VI CURSO DE EGRESADOS DE ALMA
"ACTIVIDAD FÍSICA, CAÍDAS Y FRACTURAS"
SANTA MARTA, COLOMBIA
Del 25 al 28 de febrero de 2020

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ALMA Santa Marta

Cognitive Impairment and Falls

Evidence, assumptions, and therapeutic options

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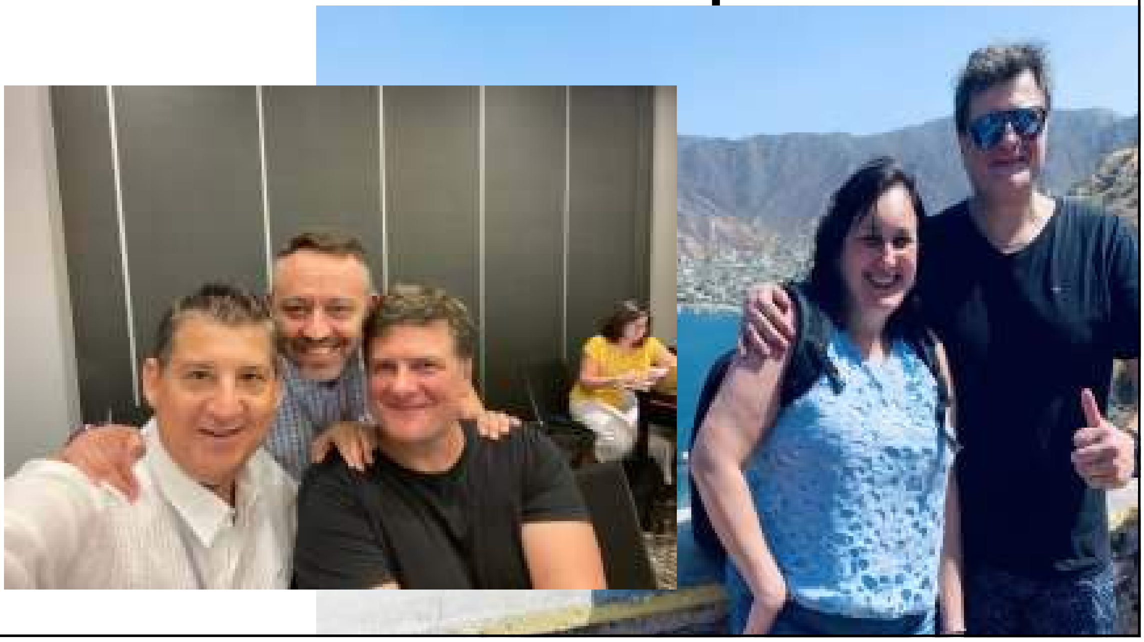
Alma 2002 (Chile) y 2003 (Mexico)




2

Alma… dos decadas despues



Outline

1- To review the role of cognitive deficits in falls risk

2- Assumptions in current fall prevention management

3- Cognitive treatment is complementary to reduce risk of falls

What makes a person look old?

- Slow Gait
- Mental Slowing

5

Falls & Fall-related Injuries Special Interest Group: a Call to Action

Manuel Montero-Odasso, MD, PhD, AGSF, FRCP[1], and David B. Hogan, MD, FRCPC[2]
[1] *Division of Geriatric Medicine, Department of Medicine, University of Western Ontario, London, ON,*
[2] *Division of Geriatric Medicine, Department of Medicine, University of Calgary, Calgary, AB, Canada*
DOI:http://dx.doi.org/10.5770/cgj.19.258

Canadian Geriatric Journal 2018

6

Gaps Identified: Falls in Cognitively Impaired

- Why are falls so common in the cognitively impaired?
- Why does fall prevention not work in this population?
- Are we assuming facts?
- Are we missing a treatment component?

Western

7

Evidence and Assumptions in Fall prevention

- **Evidence**

  Cognitive impairment is a risk factor for falls

- **Assumption**

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

Western

8

Age and Ageing (1978), 7, Supplement

ARE FALLS A MANIFESTATION OF BRAIN FAILURE?

B. ISAACS

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.

Western

9

Falls in the Cognitively Impaired - Facts

- Falls are two-fold in people with Dementia[1-3]
- Fallers with cognitive problems have

  ↑ risk of injuries & fractures
  ↓ functional outcomes
  ↓ access to rehabilitation
  ↑ institutionalization
  ↑ mortality

- Fall prevention is not successful in those with MMSE < 20[4]

Western

1.Tinetti et al. *N Engl J Med* 1988
2. Shaw. *J Neural Transm* 2007
3. Montero-Odasso et al. *JAGS* 2012, 2018
4. Oliver et al. *BMJ* 2007

10

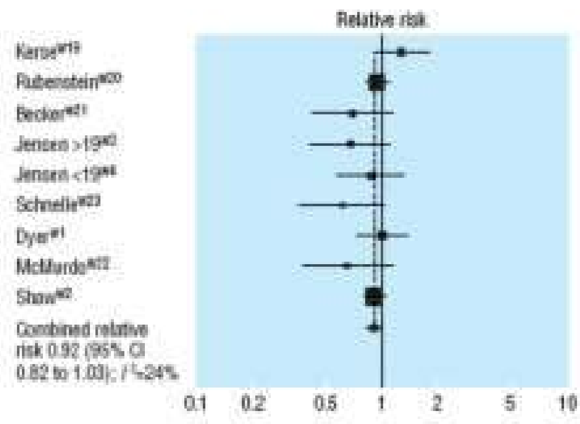
Falls in the Cognitively Impaired - Interventions

Meta-analysis for multifactorial interventions in care homes

8 Studies fulfill criteria for inclusion

The relative risk reduction for fallers was **0.92 (0.82-1.03)**

Confidence intervals included **1**



Oliver et al. *BMJ* 2007

11

SYSTEMATIC REVIEW

The role of cognitive impairment in fall risk among older adults: a systematic review and meta-analysis

Susan W. Muir, Karen Gopaul, Manuel M. Montero Odasso

Fall Outcome	Odd Ratio(95%CI)	I^2 (%)
Any fall	1.32 (1.18,1.49)	74.3%
Serious injury	2.33 (1.61,3.36)	5.9%
Fractures	1.78 (1.34,2.37)	0%
Any fall – low executive function	1.44 (1.20,1.83)	70.9%

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**

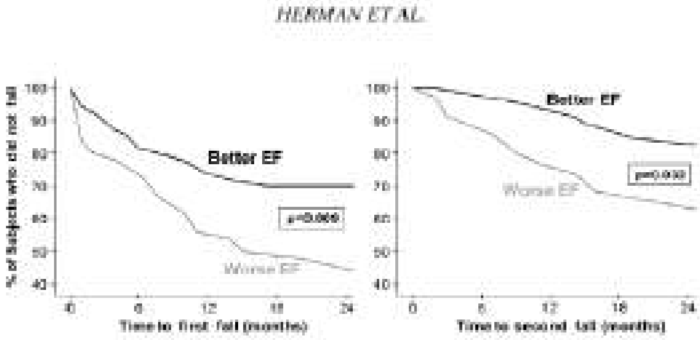
3- Executive dysfunction can be present despite normality in “global cognition”

4- Executive function should be assessed in falls risk evaluation

Age and Ageing, 2012

12

Deficits in executive function (EF) predict future falls (2 years of follow up)



Herman T, Mirelman A, Giladi N, Schweiger A, Hausdorff JM .Executive control deficits as a prodrome to fzlls in healthy older adults: a prospective study linking thinking, walking, and falling. J Gerontol A Biol Sci Med Sci. 2010 Oct;65(10):1086-92.

Herman et al. *J Gerontol Med Soc* 2010

13

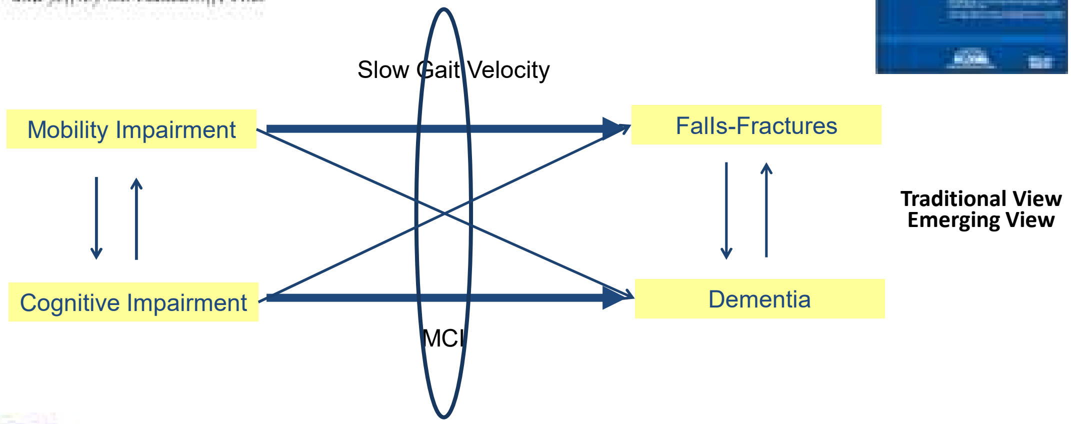
How cognitive deficits may increase risk of falls, at early stages?

14

PROGRESS IN GERIATRICS

Gait and Cognition: A Complementary Approach to Understanding Brain Function and the Risk of Falling

Manuel Montero-Odasso, MD, PhD, AGSF,[*†] Joe Verghese, MB, BS,[‡] Olivier Beauchet, MD, PhD,[§] and Jeffrey M. Hausdorff, PhD[¶**]



J Am Geriat Soc 2012; 60(11):2127-36.

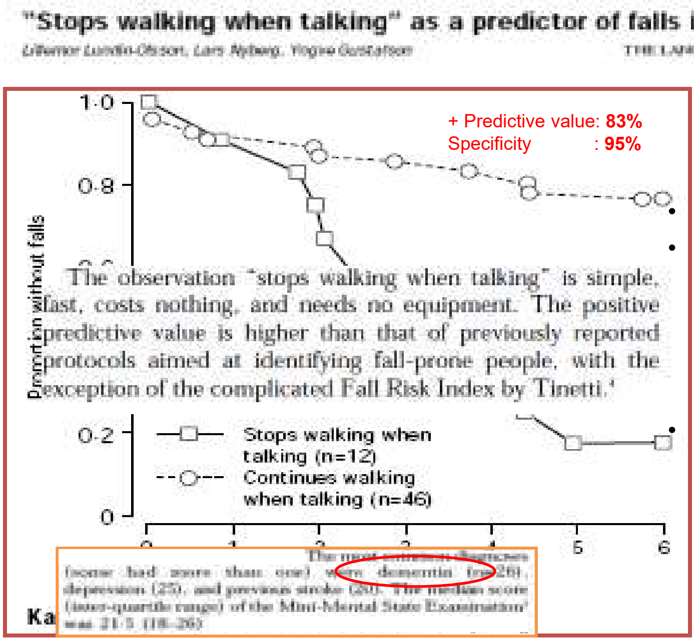
15

Gait and cognition: Is there a relationship?

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

BUT…

16



Walking When Talking

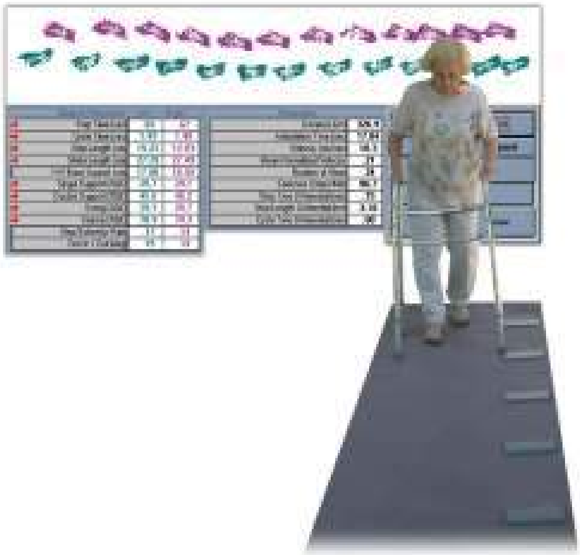
- Unmonitored conversations
- Reciting names
- Counting backward/serial subtractions
- Naming animals
- Reaction time to auditory stimuli
- Q & A
- Alphabets

Gait and cognition:
Is there a relationship?

YES!

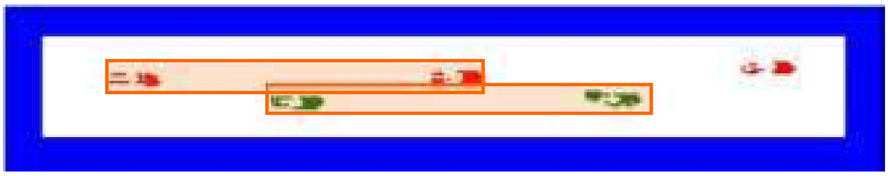
- Patients often explain that they fell when they became distracted
- While performing more that one task in the kitchen, bathroom, etc.

Gait Assessment: quantitative



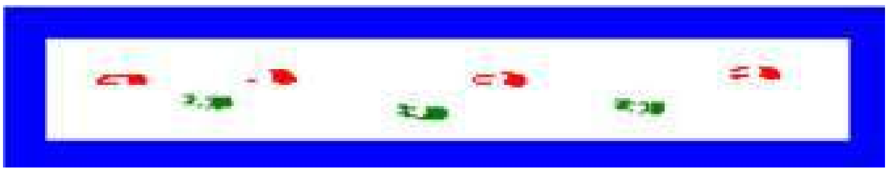
19

A. Usual gait: right and left step lengths approximately equal.



B. asymmetric gait (limp): right step length consistently shorter than left step length.

C. Variable gait: inconsistent right and left step lengths



Red = Left footprints, Green = Right footprints

20

Gait patterns and 'stress tests'

Gait variability

- With age increasing fluctuation in a gait from one step to the next = intra-individual gait variability[1]
- More sensitive predictor of falls risk[2]?
- Under less conscious control

Walk ratio (step length/cadence)

Change in speed (walking speed reserve)

Dual-task gait initiation

1 Callisaya ML et al Age and Ageing 2010
2 Callisaya ML et al Age and Ageing 2011

Gait patterns and risk of multiple falls

Preferred speed

- Step length variability[1] RR 2.01 95%CI 1.07, 3.80
- Double support phase variability[1] RR 2.08 95%CI 1.06, 4.08

Fast speed and change in speed

- Longer steps, slower cadence[2] RR 0.73 95% CI 0.63, 0.85

[1]Callisaya ML et al Age and Ageing 40 2011;
[2]Callisaya ML Gait and Posture 36 2012

Which cognitive domains are associated with increased risk of falls?

