8.0</td>
<td>8.2</td>
</tr>
<tr>
<td>Zhu 2011</td>
<td>8.1</td>
<td>8.9</td>
<td>8.0</td>
<td>8.9</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>274</td>
<td>277</td>
<td>100.0%</td>
<td>0.19</td>
</tr>
</tbody>
</table>

**Grip Strength**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Vitamin D supplementation</th>
<th>Control</th>
<th>Std. Mean Difference (IV, Fixed, 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chen 2004</td>
<td>204</td>
<td>62</td>
<td>79.7</td>
</tr>
<tr>
<td>Pfeifer 2009</td>
<td>206</td>
<td>121</td>
<td>80.6</td>
</tr>
<tr>
<td>Zhu 2011</td>
<td>176.5</td>
<td>148</td>
<td>41.7</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>312</td>
<td>314</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

**Lower Extremity Muscle Strength**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Vitamin D supplementation</th>
<th>Control</th>
<th>Std. Mean Difference (IV, Fixed, 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brunner 2008</td>
<td>-2.48</td>
<td>-2.84</td>
<td>-2.68</td>
</tr>
<tr>
<td>Grady 1983</td>
<td>0.16</td>
<td>0.51</td>
<td>0.31</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1244</td>
<td>1218</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

---

2015 International Society for Posture & Gait Research  
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June 28, 2015  
20
Evidence and Assumptions in Fall Prevention

- **Evidence 4**
  Vitamin D supplementation reduces falls by 20%

- **Assumption 4**
  This effect is mediated by a “muscle effect”

- **Emerging view 4**
  Vitamin D supplementation (>800IU/day) improves balance and neuromuscular function, but not muscle strength

- Is this a brain effect?

If we purposely target cognition, can we improve gait & reduce fall risk?

Non-pharmacological treatment
Effect of Cognitive Remediation on Gait in Sedentary Seniors

Joe Verghese,1 Jeannette Mahoney,1,2 Anne F. Ambrose,2 Cuiling Wang,4 and Rocío Holtzer1,2

• RCT
• 24 sessions, 45-60 min each, 3 times per week for 8 weeks
• N=10 intervention vs 10 control
• Computerized ‘Mindfit’ program (n = 10). Each training session included a mixture of 21 visual, auditory, and cross-modality tasks compared with wait-list (n = 10)

Benefits of Cognitive Dual-Task Training on Balance Performance in Healthy Older Adults

Karen Z. Li,1 E. Rouaida,2 M. Lussier,3,4 L. Bherer,3,4 A. Leroux,3 and P. A. McKinley6

N=20 healthy older adults, mean age 76 y/o

Transfer effect!
Effects of Single-Task Versus Dual-Task Training on Balance Performance in Older Adults: A Double-Blind, Randomized Controlled Trial

Patana Silapasuwad, PT, PhD, Anne Shumway-Cook, PT, PhD, Vignesh Lugashe, MS, Paul van Donkelaar, PhD, Li-Shan Chou, PhD, Ulrich Mayer, PhD, Margorie H. Woolacott, PhD

Dual-task gait velocity improves after 4 weeks (n=23)

Virtual Reality for Gait Training: Can It Induce Motor Learning to Enhance Complex Walking and Reduce Fall Risk in Patients With Parkinson’s Disease?

Anat Mirelman,1,2 Inbal Maldan,1 Talia Herman,1 Judith E. Deutsch,1 Nir Giladi,1,4 and Jeffrey M. Hausdorff1,2,5

Figure 2: Effects of the TT+VR intervention on overground gait speed and stride length. Percent improvement after training with TT + virtual reality compared with TT alone (18). Dual tasking performance improvements were greater after TT + VR compared with TT alone.
If we purposely target cognition, can we improve gait & reduce fall risk?

Pharmacological treatment

Cognitive Enhancers and the Effect on Gait
History of falls in Parkinson disease is associated with reduced cholinergic activity.


