Canadian Gait & Cognition Network

Presented by Manuel Montero-Odasso MD, PhD, AGSF, FRCPC
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- No conflicts of interest
Research Team

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Platform 4 – Bio-samples: Dr. R. Dixon (University of Alberta)

Theme 3 - KT: Dr. K. Rockwood (Dalhousie University)
What makes a person look old?

- Slow Gait
- Mental Slowing
- Low Mood
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 Beuchet, MD, PhD,§ and Jeffrey M. Hausdorff, PhD## *

Motor & cognitive decline collide

- Gait is not also automatic and relies on cognition
- Motor/Gait are a window to understand cognition and other brain functions
- The shared mechanisms are not completely understood
Gait / motor dysfunction

AGE  NEURODEG  VASCULAR  MOOD

DEMENTIA & FALLS & FRAILTY
Mobility and Cognition in Seniors. Report from the 2008 Institute of Aging (CIHR) Mobility and Cognition Workshop

Manuel Montero-Odasso, MD, PhD, AGSF, FRCPC, Louis Bherer, MPS, PhD, Stephanie Studenski, MD, MPH, AGSF, Karen Gopaul, MSc, Afiu Oteng-Amoako, OD, MPH, MSc, Sarah Woolmore-Goodwin, MSc, Paul Stoole, PhD, Jennie Wells, MD, FRCPC, FACPA, Timothy Doherty, MD, PhD, FRCPC, Aleksandra A. Zecevic, PhD, David Galinsky, MD, R. Jane Rylett, PhD, FCAHS, Jeffrey Jutai, PhD, Susan Muir-Hunter, PT, PhD, Mark Speechley, PhD, Richard Camicioli, MD, FRCPC

1. Cognition and mood are key contributors of the age associated mobility decline.

2. Cognition and Mobility need to be seen as combined clinical/research entity rather than separate problems.

3. Research in mobility should incorporate measures and outcomes related to cognition and vice versa.

4. Common language and common standardized assessments between researchers in the fields of mobility and cognition are needed. Evidence-based findings must be standardized.

5. Earlier detection, intervention, and assessment of cognitive and mobility decline in seniors are necessary.

6. Gait velocity and dual-task gait tests can be used as instruments to detect early changes in cognitive and mobility decline. Further consensus in measurements is needed.

7. The interaction between neuromuscular and brain function in combination with sarcopenia needs to be better explored to understand challenges to mobility in later life.

8. Interventions should have targets not only in particularly structural brain changes after exercises intervention, but also across the bio-psycho-social domain.

9. Future research that uses a unified approach of physical performance measurements, cognitive measures, and neuroimaging is needed and may be most feasible through the effective collaboration across disciplines.
How do we test the Gait and Cognition relationship?
DUAL TASK PARADIGM: “Walking While Talking”

Single-Task Gait Example

Dual-Task Gait Example (Serial 7s)

Dual task cost \[= \frac{Single\ gait - Dual\ task\ gait}{Single\ gait} \times 100\] = 30%
Dual-Task Cost

Is associated with…

1. Falls
2. Cognitive decline
3. Mortality
4. Dementia

Clinical applicability?
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
Goals of the CCNA Gait and Cognition Team

Developing Understanding

- Develop tools and assessments in cognition & motor interactions
- Characterize the “Motor Signature” of cognitive decline as a biomarker of neurodegeneration

Applying Understanding

- Advancement of diagnostic and research tools
- Advance therapeutic strategies
- Explore novel interventions combining physical exercise, cognitive training and Vitamin D supplementation

SYNERGIC Trial
2015 CCNA Gait and Cognition Team

Distinctive expertise in exercise interventions gait/physical activity cognition

Including 2 Canada Research Chairs

Bill McIlroy (U of Waterloo/Toronto)
Quincy Almeida (Laurier U)
Laura Middleton (U of Waterloo)
Manuel MonteroOdasso (Western)
Susan Muir-Hunter
Akshya Vasudev
Amer Burham
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International advisory board
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Joseph Verghese
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Olivier Beauchet

Louis Bherer (U Montreal)
Julien Doyon (U de Montreal)
Karen Li (Concordia U)
Jose Morais
Sarah Fraser (U of Ottawa)
“The results of the 2015 Consensus about testing”

- Core set of measures

<table>
<thead>
<tr>
<th>Proposed Core-Set of Measures</th>
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<tbody>
<tr>
<td><strong>Mobility measures</strong></td>
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<tr>
<td>Gait velocity (normal and fast pace)</td>
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<tr>
<td>Dual-task gait (velocity)</td>
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<tr>
<td>Gait variability</td>
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<tr>
<td>Timed Up and Go</td>
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<td>SPPB</td>
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- Minimum set of measures

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Gait as a biomarker of cognitive decline

Aβ: identified by CSF Aβ42 or PET amyloid imaging. Tau-mediated neuronal injury and dysfunction: identified by CSF tau or fluorodeoxyglucose-PET. Brain structure: measured by use of structural MRI. Aβ=β-amyloid. MCI=mild cognitive impairment.
Gait & Brain Health Program Map and Projects

Objectives
1. Develop understanding of Gait & Cognition & Mood
2. Identify mediators and moderators in C&M &M decline
3. Advance diagnostic and research tools
4. Advance therapeutic strategies and explore novel interventions