23

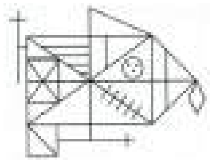
23

Cognition and falls risk

Executive function/attention

- Victoria Stroop
  Car Hat Bed
  Red Blue Yellow
- Controlled Oral Word Association Test
- Digit span

Visuospatial ability



Rey Complex Figure

Processing speed

- Digit symbol coding
- Symbol search

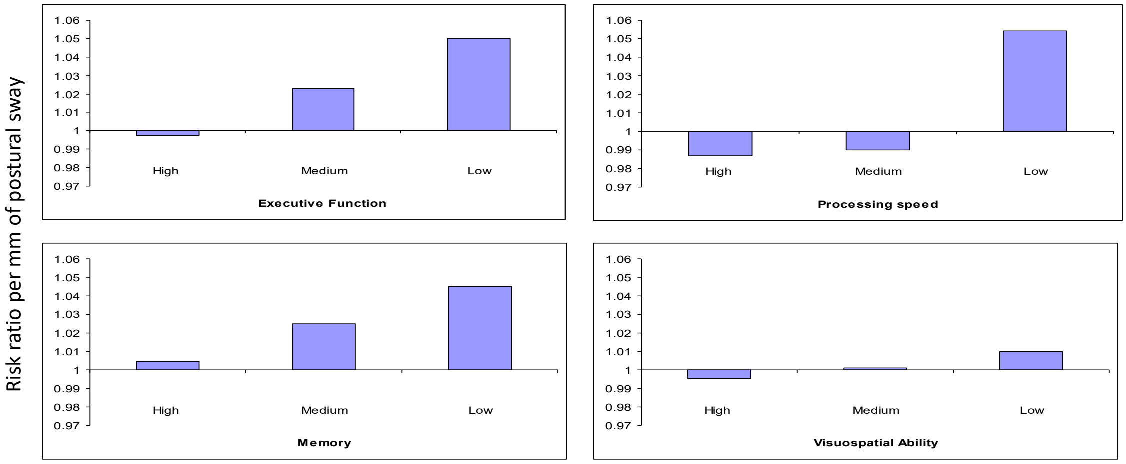
Memory

- Hopkins Verbal Learning Test
  - Immediate
  - Delay
  - Recognition
- Rey Complex Figure - Delayed

Martin K et al ..Callisaya ML J Gerontology Med Sci 2013

24

Risk of multiple falls per mm of sway at three levels of each of the four cognitive domains



High=Better performance; Low=poorer performance

Martin K et al ..Callisaya ML J Gerontology Med Sci 2013

“Gait may provide a window into the brain”

Montero-Odasso JAGS 60:2012

Cognitive domains

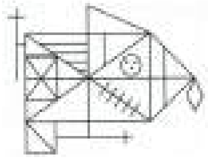
Executive function/attention

- Victoria Stroop

Car Hat Bed
Red Blue Yellow

- Controlled Oral Word Association Test
- Digit span

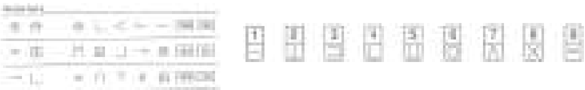
Visuospatial ability



Rey Complex Figure

Processing speed/attention

- Digit symbol coding
- Symbol search



Memory

- Hopkins Verbal Learning Test
  - Immediate
  - Delay
  - Recognition
- Rey Complex Figure - Delayed

Martin K et al ..Callisaya ML J Gerontology Med Sci 2013

Journals of Gerontology: MEDICAL SCIENCES
Cite journal as: J Gerontol A Biol Sci Med Sci.
doi:10.1093/gerona/gls224

Cognitive Function, Gait, and Gait Variability in Older People: A Population-Based Study

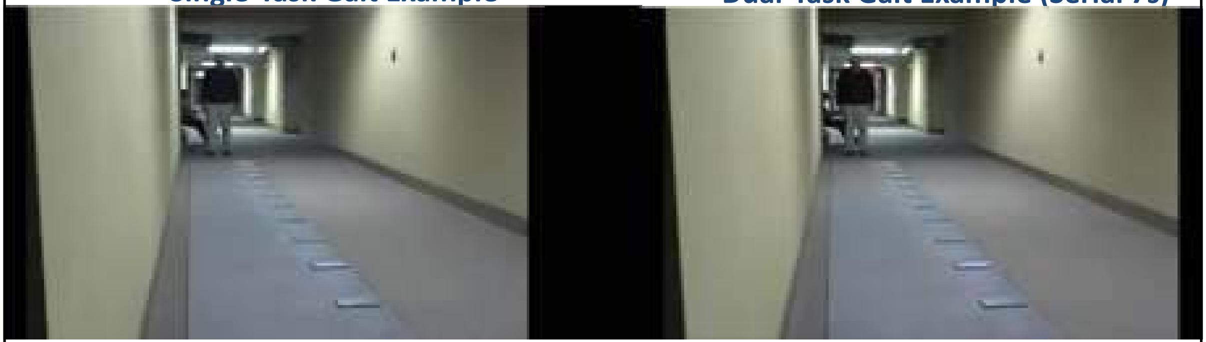
Kara L. Martin,[1] Leigh Blizzard,[1] Amanda G. Wood,[2,3] Velandai Srikanth,[1,2] Russell Thomson,[1]
Lauren M. Sanders,[2] and Michele L. Callisaya[1,2]

Multivariable linear regressions between cognition and gait measures

Gait	Processing speed	Executive function	Visuospatial function
Gait speed (cm/s)	✓	✓	
Cadence	✓		
Step length (cm)	✓	✓	
Support base (cm)	✓		
DSP (ms)	✓	✓	
Gait variability			
Step time (ms)		✓	
Step length (cm)			
Support base (cm)			
DSP (ms)	✓	✓	✓

Morris R. Neuroscience and Biobehavioural reviews 2016

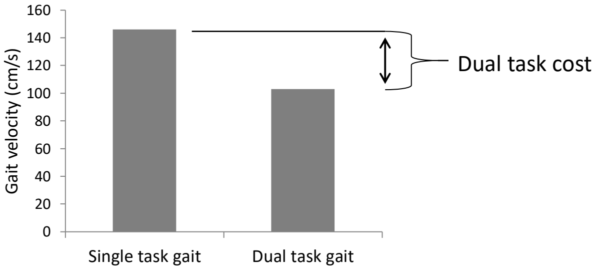
Single-Task Gait Example | **Dual-Task Gait Example (Serial 7s)**



Gait velocity: 1.46 m/sec
Gait variability: 2.83% CoV

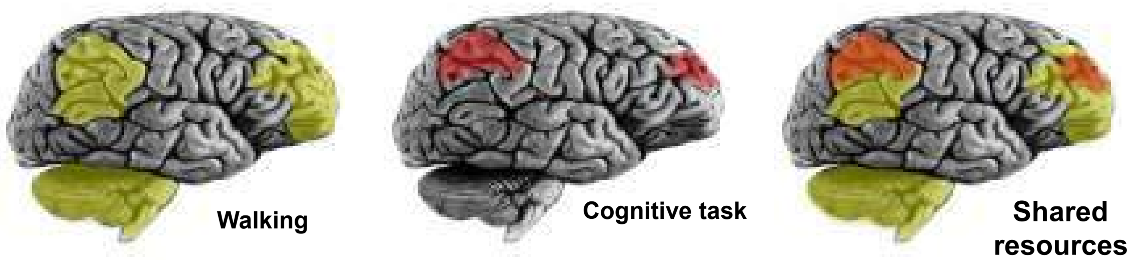
Gait velocity: 1.03 m/sec
Gait variability: 13.06% CoV

$$= \frac{Single\ gait - Dual\ task\ gait}{Usual\ gait} \times 100 = \mathbf{30\%}$$



Dual-task paradigm - How does it work?

Brain areas activated while…



Single task | Single task | Dual-task

Pashler H. Psychol Bull. 1994

Dual-Task Complexity Affects Gait in People With Mild Cognitive Impairment: The Interplay Between Gait Variability, Dual Tasking, and Risk of Falls

Manuel Montero-Odasso, MD, PhD, Susan W. Muir, PhD, Mark Speechley, PhD

DUAL-TASK COMPLEXITY ON GAIT IN MILD COGNITIVE IMPAIRMENT, Montero-Odasso 297

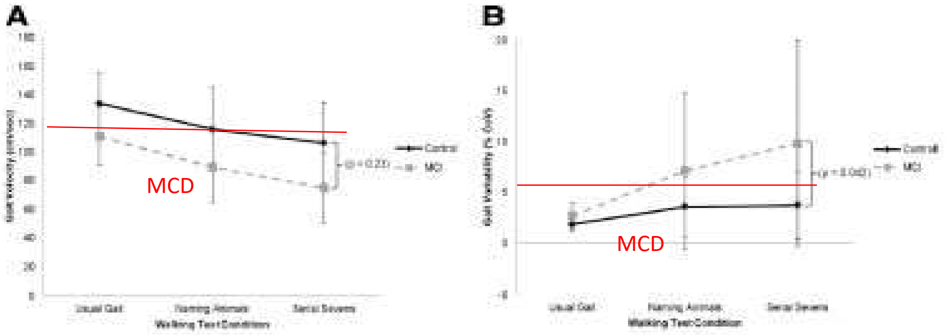


Fig 3. Interaction between cognitive status and 2 different walking conditions for gait velocity (A) and gait variability (B). Abbreviation: % CoV, percent coefficient of variation in stride time.

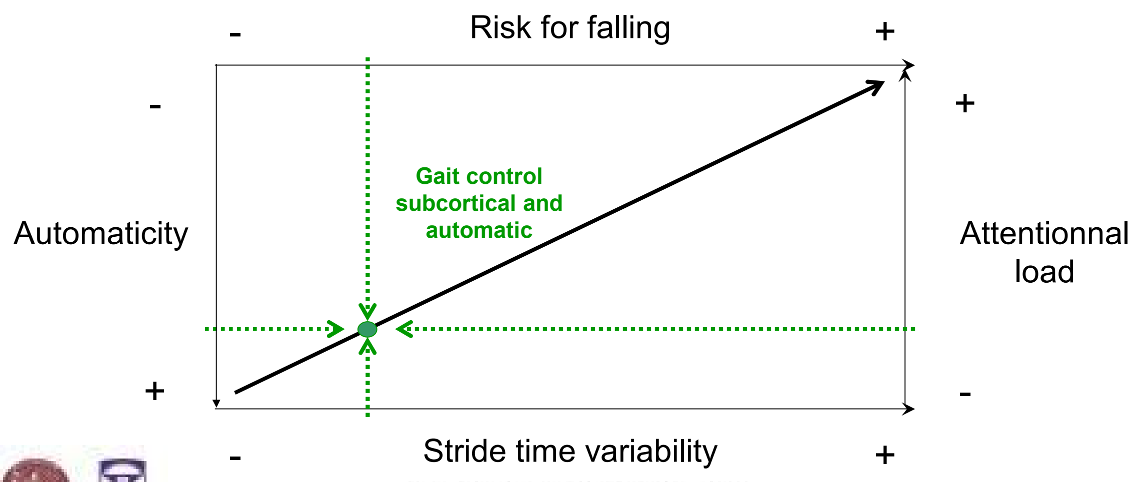
MCD: minimal clinical difference

Arch Phys Med Rehabil. 2012 Feb;93(2):293-9

31

Dual-Task Complexity Affects Gait in People With Mild Cognitive Impairment: The Interplay Between Gait Variability, Dual Tasking, and Risk of Falls

Manuel Montero-Odasso, MD, PhD, Susan W. Muir, PhD, Mark Speechley, PhD



Arch Phys Med Rehabil Vol 93, February 2012

32

Dual-Task Complexity Affects Gait in People With Mild Cognitive Impairment: The Interplay Between Gait Variability, Dual Tasking, and Risk of Falls

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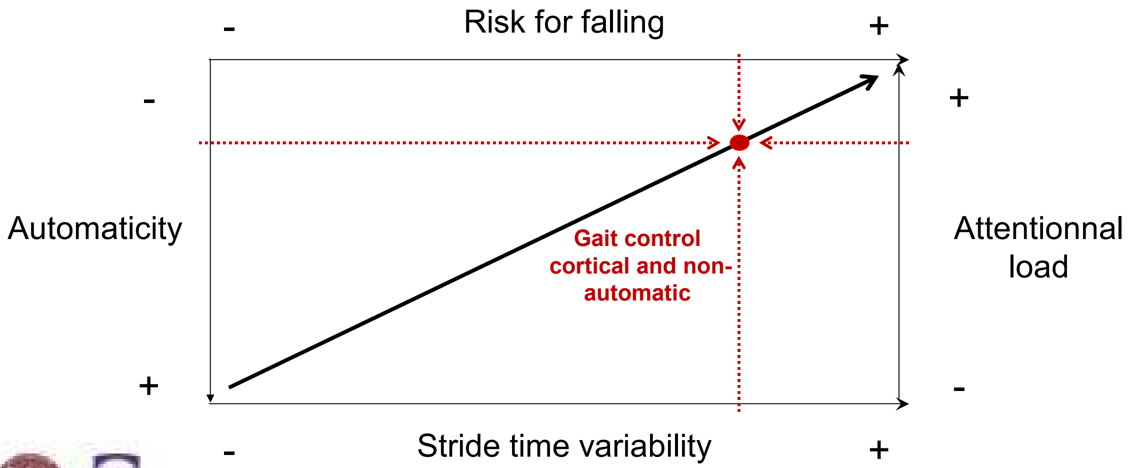
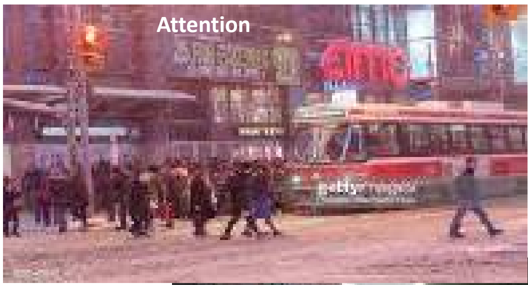


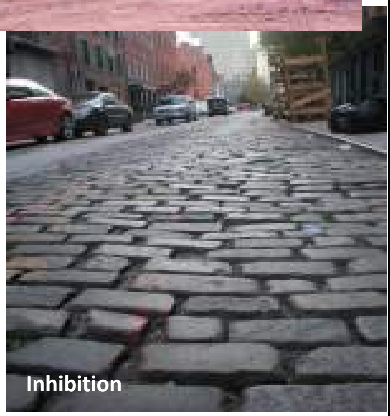
Arch Phys Med Rehabil Vol 93, February 2012

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



Walking is cognitively demanding!