<table>
<thead>
<tr>
<th></th>
<th>PD fallers (n=17)</th>
<th>PD non-fallers (n=27)</th>
<th>Group Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortical AChE</td>
<td>0.0264</td>
<td>0.0281</td>
<td>P=0.005</td>
</tr>
<tr>
<td>Thalamic AChE</td>
<td>0.0572</td>
<td>0.0617</td>
<td>P=0.006</td>
</tr>
</tbody>
</table>

No significant difference in nigrostriatal dopaminergic activity between PD fallers and non-fallers

Thalamic AChE activity represents cholinergic output of the pedunculopontine nucleus (PPN), a key node for gait control.

Effects of a central cholinesterase inhibitor on reducing falls in Parkinson disease.


- Randomized, crossover, double-blind - 6 w+ 3 w washout+6 w placebo
- N=23 pt with Parkinson’s Disease
- Donepezil/Placebo 5 mg/day of donepezil or placebo for 3 weeks and increase to 10 mg/day for the remaining 3 weeks
Pharmacological intervention for dementia: donepezil, rivastigmine, galantamine

- Modest effect on cognition but they delay placement
- Mechanism is assumed to be related to cognitive improvement
- It is unknown if it is due to an effect on mobility

• Open-label pilot study

• N=6 pt with mild AD (67%♀, age 79.9±5); 8 pt with MCI (64%♀, age 75.6±6)

• 5 mg/day donepezil for 1 month, 10 mg/day for 3 months. Follow-up of 4 months

• Donepezil improved gait velocity and variability


Donepezil in AD versus MCI (control)

MCD: minimal clinically significant difference

Donepezil Improves Gait Performance in Older Adults with Mild Alzheimer’s Disease: A Phase II Clinical Trial

**Design:** Phase II clinical trial
**Participants:** 43 seniors with mild AD received donepezil
**Primary outcome:** Gait velocity and variability under single and dual-tasking using an electronic walkway
**Secondary outcomes:** Attention and executive function
**Intervention:** 5 mg/day of donepezil for 1 month
10 mg/day for the subsequent 3 months (4 mo follow-up)

<table>
<thead>
<tr>
<th>Cognitive Enhancers &amp; Gait Phase II Study</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Table 2.</strong> Paired sample t-test; statistical significance is denoted with * and was set at <em>p</em> &lt; 0.05</td>
</tr>
<tr>
<td>Gait Velocity (mean, SD cm/s)</td>
</tr>
<tr>
<td>--------------------------------</td>
</tr>
<tr>
<td>Single gait</td>
</tr>
<tr>
<td>Counting backwards by 1s</td>
</tr>
<tr>
<td>Naming animals</td>
</tr>
<tr>
<td>Counting backwards by 7s</td>
</tr>
<tr>
<td>Stride Time Gait Variability (CoV,%)</td>
</tr>
<tr>
<td>Single gait</td>
</tr>
<tr>
<td>Counting backwards by 1s</td>
</tr>
<tr>
<td>Naming animals</td>
</tr>
<tr>
<td>Counting backwards by 7s</td>
</tr>
</tbody>
</table>
Cognitive Enhancers & Gait Phase II Study

### Table 3. Secondary Outcomes. Cognitive test changes (mean and SD) after 4 months of follow-up.

Note: Statistical significance is denoted with * and was set at p<0.05. a Final score is total time in seconds to complete task. b Final score is the sum of points from each correct trial. Maximum score is 16.

<table>
<thead>
<tr>
<th>Test</th>
<th>Baseline</th>
<th>Follow-up</th>
<th>Change</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trail Making Test A*</td>
<td>69.05 (36.81)</td>
<td>57.98 (29.82)</td>
<td>-11.08 (32.73)</td>
<td>0.030*</td>
</tr>
<tr>
<td>Trail Making Test B*</td>
<td>237.09 (138.85)</td>
<td>189.35 (139.09)</td>
<td>-51.22 (107.38)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Trail Making Test B-A</td>
<td>158.18 (110.07)</td>
<td>120.15 (100.32)</td>
<td>-38.04 (101.17)</td>
<td>0.042*</td>
</tr>
<tr>
<td>Digit Span Test – Forwardb</td>
<td>8.74 (1.83)</td>
<td>9.15 (2.03)</td>
<td>+0.41 (1.93)</td>
<td>0.051</td>
</tr>
<tr>
<td>Digit Span Test – Backwardb</td>
<td>5.32 (1.75)</td>
<td>4.91 (1.60)</td>
<td>-0.41 (1.21)</td>
<td>0.273</td>
</tr>
</tbody>
</table>