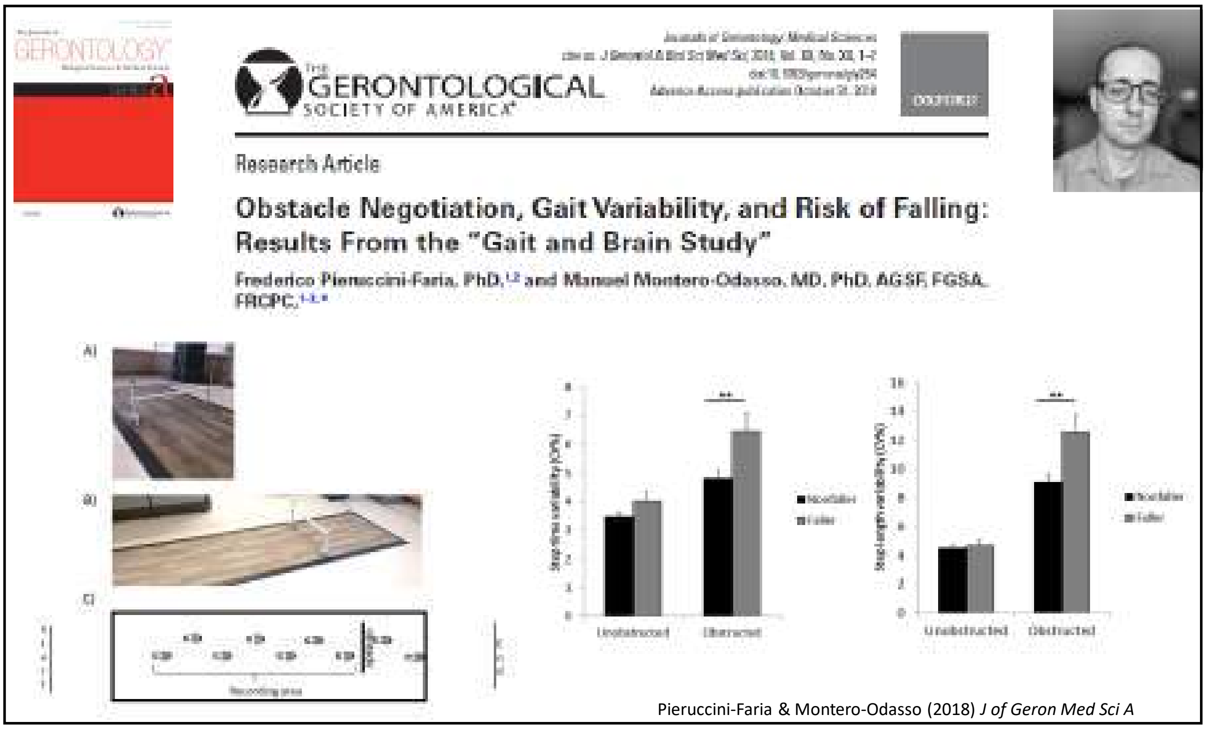


35

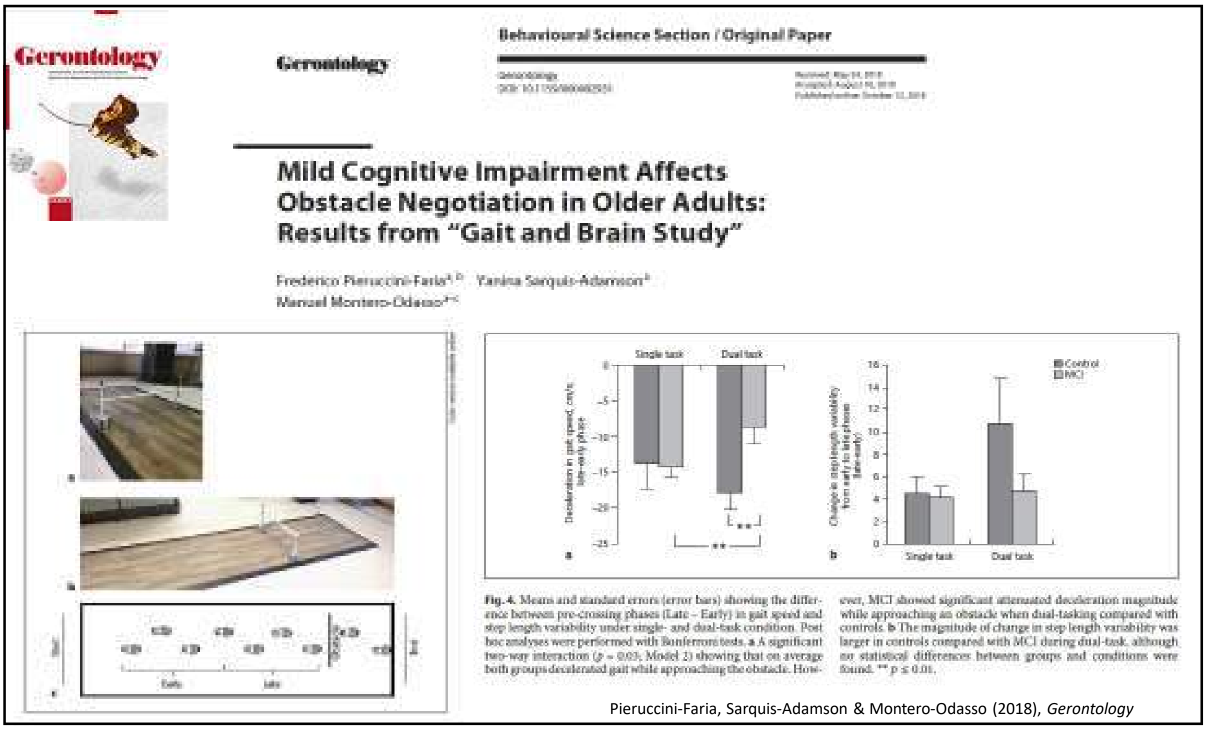
How does gait-cognitive interaction may increase the risk of falls?

Obstacle negotiation , gait variability and so on

36


The Gerontological Society of America
Research Article
Obstacle Negotiation, Gait Variability, and Risk of Falling: Results From the "Gait and Brain Study"
Frederico Pieruccini-Faria, PhD,1,2 and Manuel Montero-Odasso, MD, PhD, AGSF, FGSA, FRCPC,1-3,*
Unobstructed
Obstructed
Nonfaller
Faller
Pieruccini-Faria & Montero-Odasso (2018) J of Geron Med Sci A

37

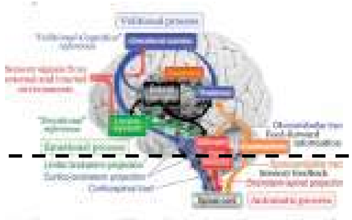

Behavioural Science Section / Original Paper
Gerontology
Mild Cognitive Impairment Affects Obstacle Negotiation in Older Adults: Results from "Gait and Brain Study"
Frederico Pieruccini-Faria Yanina Sarquis-Adamson Manuel Montero-Odasso
Single task
Dual task
Control
MCI
Fig. 4. Means and standard errors (error bars) showing the difference between pre-crossing phases (Late – Early) in gait speed and step length variability under single- and dual-task condition. Post hoc analyses were performed with Bonferroni tests. a A significant two-way interaction (p = 0.03; Model 2) showing that on average both groups decelerated gait while approaching the obstacle. However, MCI showed significant attenuated deceleration magnitude while approaching an obstacle when dual-tasking compared with controls. b The magnitude of change in step length variability was larger in controls compared with MCI during dual-task, although no statistical differences between groups and conditions were found. ** p ≤ 0.01.
Pieruccini-Faria, Sarquis-Adamson & Montero-Odasso (2018), Gerontology

38

Mapping Associations between Gait Decline and Falls Risk in MCI

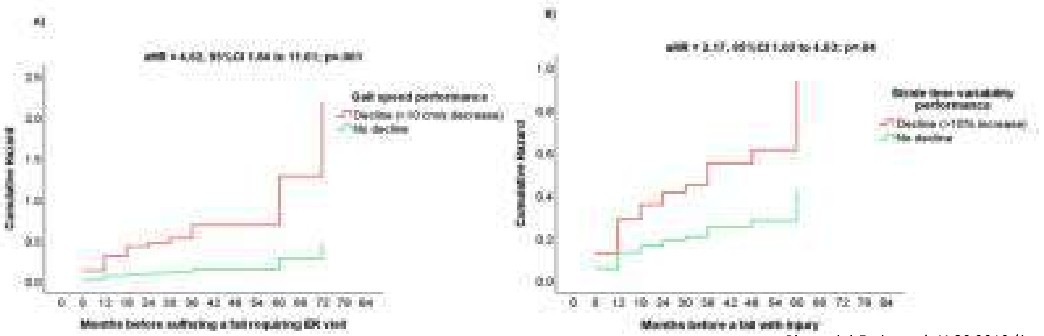
Non-rhythmic domains
- Gait speed and Stride time variability

Rhythmic domains
- Swing time and cadence



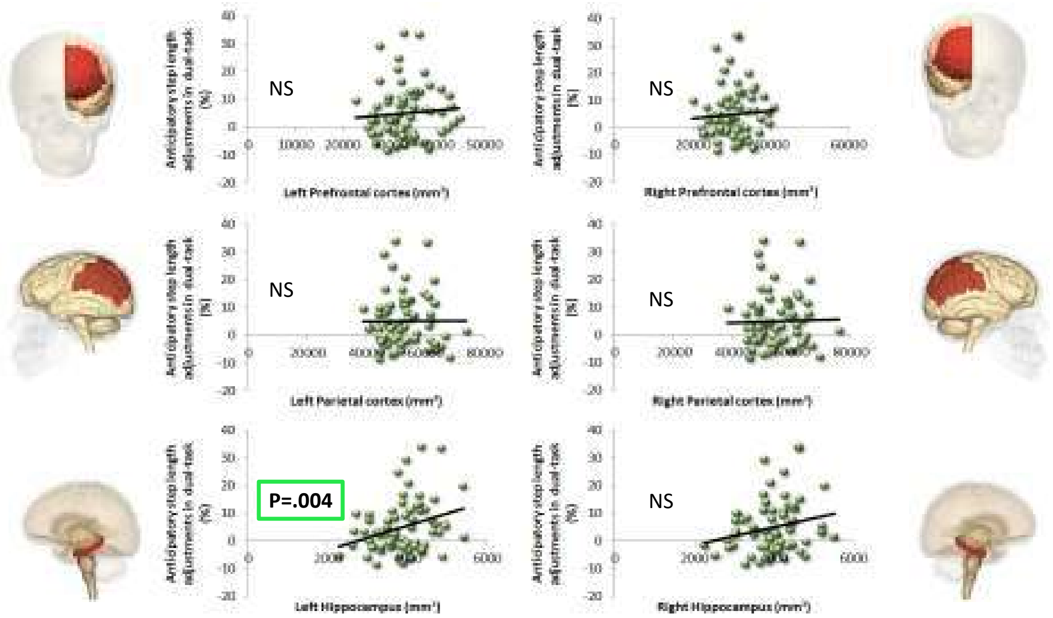
Less automatic control

More automatic control



Pieruccini-Faria et al. JAGS 2019 (*in press*)

Human Navigation Network and Obstacle Negotiation in MCI

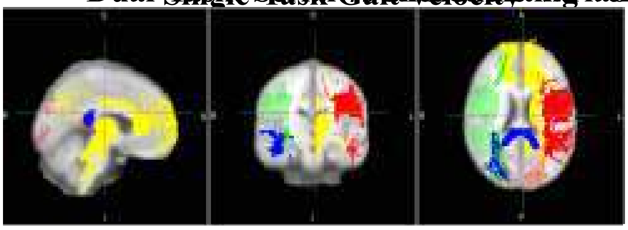


Pieruccini-Faria et al. (submitted)

White matter integrity, gait, and falls

- Corpus callosum WMI significantly ($p<0.05$) correlated(+) with single- and dual-task gait velocity and with gait variability(-).

Dual-Task: Serial 7s
Single-Task Gait Velocity



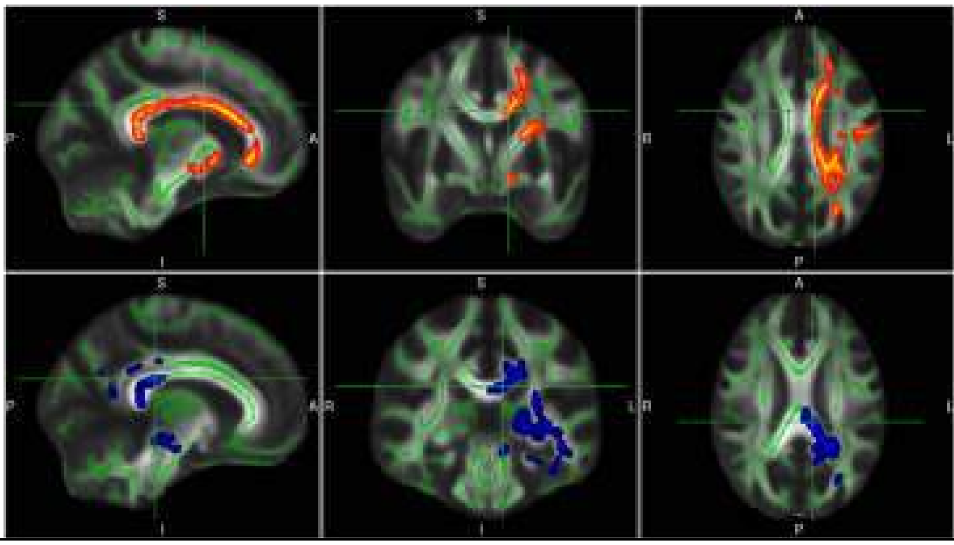
Snir J et al, Neuroimage Clin, 2019

41

Results: Voxel-wise

Lower WM integrity on the left versus right brain hemispheres (FA – red, MD – blue)

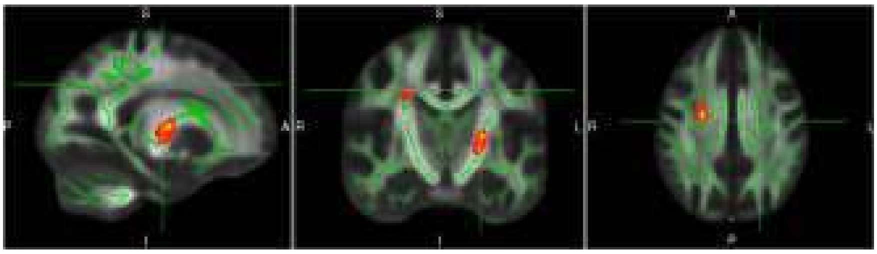
P < 0.05
Corrected for multiple comparisons



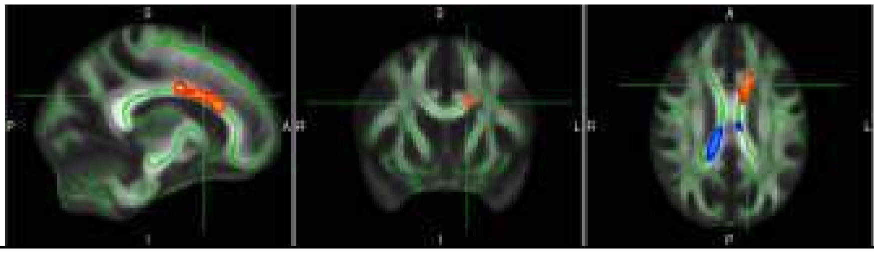
42

Results: Voxel-wise

Lower WM integrity (lower FA) correlation with falls



Lower WM integrity (higher MD) correlation with falls (positive – red; negative – blue)



White matter integrity, gait, and falls

- Poor WM integrity in the corpus callosum predicted a 3 year gait decline.

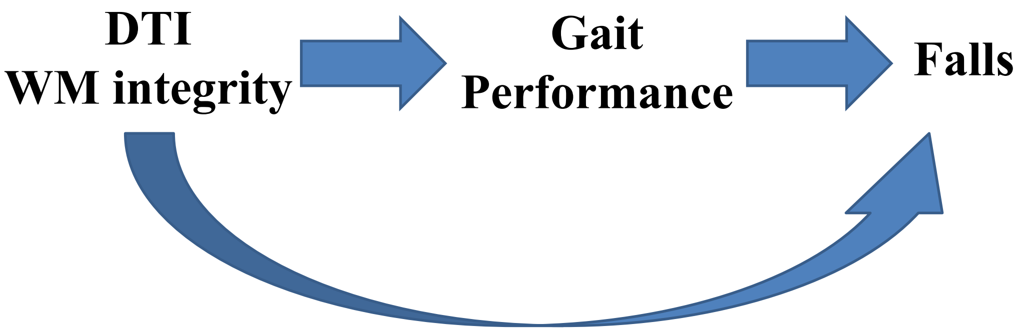
↓ FA ↑ MD → ↓ Gait velocity ↑ Gait variability

- Poor WM integrity predicted fall incidence.