BMC Neurology

**Study protocol**

*Can cognitive enhancers reduce the risk of falls in older people with Mild Cognitive Impairment? A protocol for a randomised controlled double blind trial*

Manuel Montero-Odasso*1,2,3, Jennie L. Wells1,3, Michael J. Borrie1,3 and Mark Speechley2,3

Address: 1Department of Medicine, Division of Geriatric Medicine, Parkwood Hospital, University of Western Ontario, London, ON, Canada; 2Department of Epidemiology and Biostatistics, University of Western Ontario, London, ON, Canada; 3Maasen Health Research Institute, London, ON, Canada

Email: Manuel.Monteiro-Odasso@uwo.ca; Jennie.L.Wells@sch.ca; Michael.J.Borrie@sch.ca; Mark.Speechley@sch.ca

* Corresponding author

ClinicalTrials.gov Identifier: NCT00054531
Approached to be in Study (n=216)

- Ineligible (n=78)
  - Screen failed
  - Did not meet inclusion

Consented (n=46)

Refused (n=72)
  - Not interested
  - Withdrew from the screening

Randomized (n=46)

Allocated to Donepezil (n=24)
  - Baseline Assessment (T0) (n=23)
  - 1 month Assessment (T1) (n=19)
  - 6 month Assessment (T6) (n=19)
  - Included in Preliminary Analysis (n=19)

Allocated to Placebo (n=22)
  - Baseline Assessment (T0) (n=20)
  - 1 month Assessment (T1) (n=20)
  - 6 month Assessment (T6) (n=19)
  - Included in Preliminary Analysis (n=19)

Consort Diagram

ClinicalTrials.gov Identifier: NCT00934531

Dual-task Gait

- Mean Change in Naming Animals Gait Velocity (cm/sec) from Baseline

Dual-task Variability

- Serial Sevens Gait Variability (CV\%) from Baseline

Donepezil and Gait in MCI: An RCT. Preliminary Results
Conclusions

- Donepezil modestly improved GV and reduced Gva in the range 5 cm/s
- Changes are clinically meaningful and similar to the gait improvement seen after exercise intervention protocols
- Changes were of higher magnitude in dual-task gait
- Improvements were found early, 1 month, and sustained during 6 months
- Dose-response pattern
Final Summary

- Walking (gait) is not automatic and relies on cognition
- Dual-task affects gait, and falls are likely to occur while multitasking
- Subtle cognitive deficits likely exacerbate falls risk even in those labeled as “cognitively normal”
- The effect of proven strategies to reduce falls, including exercise and vitamin D, can be mediated via cognitive enhancement

Novel Approach: Improve Cognition to Improve Mobility
Enhancing attention/executive function may reduce falls risk
(caution: publication bias, small studies, larger RCTs are needed)

- Not the only approach and it is complementary of existing strategies

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Guillaume Limfat

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Dr Mark Speechley
Dr Tim Doherty
Dr Michael Borrie
Dr Jennie Wells
Dr Kevin Shoemaker
Dr Amer Burhan
Dr Akshya Vasudev

WALK Collaboration
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Dr Cedric Anweiller - Univ of Angers

Montreal Collaboration
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Dr Louis Bherer - Concordia University
Dr Karen Li - Concordia University

Web: www.gaitandbrain.com
Email: mmontero@uwo.ca

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Ontario Ministry of Research and Innovation
The Physicians Services Incorporated Foundation (PSI)
The Drummond Foundation
Lawson Health Research Institute (LHRI)
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Including 2 Canada Research Chairs
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www.geron.org/cns

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In conjunction with The Gerontological Society of America’s Annual Scientific Meeting, the yearly workshop built on the information from the prior workshops:

- 2014: Prevention and Intervention
- 2013: Neural Mechanisms of Mobility Impairments
- 2012: Evidence on changes in central nervous system control of movement across the life span and in aging

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