↓ FA ↑ MD → ↑ Falls

Snir J et al, Neuroimage Clin, 2019

White matter integrity, gait, and falls



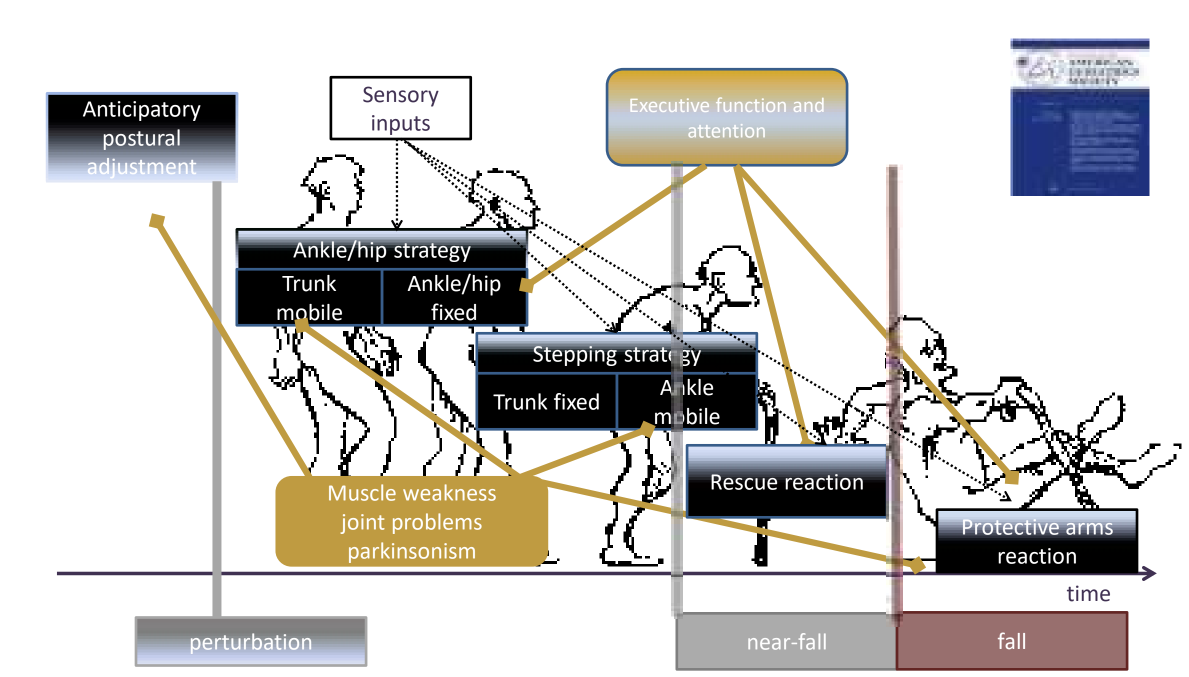
Precursor of White Matter Lesions

Snir J et al, Neuroimage Clin, 2019

Conclusion and framework

How cognition, executive processes, may affect gait and posture before falling?

How is the neurobiology of falls ?



Montero-Odasso & Speechley. *J Am Geritr Soc* 2018

47

If we purposely target cognition,

can we improve gait & reduce falls?

48

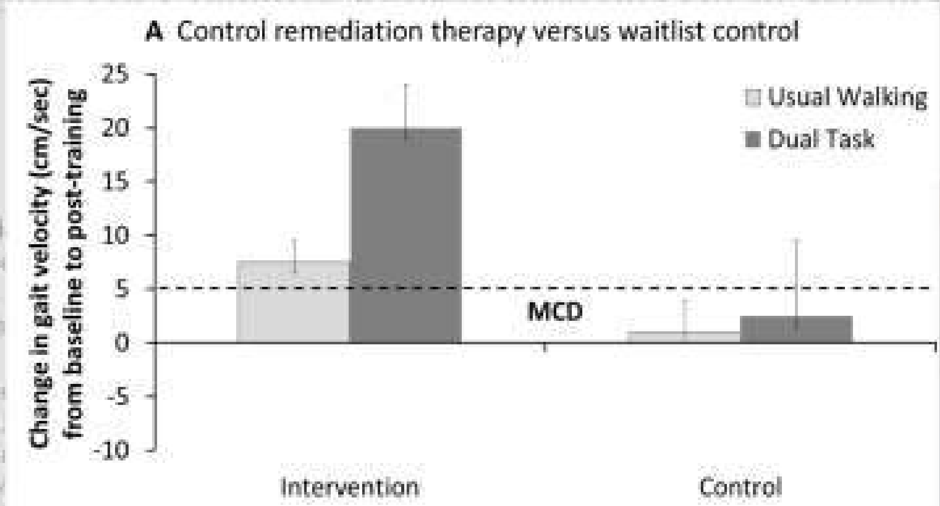
Effect of Cognitive Remediation on Gait in Sedentary Seniors

Joe Verghese,[1] Jeannette Mahoney,[1,2] Anne F. Ambrose,[3] Cuiling Wang,[4] and Roee Holtzer[1,2]

RCT

- 24 sessions, 45-60 min each, 3 times/week for 8 weeks
- N= 10 intervention/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 controls (n= 10)

49



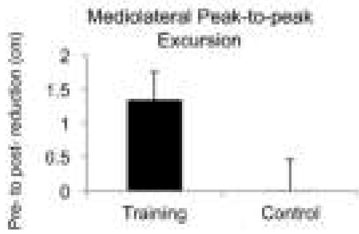
50

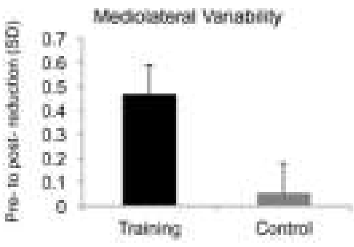
Journal of Gerontology: MEDICAL SCIENCES
Cite journal as: J Gerontol A Biol Sci Med Sci
doi:10.1093/gerona/glq151

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

Karen Z. H. Li,[1] E. Roudaia,[2] M. Lussier,[3,4] L. Bherer,[3,4] A. Leroux,[5] and P. A. McKinley[6]

- N=20 healthy older adults (76y/o)
- Randomly assigned to attentional training or no-treatment
- 5 (1-hour) sessions x 3 weeks





Transfer effect!

51

Attentional training method

(Bherer, Kramer, et al., 2005; Erickson et al., 2008)

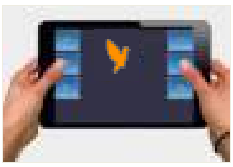
Cognitive Training

- 30 minutes of single and dual-task blocks
- Task A: celestial bodies
- Task B: Animals
- Adaptive increase in difficulty over sessions

Single tasks

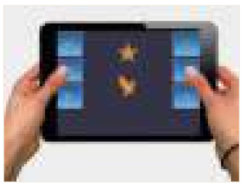
A

B



Dual task

A+B



52

Journal of Alzheimer's Disease 43 (2015) 193–199
DOI 10.3233/JAD-140759
IOS Press

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

Manuel Montero-Odasso[a,b,c,*], Susan W. Muir-Hunter[a,b], Afua Oteng-Amoako[a], Karen Gopaul[a], Anam Islam[a], Michael Borrie[b], Jennie Wells[b] and Mark Speechley[c]
[a] "Gait and Brain Lab", Parkwood Hospital and Lawson Health Research Institute, London, ON, Canada
[b] Department of Medicine, Division of Geriatric Medicine, Schulich School of Medicine and Dentistry, University of Western Ontario, London, ON, Canada
[c] Department of Epidemiology & Biostatistics, Schulich Interfaculty Program in Public Health, University of Western Ontario, London, ON, Canada

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 month follow-up)

Donepezil Study

Participants took donepezil/placebo for 6 months

Donepezil group had lower number of falls, lower participants who fell, and lower risk of falls

	6 months prior to intervention		6 months after intervention		
	Placebo (n= 29)	Donepezil (n= 31)	Placebo (n= 25)	Donepezil (n= 20)	p value
Total # of falls	6	5	21	13	0.209
# participants who fell (%)	5 (17%)	5 (17%)	12 (41%)	7 (23%)	0.159
Falls per participant	0.21	0.17	0.72	0.42	

Phase III RCT Study
2013-2018

BMC Neurology

BioMed Central

Study protocol

Open Access

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 Wells[1,3], Michael J Borrie[1,3] and Mark Speechley[2,3]

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

Email: Manuel Montero-Odasso* - Manuel.MonteroOdasso@sjhc.london.on.ca; Jennie L Wells - Jennie.Wells@sjhc.london.on.ca; Michael J Borrie - Michael.Borrie@sjhc.london.on.ca; Mark Speechley - Mark.Speechley@schulich.uwo.ca

* Corresponding author

Montero-Odasso, M et al *BMC neurology* 9.1 (2009): 42. **ClinicalTrials.gov Identifier: NCT00934531**

ORIGINAL ARTICLE

Donepezil for gait and falls in mild cognitive impairment: a randomized controlled trial

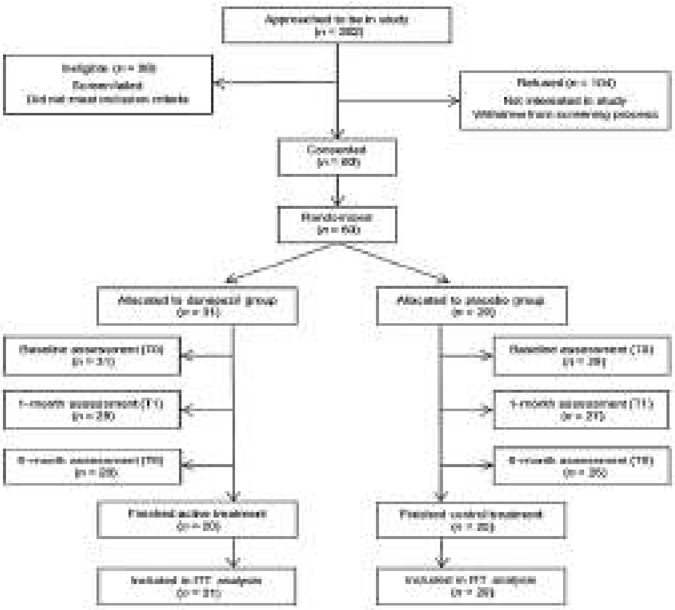
M. Montero-Odasso, M. Speechley, H. Chertkow, Y. Sarquis-Adamson, J. Wells, M. Borrie, L. Vanderhaeghe, G. Y. Zou, S. Fraser, L. Bherer and S. W. Muir-Hunter

Montero-Odasso et al. *Eur J Neurol. 2019 Apr;26(4):651-659*. doi: 10.1111/ene.13872. Epub 2018 Dec 26.

57

Consort Diagram

ClinicalTrials.gov Identifier: NCT00934531



58

Mixed effects model with repeated measures for the primary outcomes comparing the effect between placebo and donepezil treatments at T6.

	Full sample (n = 45)	Placebo (n = 25)	Donepezil (n = 20)	P-value[a]	P-value[b]
Gait speed (cm/s)					
Single-task	110.35 (20.49)	111.60 (18.80)	108.85 (22.76)	0.362	0.137
Dual-task					
Counting	102.91 (23.44)	101.26 (24.93)	104.80 (22.07)	0.263	0.511
Serial 7	87.66 (19.39)	88.09 (20.77)	87.20 (18.41)	0.323	0.533
Naming animals	90.73 (20.86)	90.71 (22.62)	90.75 (19.49)	0.459	0.642
DTC (%)					
Counting	6.30 (16.94)	10.25 (12.35)	1.75 (20.43)	**0.048**	0.056
Serial 7	18.10 (21.14)	21.38 (14.92)	14.64 (26.19)	**0.033**	**0.037**
Naming animals	15.50 (21.15)	18.84 (17.97)	11.78 (24.19)	0.282	0.269
Gait variability (CoV)					
Single-task	4.10 (2.61)	3.77 (1.28)	4.51 (3.66)	0.223	0.239
Dual-task					
Counting	5.35 (5.06)	5.26 (4.15)	5.45 (6.09)	0.221	0.389
Serial 7	6.31 (6.63)	5.80 (6.84)	6.93 (6.51)	0.133	0.201
Naming animals	4.72 (3.79)	4.82 (4.47)	4.59 (2.76)	0.526	0.370

CoV, coefficient of variation; DTC, dual-task gait cost; [a]Mixed model adjusted for baseline values of each variable; [b]Mixed model adjusted for baseline values of each variable plus age, sex and previous falls. Data are given as mean (SD). Values in bold are statistically significant.

Donepezil Study and Falls

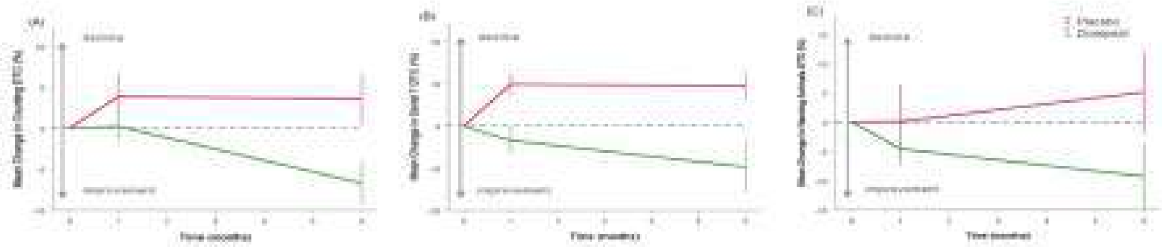
Donepezil group had lower number of total falls and lower participants who fell, although not significant

	6 months prior to intervention		6 months after intervention		
	Placebo (n = 29)	Donepezil (n = 31)	Placebo (n = 25)	Donepezil (n = 20)	P-value
Total no. of falls	6	5	21	13	0.209
No. of participants who fell (%)	5 (17%)	5 (17%)	12 (41%)	7 (23%)	0.159
Falls per participant	0.21	0.17	0.72	0.42	

Western

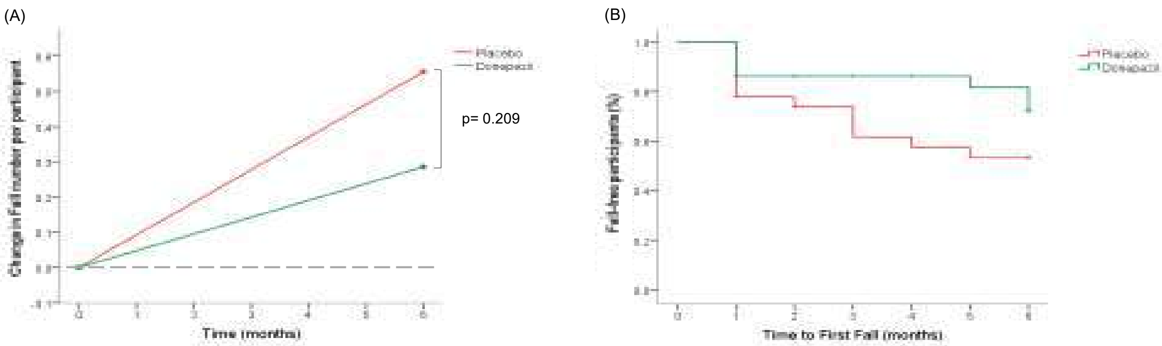
Donepezil Study and Falls

Dual-task cost (DTC) mean change for A) counting, B) serial sevens subtractions, and C) naming animals conditions. Error bars represent ±1 S.E.



Donepezil Study and Falls

Falls during intervention/follow up
A) changes in number of falls after intervention
B) Kaplan-Meier survival curve for falls.



Final Summary

- Cognitive deficits exacerbate falls risk even in “cognitively normal”
- Falls risk screening should include assessment of cognitive processes, in particular selective attention, inhibition, conflict resolution, and dual-tasking
- Falls prevention should consider intervention components that target cognition, specifically executive function
- **Complementary Approach: Improve Cognition to Reduce Falls**
  Enhancing attention/executive function may reduce falls risk
  (caution: publication bias, small studies, larger RCTs are needed)

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63

Final Summary

Neurol Sci
DOI 10.1007/s10072-013-1613-4

NEUROLOGICAL DIGRESSION

Preludes to brain failure: executive dysfunction and gait disturbances

Manuel Montero-Odasso · Vladimir Hachinski

- Impairment in cognition and gait and falls may have a common pathological mechanism
- Evidence show this machains can be at brain shared networks betrem motro control and cogntive processes
- White matter disease affects theses networks , but is not the only mechanism

Neurol Sci. 2014 Apr;35(4):601-4. doi: 10.1007/s10072-013-1613-4. Epub 2013 Dec 24.

64

CCNA Motor, Exercise & Cognition (MEC) Team 12

Distinctive expertise in, **motor/cognitive interaction**, **interventions exercise, gait/physical activity, cognition**

Including 2 Canada Research Chairs

International advisory board
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Caterina Rosano
Joseph Verghese
Jeffrey Hausdorff
Olivier Beauchet

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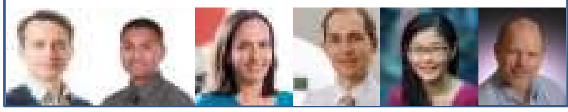
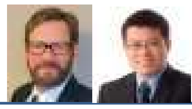
Site leaders



Methodologists



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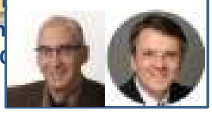

Acknowledgements

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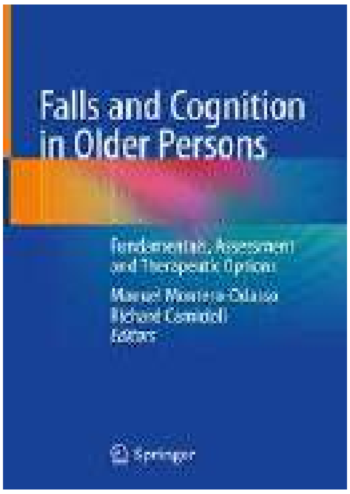
If you want to learn more!



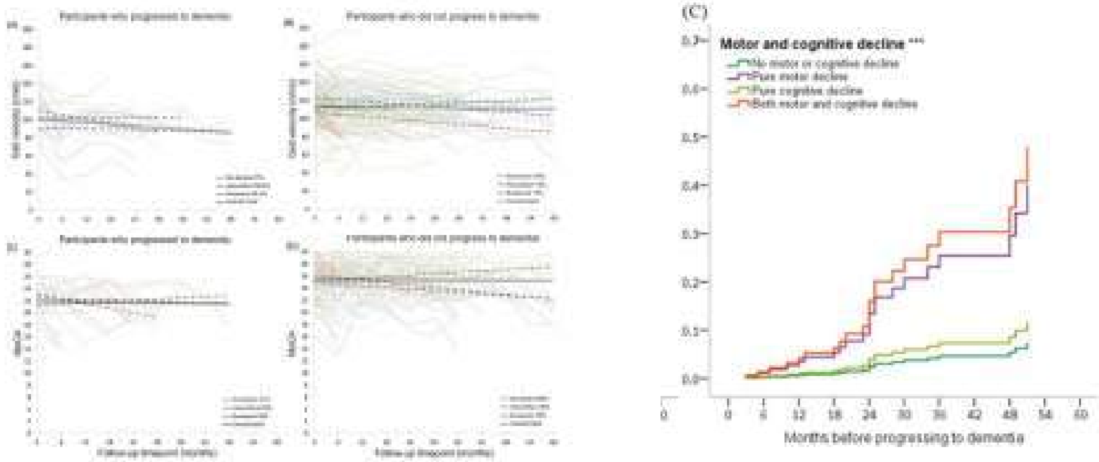
Thank you!!!!

mmontero@uwo.ca

CLINICAL INVESTIGATION

Motor and Cognitive Trajectories Before Dementia: Results from Gait and Brain Study

Manuel Montero-Odasso, MD, PhD, AGSF, Mark Speechley, PhD, Susan W. Muir-Hunter, PT, PhD, Yanina Sarquis-Adamson, PhD, Luciano A. Sposato, MD, MBA, Vladimir Hachinski, MD, DPhil, Michael Borrie, MBBS, Jennie Wells, MD, Alanna Black, MSc, Ervin Sejdić, PhD, Louis Bherer, PhD, Howard Chertkow, MD, and The Canadian Gait and Cognition Network



Summary, so far!

- Cognitive frailty = slow gait + cognitive impairment
- Common brain mechanisms underlie gait and cognitive impairments before dementia
- Identification of common modifiable risk factors for gait, motor and cognitive interaction will help develop targeted interventions to prevent cognitive decline and delay progression to dementia
- **How can we treat these impairments together?**

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69

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

Western

70

CLINICAL MANAGEMENT OF THE OLDER ADULT

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

Manuel Montero-Odasso, MD, PhD, AGSF,[*†‡] *and Mark Speechley, PhD*[*‡]

71

If we purposely target cognition,

can we improve gait & reduce falls?

72

Donepezil Study

Participants took donepezil/placebo for 6 months

Donepezil group had lower number of falls, lower participants ... ls

Come tomorrow to session 16 to learn more!!!

SYMPOSIA SESSION 16

Cognitive Motor Approaches To Assessing and Treating Gait and Falls

Hall 6B, Level 1

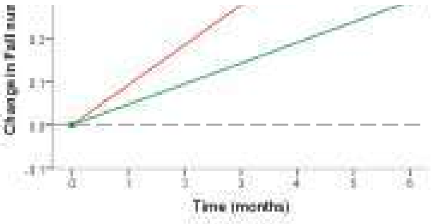
Chair: Devinder Kaur Ajit Singh, Organizing Co-chair, WCFPS 2019

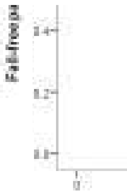
Co-Chair: Dawn Skelton, Professor, Glasgow Caledonian University

1100 – 1120
Motoric Cognitive Risk Syndrome
Joe Verghese, Albert Einstein College of Medicine, United States of America

1120 – 1140
Cognitive Enhancers yo Reduce Falls, What is the Evidence?
Manuel Montero-Odasso, University of Western Ontario, Canada

1140 – 1200
Novel and Emerging Rehabilitation Approaches to Gait / Falls Training
Felicia Ambrose, Burke Rehabilitation Hospital, United States of America





Final Summary

- Cognitive deficits exacerbate falls risk even in “cognitively normal”
- The effect of proven strategies to reduce falls, including **exercises** and **vitamin D**, can be also mediated via cognitive enhancement
- **New Approach: Improve Cognition to Reduce Falls**
  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

Take Home Messages

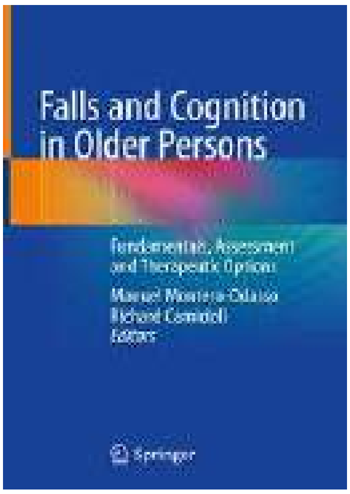
1- Falls risk screening should include assessment of cognitive processes, in particular selective attention, conflict resolution, and dual-tasking

2- Falls prevention strategies should consider intervention components that target cognition, specifically executive function

Thank you!!!!

75

If you want to learn more!



Thank you!!!!

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76

Gait & Brain Team

Parkwood Institute, London ON

Alanna Black	*Shay Nejim*
Frederico Faria	*Yanina Sarquis-Adamson*
Stephanie Cullen	*Nick Bray*
Josh Titus	*Korbin Blue*
Ryota Sakurai	*Susan Muir-Hunter*

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Canadian Consortium on Neurodegeneration in Aging
ONTARIO BRAIN INSTITUTE / INSTITUT ONTARIEN DU CERVEAU

77

Journal of Gerontology: MEDICAL SCIENCES

Effect of Cognitive Remediation on Gait in Sedentary Seniors

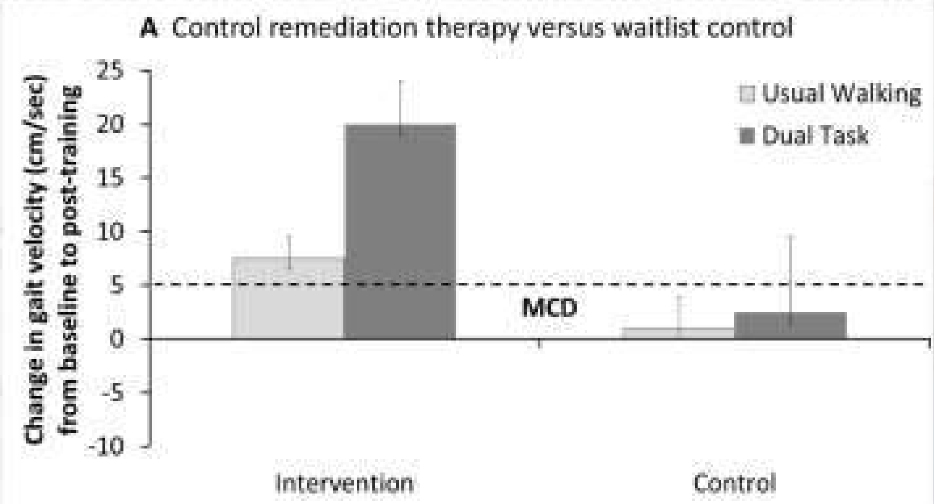
Joe Verghese,[1] Jeannette Mahoney,[1,2] Anne F. Ambrose,[3] Cuiling Wang,[4] and Roee Holtzer[1,2]

RCT

- 24 sessions, 45-60 min each, 3 times/week for 8 weeks
- N= 10 intervention/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 controls (n= 10)

Western

78



79

Journal of Gerontology: MEDICAL SCIENCES
Cite journal as: J Gerontol A Biol Sci Med Sci
doi:10.1093/gerona/glq151

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

Karen Z. H. Li,[1] E. Roudaia,[2] M. Lussier,[3,4] L. Bherer,[3,4] A. Leroux,[5] and P. A. McKinley[6]

- N=20 healthy older adults (76y/o)
- Randomly assigned to attentional training or no-treatment
- 5 (1-hour) sessions x 3 weeks

Transfer effect!

80

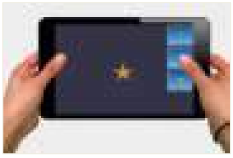
Attentional training method
(Bherer, Kramer, et al., 2005; Erickson et al., 2008)

Cognitive Training

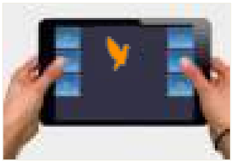
- 30 minutes of single and dual-task blocks
- Task A: celestial bodies
- Task B: Animals
- Adaptive increase in difficulty over sessions

Single tasks

A

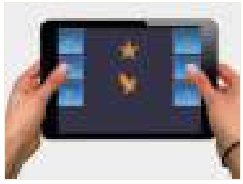


B

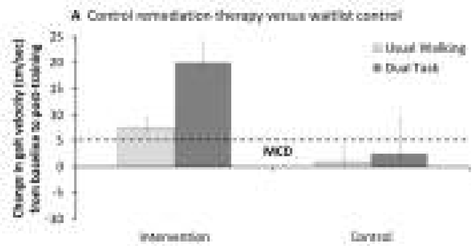


Dual task

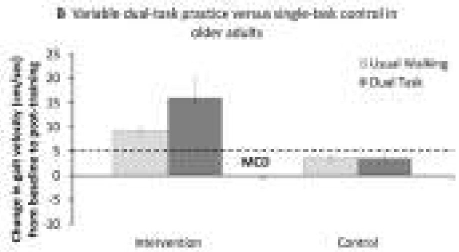
A+B



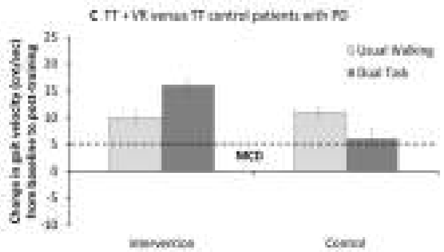
Summary of Interventions Targeting Cognition to Improve Mobility



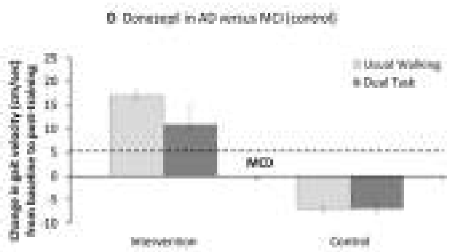
Verghese et al JGMS 2010



Silsupadol et al APMR 2009



Mirelman et al JGMS 2011



Montero-Odasso et al JAGS 2009

J Am Geriat Soc 2012

Final Summary

- Cognitive deficits likely exacerbate falls risk even in those labeled as "cognitively normal"
- The effect of proven strategies to reduce falls, including **exercises** and **vitamin D**, can be also 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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Distinctive expertise in, **motor/cognitive interaction, interventions exercise, gait/physical activity, cognition**

Including 2 Canada Research Chairs

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Quincy Almeida (Laurier U)
Laura Middleton (U of Waterloo)
Manuel Montero-Odasso (Western)
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Karen Li
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Sarah
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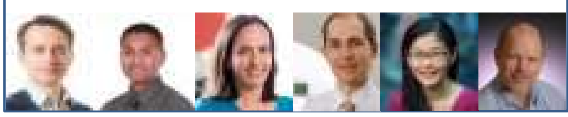
Site leaders



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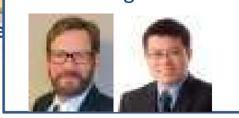

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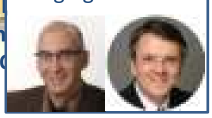

84

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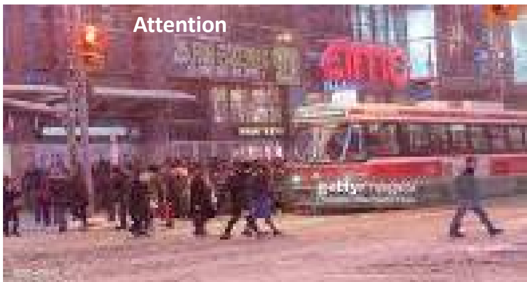
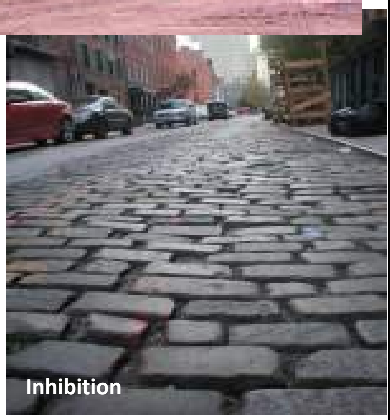




Walking is cognitively demanding!

86

Evidence and Assumptions in Fall prevention

- **Evidence 1**

  Cognitive impairment is a risk factor for falls

- **Assumption 1**

  Falls are not related to cognition when a normal MMSE/MoCA is present

- **Emerging view 1**

  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

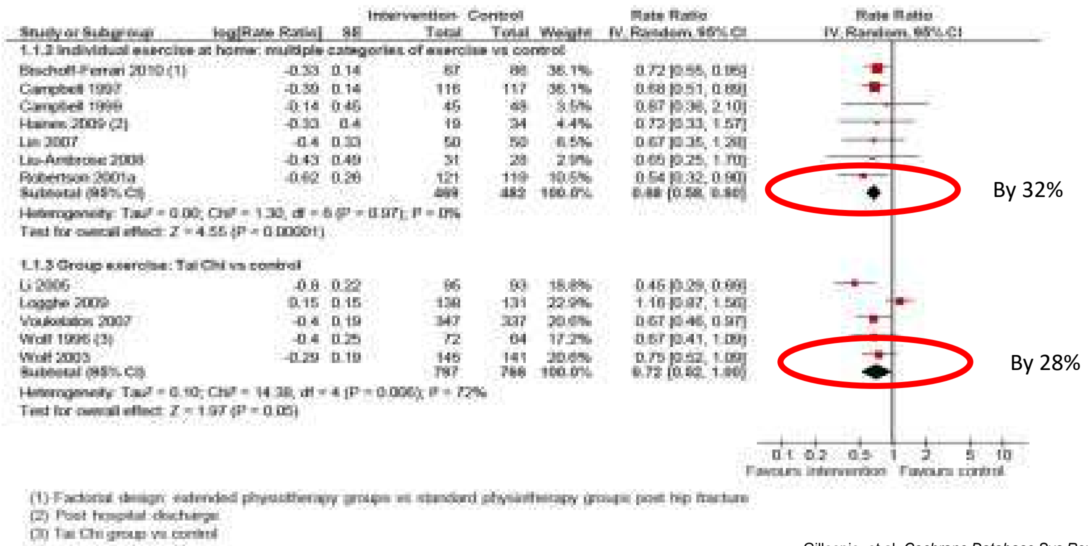
- **Evidence 2**

  Exercise reduces falls

- **Assumption 2**

  Exercise reduces fall due to a physical effect

Results: Exercise Programs to Reduce Falls



Gillespie et al. *Cochrane Database Sys Rev* 2012
www.cochranejournalclub.com

Multi-component Exercise Programs Reduce Falls

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

Gillespie et al. *Cochrane Database Sys Rev* 2012
www.cochranejournalclub.com

Meta-analyses on Exercise to Improve Cognition

- Etnier JL, Salazar W, Landers DM, et al. ***Journal of Sport & Exercise Psychology, 1997;19:249-77***
- Colcombe S, Kramer AF ***Psychol Sci 2003;14(2):125–30***
- Heyn P, Abreu BC, Ottenbacher KJ. ***Arch Phys Med Rehabil 2004;85(10):1694 –704***
- Etnier JL, Nowell PM, Landers DM, et al***. Brain Res Rev. 2006 Aug 30;52(1):119-30***
- Angevaren M, et al. Physical activity and fitness to improve cognitive function. ***COCHRANE Review, 2008***

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

Michelle E. Kelly[a,*], David Loughrey[a], Brian A. Lawlor[a], Ian H. Robertson[a], Cathal Walsh[b], Sabina Brennan[a]

[a] The NEIL Programme, Institute of Neuroscience, Trinity College Dublin, Dublin 2, Ireland
[b] Department of Statistics, Trinity College Dublin, Dublin 2, Ireland

Ageing Research Reviews 16 (2014)

Table 1. *Results for significant moderating variables*

Moderator variable	Effect size	SE	n	p
Overall				
Control	0.164	0.028	96	*
Exercise	0.478[1]	0.029	101	*
Exercisers				
Training characteristics				
Training type				
Combined	0.59[2]	0.049	49	*
Cardiovascular only	0.41	0.037	52	*
Program duration				
Short (1–3 mo)	0.522[2]	0.067	38	*
Medium (4–6 mo)	0.269	0.047	56	*
Long (6+ mo)	0.674[1,2]	0.048	27	*
Session duration				
Short (15–30 min)	0.176	0.089	13	
Moderate (31–45 min)	0.614[1,3]	0.052	24	*
Long (46–60 min)	0.466[1]	0.041	53	*
Participants' characteristics				
Sex				
High female (>50% female)	0.604[2]	0.036	67	*
High male (≥50% male)	0.150	0.055	27	*
Age				
Young-old (55–65)	0.298	0.044	31	*
Mid-old (66–70)	0.693[1,3]	0.056	37	*
Old-old (71–80)	0.549[1]	0.058	33	*

Note. All listed categorical effects were, as a group, reliably different from zero. A superscript 1, 2, or 3 indicates that the effect size was statistically greater (after Bonferroni correction) than the effect size for the 1st, 2nd, or 3rd item, respectively, listed in that category (e.g., a "1,3" superscript means that the value in that cell was statistically greater than the 1st and 3rd listed items in that category). Asterisks indicate which categories were significantly different from zero.

Colcombe & Kramer (2003)

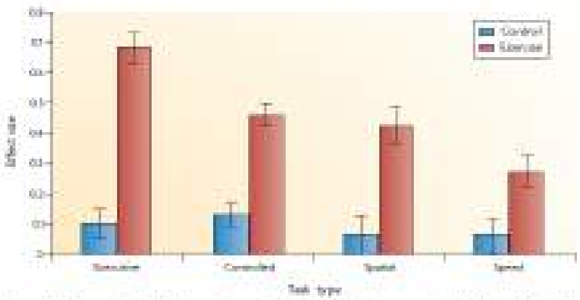


Figure 1 | **Meta-analytic findings of exercise-training effects on cognition in older adults.** The results of a meta-analysis of the effects of fitness training on cognition showed that the benefits of fitness training on four different cognitive tasks were significant. As illustrated in the figure, fitness training has both broad and specific effects. The effects are broad in the sense that individuals in aerobic fitness training groups (represented by the red bars) showed larger fitness training effects across the different categories of cognitive processes illustrated on the x-axis. They are specific in the sense that fitness training effects were larger for some cognitive processes, in particular executive control processes, than for other cognitive processes. Figure reproduced, with permission, from REF. 52 © (2003) Blackwell Publishers.

Otago Home-Based Strength and Balance Retraining Improves Executive Functioning in Older Fallers: A Randomized Controlled Trial

Teresa Liu-Ambrose, PhD, PT,[*†‡] *Meghan G. Donaldson, PhD,*[*§‖] *Yasmin Ahamed, MSc,*[*‡] *Peter Graf, PhD,*[†] *Wendy L. Cook, MD,*[*] *Jacqueline Close, MD,*[**] *Stephen R. Lord, PhD,*[**] *and Karim M. Khan, MD, PhD*[*††]

Table 2. Physiological Falls Risk, Functional Mobility, and Executive Functions at Baseline and 6-Month Follow-Up (N = 52)

Outcome Measures	OEP Group (n = 28) Baseline	OEP Group (n = 28) Six Months	Control Group (n = 24) Baseline	Control Group (n = 24) Six Months
	Mean ± Standard Deviation			
Physiological Profile Assessment z-score	2.0 ± 1.3	1.9 ± 1.2	1.9 ± 1.3	1.9 ± 1.2
Timed Up and Go Test, seconds	14.2 ± 4.6	13.6 ± 4.3	17.4 ± 10.4	18.1 ± 10.5
Trail Making Test Part B, seconds	222.4 ± 200.1	203.1 ± 262.3	224.7 ± 106.4	232.9 ± 127.1
Verbal Digits Backward Test (maximum 14 points)	[illegible]	[illegible]	3.1 ± 1.8	2.8 ± 1.6
Stroop Color-Word Test, seconds	157.6 ± 83.0	137.4 ± 49.5	151.7 ± 44.0	167.2 ± 103.4*

* Significantly different from Otago Exercise Program (OEP) group at P = .05.

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

Liu-Ambrose et al. *J Am Geriatr Soc* 2008

Evidence and Assumptions in Fall prevention

- **Evidence 2**

  Exercise reduces falls

- **Assumption 2**

  Exercise reduces fall due to a physical effect

- **Emerging view 2**

  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 3**

  Vitamin D supplementation may reduce falls

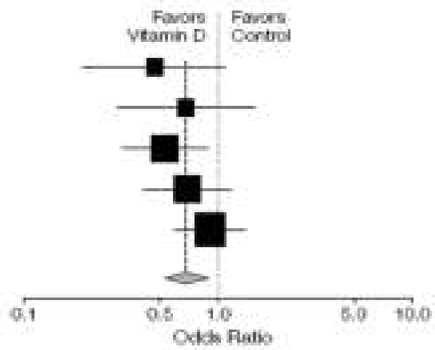
- **Assumption 3**

  This effect is mediated by a “muscle effect”

Effect of Vitamin D on Falls A Meta-analysis

Primary Analysis

Source	Odds Ratio (95% CI)
Pfeifer et al,[11] 2000	0.47 (0.20-1.10)
Bischoff et al,[12] 2003	0.68 (0.30-1.54)
Gallagher et al,[17] 2001	0.53 (0.32-0.88)
Dukas et al,[18] 2004	0.69 (0.41-1.16)
Graafmans et al,[19] 1996	0.91 (0.59-1.40)
Pooled (Uncorrected)	0.69 (0.53-0.88)



- 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.

Bischoff-Ferrari et al. *JAMA. 2004*

Vitamin D Supplements

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

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

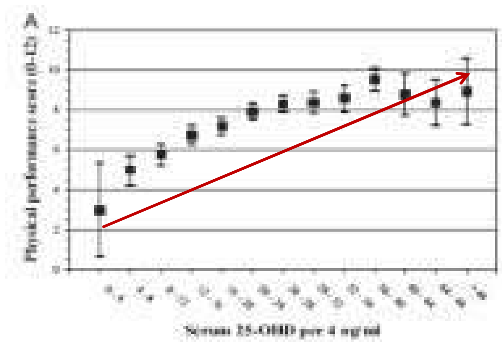
Gillespie LD et al. *Cochrane Database Sys Rev* 2012
Cameron ID et al. *Cochrane Database Sys Rev* 2012

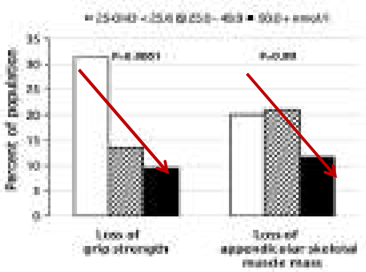
Vitamin D and Muscle function

LASA Study

- 1008 older adults
- 3y follow-up

Higher vitamin D levels predicted physical performance (SPPB)





Vitamin D deficiency predicted loss muscle mass and strenght

Visser et al. *JCEM* 2003

Vitamin D and Brain Function

OPEN ACCESS Freely available online PLOS ONE

Vitamin D and Caudal Primary Motor Cortex: A Magnetic Resonance Spectroscopy Study

Cedric Annweiler[1,2,3]*, Olivier Beauchet[2], Robert Bartha[3], Vladimir Hachinski[4], Manuel Montero-Odasso[1], on behalf of the WALK Team (Working group Angers-London for Knowledge)

1 Gait and Brain Lab, Lawson Health Research Institute, Parkwood Hospital, The University of Western Ontario, London, Ontario, Canada, 2 Division of Geriatric Medicine, University Hospital; Memory Clinic; UPRES EA 4638, University of Angers, Angers, France, 3 Robarts Research Institute, the University of Western Ontario, London, Ontario, Canada, 4 Department of Clinical Neurological Sciences, University Hospital, the University of Western Ontario, London, Ontario, Canada

Abstract

Background: Vitamin D is involved in brain physiology and lower-extremity function. We investigated spectroscopy in a cohort of older adults to explore the hypothesis that lower vitamin D status was associated with impaired neuronal function in caudal primary motor cortex (cPMC) measured by proton magnetic resonance spectroscopic imaging.

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

Cedric Annweiler, Manuel Montero-Odasso, David J. Llewellyn, Stéphane Richard-Devantoy, Gaetano Duque and Olivier Beauchet

Low Vitamin D/ Vitamin D deficiency is associated with:

1: Low cognitive function

2: Brain structural changes

Effect of Vitamin D Supplementation on Muscle Strength, Gait and Balance in Older Adults: A Systematic Review and Meta-Analysis

Susan W. Muir, PhD, and Manuel Montero-Odasso, MD, PhD, AGSF*†‡*

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.

demonstrated, although further evaluation is recommended. J Am Geriatr Soc 59:2291–2300, 2011.

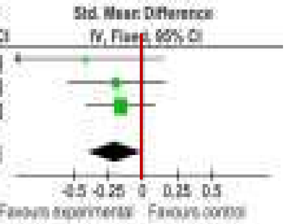
Key words: vitamin D; aged; systematic review; randomized controlled trials; muscle strength; balance; gait

Muir & Montero-Odasso J Am Geriatr Soc 2011

Balance Sway

Study or Subgroup	Vitamin D supplementation Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Burout 2006	119.8	38.3	24	134.7	31.8	24	11.4%	-0.42 [-0.99, 0.16]
Dhesi 2004	0.0899	0.046	62	0.0999	0.057	61	29.8%	-0.19 [-0.55, 0.16]
Pfeifer 2000	81	32	121	88	30	121	58.8%	-0.16 [-0.41, 0.09]
Total (95% CI)			207			206	100.0%	-0.20 [-0.38, -0.01]

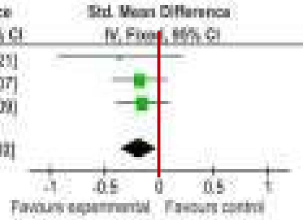
Heterogeneity: $Chi^2 = 0.64$, $df = 2$ ($P = 0.73$); $I^2 = 0\%$
Test for overall effect: $Z = 2.02$ ($P = 0.04$)



Timed Up & Go Test

Study or Subgroup	Vitamin D supplementation Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Burout 2008	13.8	2.5	24	15.2	4.7	24	8.6%	-0.37 [-0.94, 0.21]
Pfeifer 2009	7.5	3.4	121	8.2	5.1	121	44.0%	-0.18 [-0.44, 0.07]
Zhu 2010	8.1	3.9	129	9	7	132	47.4%	-0.16 [-0.40, 0.09]
Total (95% CI)			274			277	100.0%	-0.19 [-0.35, -0.02]

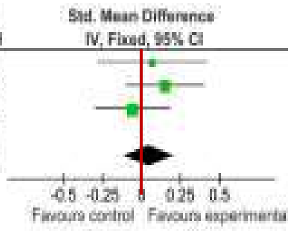
Heterogeneity: $Chi^2 = 0.43$, $df = 2$ ($P = 0.81$); $I^2 = 0\%$
Test for overall effect: $Z = 2.19$ ($P = 0.03$)



Grip Strength

Study or Subgroup	Vitamin D supplementation Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Dhesi 2004	204	92.4	62	198	79.7	61	19.7%	0.07 [-0.28, 0.42]
Pfeifer 2009	236	75	121	224	83	121	38.6%	0.15 [-0.10, 0.40]
Zhu 2010	176.6	49	129	179.6	54	132	41.7%	-0.06 [-0.30, 0.18]
Total (95% CI)			312			314	100.0%	0.05 [-0.11, 0.20]

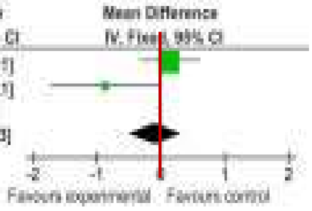
Heterogeneity: $Chi^2 = 1.39$, $df = 2$ ($P = 0.50$); $I^2 = 0\%$
Test for overall effect: $Z = 0.60$ ($P = 0.55$)



Lower Extremity Muscle Strength

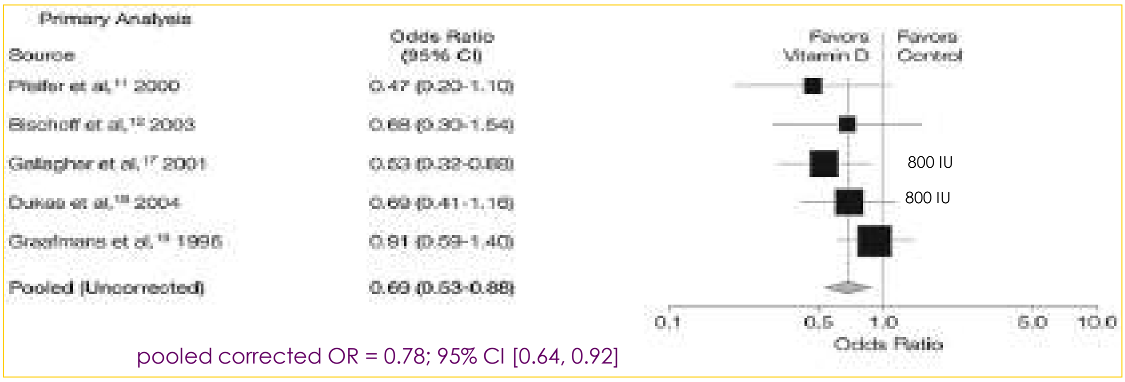
Study or Subgroup	Vitamin D supplementation Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Brunner 2008	-2.49	5.81	1194	-2.64	5.69	1170	77.5%	0.15 [-0.31, 0.61]
Grady 1991	0.64	1.9	50	1.51	2.4	48	22.5%	-0.87 [-1.73, -0.01]
Total (95% CI)			1244			1218	100.0%	-0.08 [-0.49, 0.33]

Heterogeneity: $Chi^2 = 4.19$, $df = 1$ ($P = 0.04$); $I^2 = 76\%$
Test for overall effect: $Z = 0.38$ ($P = 0.70$)



Forest Plot Meta-analysis: Effect of vitamin D on falls

Bischoff-Ferrari HA et al.; JAMA 2004



Cochrane review on falls 2009 (13 studies)

- No significant reduction in fall rates or risk
- Subgroup analysis showed significant reduction in fall rate of 43% if participants had low Vitamin D levels at recruitment

Recent Vitamin D Data

- **2017 JAMA** meta-analysis of 33 RCTs comparing "calcium, vitamin D or combined calcium and vitamin D" in community-dwelling adults aged 50+ reports no effect on fracture incidence *(Zhao J-G, JAMA 2017;318:2466)*
- **2017 Lancet Diab Endocr**: Primary RCT of 100,000 IU monthly oral D_3 vs placebo did not reduce falls or fracture incidence despite good adherence and tolerance *(Khaw K-T, Lancet Diab Endocr 2017;5:438)*
- **2017 JAMA**: Primary RCT of 2000 IU/d of vitamin D3 and 1500mg/d of calcium for 4y in women aged 55+ did not significantly reduce cancer outcomes (HR 0.70; 95% CI 0.47 to 1.02, p=0.06) *(Lappe J, JAMA 2017; 317(12):1234)*
- **2018 Lancet Diab Endocr**: Meta-analysis and trial-sequential analalysis of vitamin D studies finds intervention "does not prevent fractures or falls, or have clinically meaningful effects on bone mineral density" *(Bolland, Lancet Diab Endocr 2018)*.
- **2018 NEJM** VITAL study (fracture data not yet available) D_3 2,000 IE daily did not result in a lower incidence of invasive cancers or cardiovascular events. *(Manson JE, NEJM 2018)*

Evidence and Assumptions in Fall prevention

- **Evidence 3**

  Vitamin D supplementation may reduce falls

- **Assumption 3**

  This effect is mediated by a “muscle effect”

- **Emerging View 3**

  Vitamin D supplementation (>800IU/day) improves balance and neuromuscular function, but not muscle strength, mainly in those with deficiency

  Is this a brain effect?

Gait & Brain Study - Design and follow-up

N = 130
(1st wave
2007-2010)

→

N = 270
(2^{nd} wave
2010-ongoing)

↓

Total Since 2007
N = 414
MCI=211, SCI=115,Controls=88

↓

N = 250
in follow- up

N = 57 progressed to dementia
N = 77 drop out
N = 16 deceased

Design and Participants:
- Ongoing cohort, up to 15 years
- Seniors (>65 y/o) with SCI, MCI, Cognitive Healthy controls
- No frailty, no dementia at baseline, able to ambulate independently

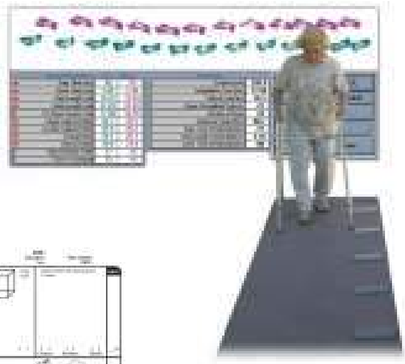
Mean follow-up: 34 months
Range follow up: 6 months to 78 months

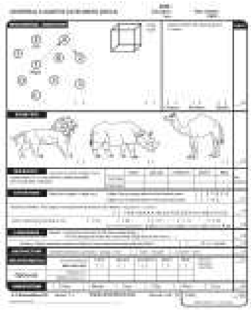
Bi annual assessments:
- Battery of Cognitive tests
- Gait (electronic walkway), Balance, Blood tests, MRIs every 18 mo

Montero-Odasso M, et al. BMC Geriatr. 2009 Sep 1;9:41
Montero-Odasso M et al. *J. Am Geriatr Soc* 2012

Gait & Brain Study – Methods and Assessments

- **Gait performance**
  - Electronic walkway (Zeno Mat® and GAITRite® System)
    - Gait velocity (cm/s)
    - Dual-task gait test
- **Cognitive Assessments:**
  - MoCA, MMSE , CDR, Neuropsy battery
- **Brian Magnetic Resnce Imaging:**
  - Structural, Spectrospcopy, Tension Diffusion, and Resting State



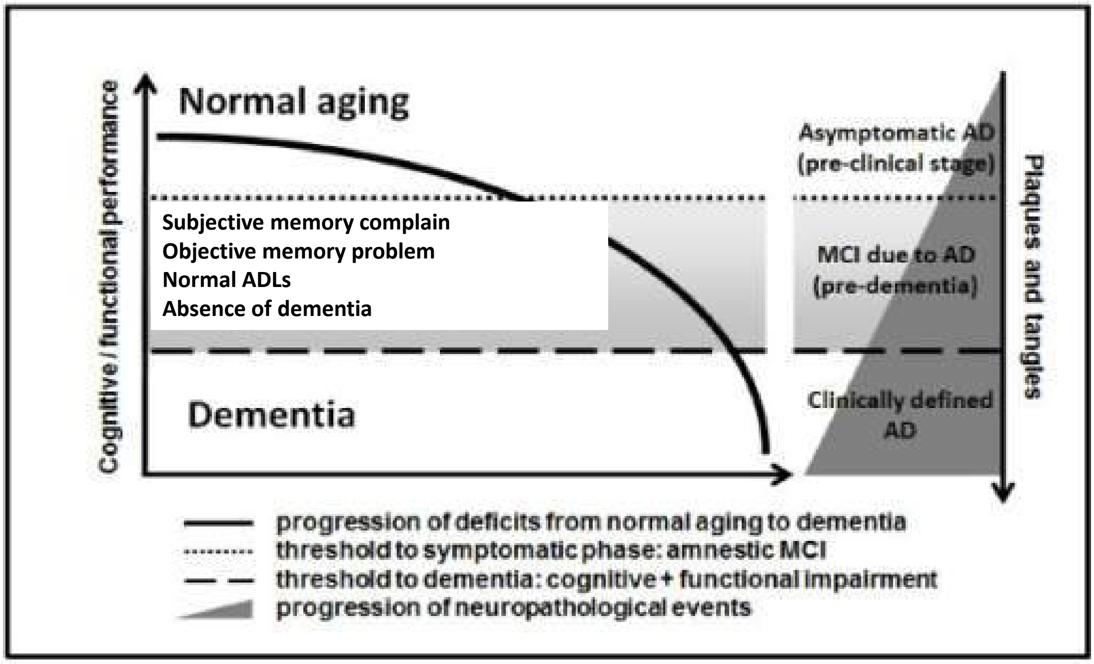


107

Mild Cognitive Impairment & Gait Velocity (GV)

Montero-Odasso M, Bergman H, Phillips NA, Wong CH, Sourial N, Chertkow H. BMC Geriatr. 2009 Sep 1;9:41.

108



Petersen RC. Mild cognitive impairment as a diagnostic entity. J Intern Med. 2004 Sep;256(3):183-94.

109

Mild Cognitive Impairment as a Predictor of Falls in Community-Dwelling Older People

Kim Delbaere, Ph.D., Nicole A. Kochan, Ph.D., Jacqueline C.T. Close, M.D., Jasmine C. Menant, Ph.D., Daina L. Sturnieks, Ph.D., Henry Brodaty, D.Sc., Perminder S. Sachdev, M.D., Stephen R. Lord, D.Sc.

TABLE 3. Univariate Logistic Regression Output of Factors Associated With (Multiple or Injurious) Falls During the 1-Year Follow-up Period in 419 Participants

	OR (95% CI)[a]	OR (95% CI)[b]	OR (95% CI)[c]
MCI (yes)	1.72 (1.03–2.89)[d]	1.63 (0.97–2.75)[e]	1.54 (0.90–2.63)
Amnestic MCI (yes)	1.18 (0.39–2.99)	1.12 (0.40–3.12)	0.85 (0.28–2.57)
Nonamnestic MCI (yes)	1.98 (1.11–3.55)[d]	1.83 (1.02–3.29)[d]	1.82 (1.00–3.31)[d]
Attention domain composite (z score)	1.10 (0.88–1.37)	1.03 (0.82–1.29)	1.02 (0.81–1.28)
Language domain composite (z score)	1.23 (0.98–1.56)[e]	1.19 (0.94–1.52)	1.17 (0.92–1.50)
Executive function domain composite (z score)	1.27 (1.02–1.59)[d]	1.22 (0.98–1.53)[e]	1.23 (0.97–1.55)[e]
Memory domain composite (z score)	0.94 (0.76–1.18)	0.92 (0.73–1.15)	0.90 (0.71–1.13)

Notes: 95% CI: 95% confidence interval; OR: odds ratio.
[a]The output of univariate logistic regression analyses ($df = 1$) after controlling for age and education.
[b]The output of univariate logistic regression analyses ($df = 1$) after controlling for age, education, and PPA.
[c]The output of univariate logistic regression analyses ($df = 1$) after controlling for age, education, PPA, WHODAS, and medication use.
[d]$p \leq 0.05$.
[e]$p \leq 0.10$.

110

Gait Assessment

Gait Velocity was measured as the time taken to walk 6 meters.
Subjects were instructed to perform 3 walking tasks:

Gait Test	Pace	Dual-Task
Usual Gait (uGV)	Usual and comfortable pace	None
Verbal Gait (vGV)	Usual pace, participant can be prompted	Naming animals
Counting Gait (cGV)	Usual pace, participant can be prompted	Counting backwards from 100

6 m

10 m

1.Montero Odasso M et al. J Nutr Health Aging. 2004;8(5):340-3.
2.Montero Odasso M, Schapira M, Duque G et al. BMC Geriatrics, 2005. *5:15*

Gait & MCI

<u>Hypotheses</u>

1. Gait is affected by specific cognitive domains in MCI

2. Dual-task cost is associated to specific cognitive domains

<u>Methods</u>

60 participants with MCI
mean age 75.2 y/o

Associations between performance in cognitive tests and GV under single and dual-task (multivariate logistic regression adjusted by age, sex and history of falls)

Cognitive Tests	Usual GV *p*-value	Verbal GV *p*-value	Count GV *p*-value
MoCA (memory)	0.37	0.75	0.77
TMT A (attention)	0.61	0.24	0.10
TMT B (executive)	0.13	0.06	0.04*
TMT B-A (pure executive)	0.18	0.12	0.09
Digit Symbol (speed)	0.361	0.065	0.06
LNS (working memory)	0.009*	0.017*	0.017*

Montero-Odasso M, Bergman H, Phillips NA, Wong CH, Sourial N, Chertkow H. BMC Geriatr. 2009 Sep 1;9:41.

* Statistically significant

Gait & MCI

Associations between performance in cognitive tests and GV under single and dual-task (multivariate logistic regression adjusted by age, sex and history of falls)

<u>Hypotheses</u>

1. Gait is affected by specific cognitive domains in MCI

2. Dual-task cost is associated to specific cognitive domains

<u>Methods</u>

60 participants with MCI

mean age 75.2 y/o

MMSE>26

MoCA<26

Cognitive Tests	Usual GV *p*-value	Verbal GV *p*-value	Count GV *p*-value
MoCA (memory)			
TMT A (attention)			
TMT B (executive)			0.04*
TMT B-A (pure executive)			
Digit Symbol (speed)			
LNS (working memory)	0.009*	0.017*	0.017*

* Statistically significant

Montero-Odasso M, Bergman H, Phillips NA, Wong CH, Sourial N, Chertkow H. BMC Geriatr. 2009 Sep 1;9:41.

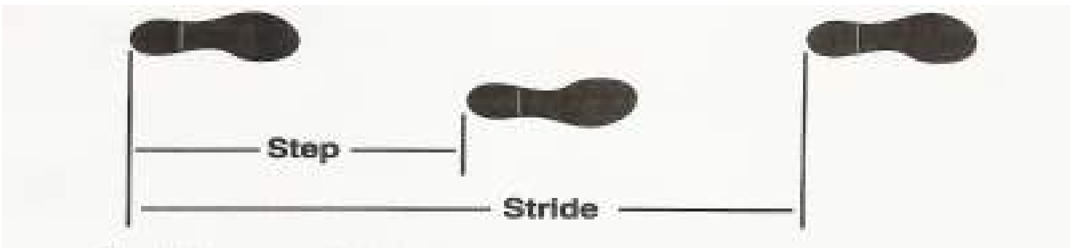
113

Dual-tasking in MCI: first results

- Cognitive correlates of gait are complex and NOT limited to attention.
- Association between cognition and gait varies as a function of walking condition
- Working memory was constantly associated with gait slowing
- Possible shared brain networks of cognitive and motor function

114

Mild Cognitive Impairment & Gait Variability (Gva)



Step length
Stride length
Velocity
Cadence
Cycle time
Stance time
Swing time
Double support time

Walking is fundamental

Unrecognized Clinical Reality

An 86 year old man is brought to clinic for several years history of decline. He has withdrawn from life and spends all his time sitting in a chair dozing. He has had several recent falls.

PMH: II Diabetes, HTN

Meds: HCTZ, glipizide

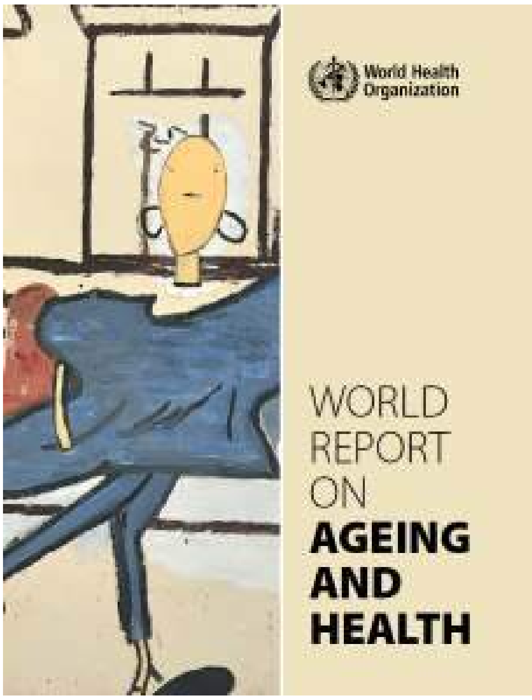
Exam shows deficits in cognition, construction, sequencing, recall and language. He has a slow shuffling gait and increased tone. His affect is flat, he states that life is not worth living.

He is diagnosed with dementia and depression and given a cane.

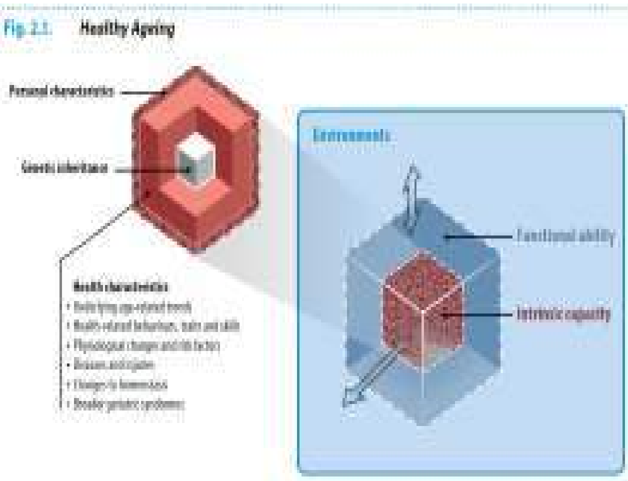
Brain-related gait abnormalities in older people are often ignored or attributed to "normal aging".

"senile gait"

World Health Organization



119



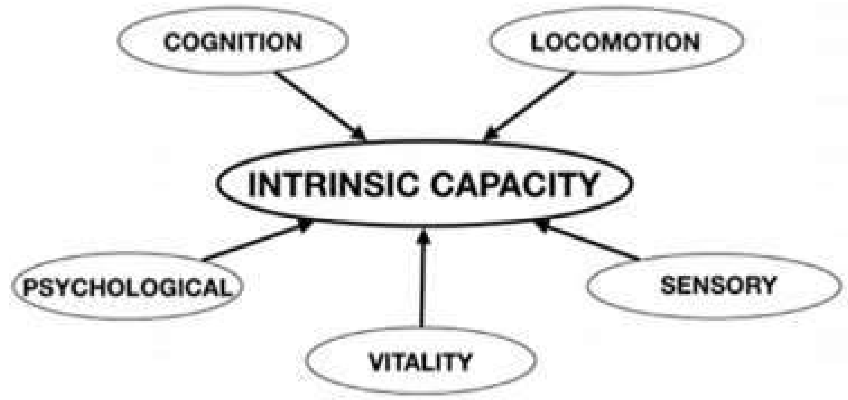
Healthy Ageing: the process of developing and maintaining the functional ability that enables well-being in older age.

It is made up of the **intrinsic capacity** of the individual, relevant **environmental characteristics** and the interactions between the individual and these characteristics.

Intrinsic capacity: composite of all the physical and mental capacities of an individual.

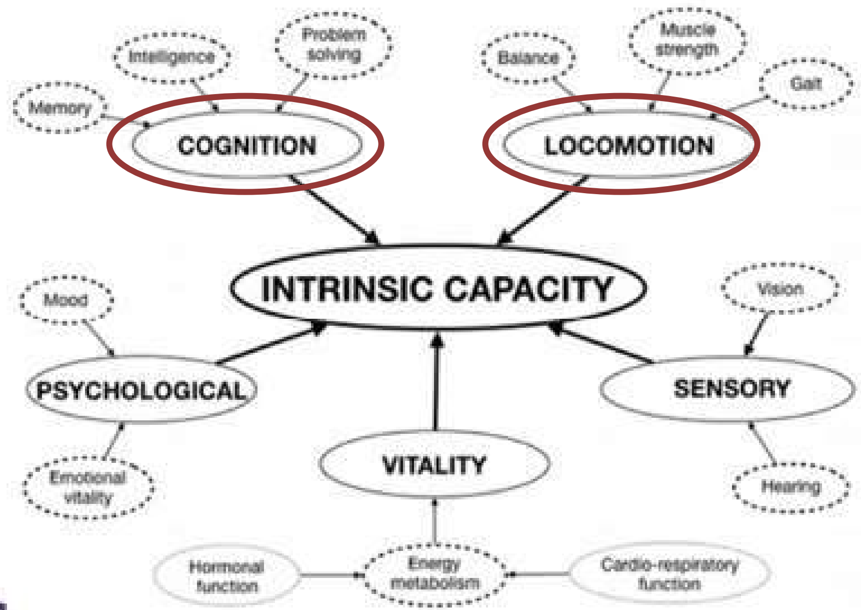
Environments: factors in the extrinsic world that form the context of an individual's life.

120



Cesari M et al. *J Gerontol A Biol Sci Med Sci* 2019

121



Cesari M et al. *J Gerontol A Biol Sci Med Sci* 2019

122

What about in the clinic?

123

La parte de imagen con el identificador de relación rId3 no se encontró en el archivo.

La parte de imagen con el identificador de relación rId4 no se encontró en el archivo.

La parte de imagen con el identificador de relación rId5 no se encontró en el archivo.

124

Single and dual task gait are equivalent in predicting falls risk

- Single and dual task were equivalent in predicting falls
- No change in subgroups (e.g slow vs fast walkers)
- Types of secondary cognitive tasks not important

Menant J   et al Ageing Res Rev 2014

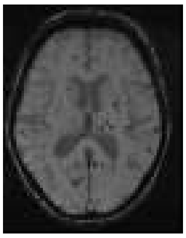
Clinical observation

Possible underlying mechanisms of cognition, gait & falls

Cerebral small vessel disease

Subcortical Infarcts

White matter hyperintensities (WMH)

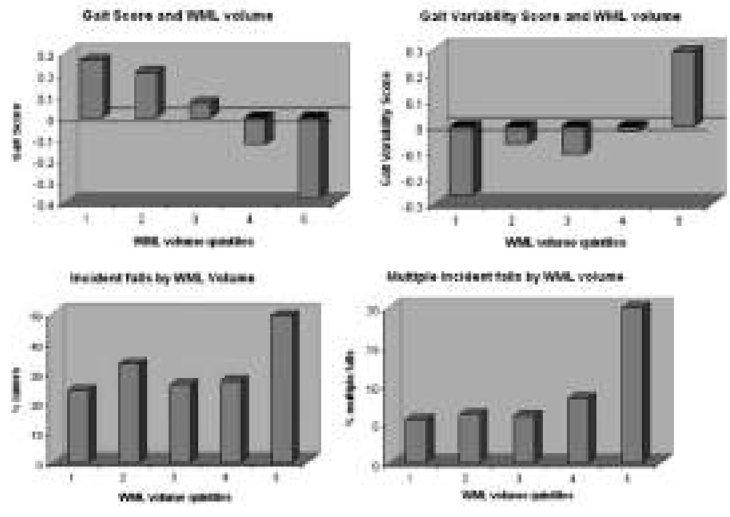


Microbleeds

Healthy brain

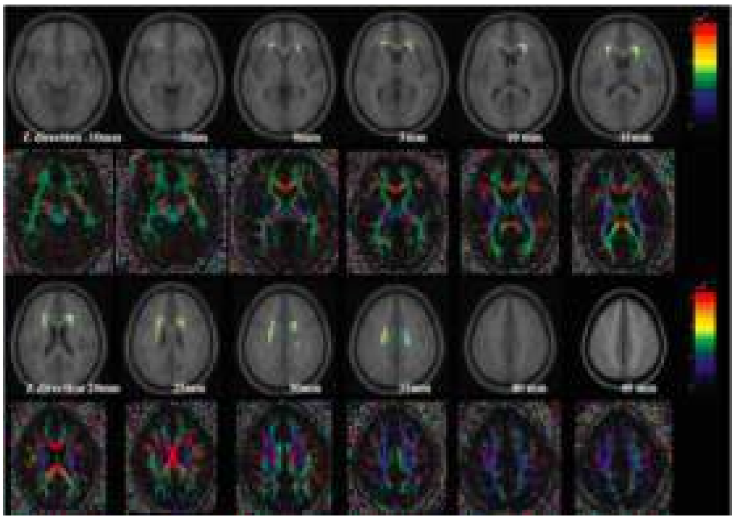
Atrophic brain

WMH are associated with cognition (EF and processing speed)[1]
WMH are associated with gait[2,3], gait variability and falls[2,4]



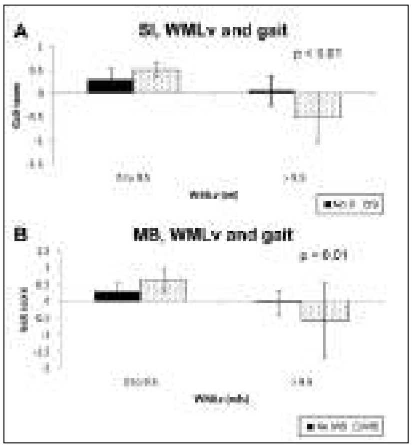
1 Debette BMJ 2010
2 Srikanth Stroke 2009;40;175-180
3 Callisaya ML et al 61:2013
4 Callisaya ML J Gerontol A Biol Sci Med Sci 2015

Bilateral frontal and periventricular WMH are associated with poorer gait



Srikanth V et al Annals Neurology 2010

Subcortical infarct are associated with cognition (EF & processing speed)
Subcortical infarcts are associated with gait[1] and falls[2]

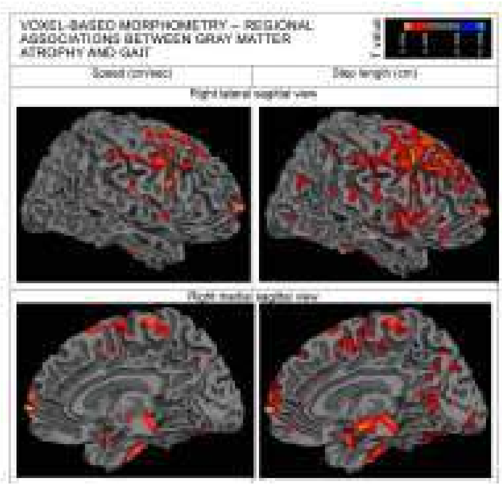


TASCOG and MAS	Multiple falls	
Subcortical infarcts	RR	95% CI
0	1.00	
1	1.15	0.69, 1.90
2	1.15	0.57, 2.31
≥3	1.89	1.03, 3.46

Highest infarct probability: frontal, subcortical (claustrum, putamen)

1 Choi P..Callisaya ML...Srikanth Stroke 2012
2 Callisaya ML...K. Delbaere Int J of stroke 2014

Lower brain volume in multiple areas is associated with gait speed (step length)



Attention/cognitive control
- prefrontal, insula, temporal lobe, subcortical nuclei, limbic

Gait initiation and regulation
- basal ganglia, Supplementary motor area (SMA)

Execution
- premotor, SMA

Sensory
- parietal, precuneus, thalamus, occipital, cuneus

Balance
- cerebellum

Consistent with the notion that gait requires the complex interaction of distributed brain cortical networks

Callisaya ML ....Srikanth VL PLOS ONE 2014
Callisaya ML Brain Structural Change and Gait Decline: A Longitudinal Population-Based Study JAGS 61:2013

131

Disruption of frontal-subcortical circuits

Motor circuit	Cognitive	Apathy	Disinhibition
Primary motor, SMA, premotor	Dorsolateral prefrontal	Medial frontal	Orbital frontal
Putamen	Caudate	Nucleus accumbens	Caudate
Globus pallidus	Globus pallidus	Globus pallidus	Globus pallidus
Thalamus	Thalamus	Thalamus	Thalamus

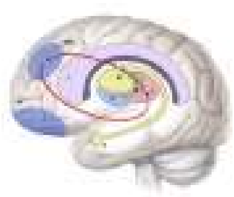


Figure adapted from Bonelli R Translational Research 2007

132

What scope do we have for interventions (non-pharmacological)

Osteoporosis

Osteo-cise[1]

- High-challenge balance exercises
- Moderate impact weight-bearing (e.g., step-ups or mini jumps).
- High speed ("power training"), with a focus on the muscles around the hips

Vascular risk factors

- Physical activity – aerobic/resistance
- Blood pressure management
- Diet
- Weight loss

[1]Gianoudis J, …Daly RM. J Bone Miner Res. 2013 Jun

Balance exercise

Exercise to prevent falls in older adults: an updated systematic review and meta-analysis

Summary/conclusions Exercise as a single intervention can prevent falls in community-dwelling older people. Exercise programmes that challenge balance and are of a higher dose have larger effects. The impact of exercise as a single intervention in clinical groups and aged care facility residents requires further investigation, but promising results are evident for people with Parkinson's disease and cognitive impairment.

Br J Sports Med. 2016 Oct 4. pii: bjsports-2016-096547. doi: 10.1136/bjsports-2016-096547.

135

Weight Bearing Exercise for better balance (WEBB)

1. Movement of the centre of mass,
2. Narrowing of the base of support
3. Minimising upper limb support

Prof Catherine Sherrington et al

The LIFE principles of improving your balance are:

1. Reduce your base of support
2. Shift weight to the limits of sway
3. Shift weight from foot to foot
4. Stepping over objects
5. Turning and changing direction

NoFalls

Randomised factorial trial of falls prevention among older people living in their own homes

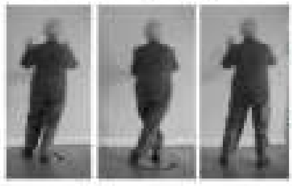
Lesley Day, Brian Fildes, Ian Gordon, Michael Fitzharris, Harold Flamer, Stephen Lord

NoFalls program. These emphasise:

- muscle extensibility, and to a lesser degree, joint flexibility
- strength of muscles critical for posture and balance
- proprioception (through the use of rockerboards)
- visual and vestibular stimulation (eye tasks)
- reaction time (rockerboards and group work)
- relearning the elements of a balance task.

13 Front-to-Back Balance

17 Balance Recovery Sideways



137

137

What makes a person look old?

- Slow Gait
- Mental Slowing

138

Prevalence of falls

Community setting

- + 65 yrs: 28-35% at least one fall over one year
- + 75 yrs: 32-42%
  - between 10 and 31% are recurrent fallers

with dementia: up to 66%

- Alzheimer's disease: 47%
- vascular dementia: 47%
- Lewy body dementia: 77%
- Parkinson's disease dementia: 90%

Masud et al, Age Ageing 2001; Milisen et al, TGG 2004; CBO/NVKG guideline 2004; Kannus et al, Lancet 2005; Allan et al, PLoS 2009

Falls & Fall-re

Group: a Call t

Manuel Montero-Odasso, MD

[1] *Division of Geriatric Medicin*

[2] *Division of Geriatric Medicin*

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DOI: http://dx.doi.org/10.5770/

1. A desire to eradicate the term mechanical fall.(5)
2. There was an identified need for clear and accessible resources on fall prevention for busy clinicians. This could take the form of updated fall prevention guidelines for primary care physicians and easy-to-find material on, for example, the CGS website about falls and fall prevention.
3. The observation that syncopal falls are under-recognized and undertreated.
4. There were a number of comments made about exercise. There was uncertainty on how to prescribe exercise to prevent falls and who should participate in a fall prevention exercise program. Should all persons above a certain age (e.g., 65 years or older) be encouraged to participate in an exercise program (a reasonable suggestion, given the 30% fall rate in this age group), or should it be the subset of older adults with an elevated risk for a fall injury? What type of exercise program should be recommended? Who can be advised to exercise on their own? Who should attend a supervised program at sites such as senior centres or gyms? Who would require supervision, at least initially, by a health professional (e.g., physiotherapist)?
5. Are there valid, reliable, and practical clinical screening tests that should be used to identify high-risk populations in a variety of settings?
6. How to deal with falls in ERs?
7. How early should fall prevention strategies start? 40s? 50s? Is it too late when individuals are older?

Gaps Identified: Falls in Cognitively Impaired

- Why are falls so common in the cognitively impaired?
- Why does fall prevention not work in this population?
- Are we missing a treatment component?

Western

141

Age and Ageing (1978), 7, Supplement

ARE FALLS A MANIFESTATION OF BRAIN FAILURE?

B. Isaacs

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.

Western

142