Projects
1a. Build evidence, interventions and outcomes to link gait, cognition, motor learning, exercise and brain health
1b. Establish “core measures” and apply to current and future cohorts studying C&M in Canada
2a. Role of vascular factors, genomics, mood, Vit D, inflammation in C&M
2b. Frontal-executive, motor function and learning with aging and neurodegeneration
2c. Role of motor learning in use of assistive devices
2d. Assess how “motor imagery” alters mobility
2e. Phenotype of cognitive/gait disorders
3a. Motor signature as a predictor of dementia
3b. Indices of vascular predictors of C&M decline
3c. Characterize optimal exercise interventions for cognitive and mobility decline
4a. Dual-Task training and Multimodal exercise trials to improve cognition
4b. Proof of principle trials using TBM on mobility & cognition
4c. Cognitive enhancers to reduce falls. RCT
4d. Exercise + Vitamin D + Cognitive remediation
5a. Use and apply gait assessment as a clinical tool for C&M decline
5b. Translate “motor signature” into a test to detect vulnerable older people
5c. Apply clinical tools to predict dementia progression
5d. Translate results to areas of stroke and brain injury
5e. Guidelines on prescribing exercises (alone or combined) to reduce disability related to C&M decline

Methods
- Systematic reviews (distillation of knowledge), consensus panels, technology development, identification of mediators and moderators
- Cross-sectional/prospective studies across C&M spectrum
- Use imaging (fMRI, BOLD, NiRS, and blood markers (BDNF) to elucidate factors
- Prospective cohort studies
- Logistic Pilots of the SYNERGIC Trial phase III
- SYNERGIC RCT: Phase II & III trials combining Exercise + Vit D + Cognitive Remediation
- Pilot studies
- Proof of principle studies


Alphanumeric refers to projects outlined in my CV.
Motor and cognitive decline patterns in participants who progressed to dementia and those who did not.

(A) Motor decline
- No decline
- Intermittent
- Sustained

(B) Cognitive decline
- No decline
- Intermittent
- Sustained

(C) Motor and cognitive decline
- No motor or cognitive decline
- Pure motor decline
- Pure cognitive decline
- Both motor and cognitive decline

Cumulative Hazard

Months before progressing to dementia

Follow-up timepoint (months)
SYNERGIC Trial

SYNchronizing, Exercises, Remedies in GaIt and Cognition

A randomized controlled double blind trial

NCT02808676  HC6-24-c195918
Exercise is Medicine

BRAIN AFTER SITTING QUIETLY

BRAIN AFTER 20 MINUTE WALK

Research/scan compliments of Dr. Chuck Hillman University of Illinois
What is good for your heart, is good for your brain!

• The brain is the best customer of our heart and lungs
  Weight 1.5 kgs but consumes 20% of energy

• “Mens sana in corpore sano”
  A healthy body provides the basis for a healthy brain
  – Blood flow
  – Growth factors
  – Reduction of risk factors: hypertension, diabetes

Photo courtesy of SYNERGIC participants, London site
What is good for your heart, is good for your brain!

- Types of Exercise
  - Aerobic Training
    - Running, walking, swimming
  - Resistance Training
    - Lifting weights
  - Anaerobic Training
  - Balance/Agility Training
  - Others: Yoga, Tai Chi, dance

Photo courtesy of SYNERGIC participants, London site
SYNERGIC Trial
Interventions

3 interventions… in 200 individuals with MCI

Cognitive training  +  Physical exercises  +  Vitamin D
SYNERGIC Trial
Interventions

3 interventions… in 200 individuals with MCI

Cognitive training + Physical exercises + Vitamin D

Cognitive Training

- Cognitive Training (CT) intervention will involve tablet-based multimodal and multi-domain dual-task training with memory load
- Training sessions will take place before each of the fitness-training sessions for a duration of 30 min
- Selected by our experts Karen Li and Louis Bherer
SYNERGIC Trial

Interventions

3 interventions… in 200 individuals with MCI

Cognitive training + Physical exercises + Vitamin D

Multimodal Exercise
- 3 weekly sessions, 60 min each
- 40 min Progressive Resistance training + 20 min Aerobic
- Selected by our experts Teresa Liu-Ambrose, Karen Li and Louis Bherer
SYNERGIC Trial

Interventions

3 interventions… in 200 individuals with MCI

Cognitive training  +  Physical exercises  +  Vitamin D

Improve Cognition and Mobility

Vitamin D

• 10,000 IU of Vitamin D3 or matching placebo 3 times per week
• Weekly cumulative dose: 30,000 IU
• Daily dose: 4,258 IU
• Current daily maximum dose approved by Health Canada as a supplementation is 10,000 IU
SYNERGIC Trial
Summary

- Cognitive and mobility decline cause most of the disability of aging

- **Clinical Trial** to test the combined effect of exercise + cognitive remediation + vitamin D + medications to improve cognition and mobility/gait decline

- The gained knowledge will be translated in combined interventions based on **exercises** to prevent cognitive decline/progression to **dementia and mobility decline and falls**
Canadian Gait and Cognition Network
A 10 years history tale

2008  Identified gaps in knowledge but also in clinical applicability

2011-2014  It went through a peer-reviewed process to get scientific approval

2014-2015  Obtained peer-reviewed funding

2015-2018  Successfully leveraged funds from other organizations and harmonized measures in two Canadian Cohorts Studies: ONDRI and CCNA

Since 2012  Leading 3 longitudinal studies that include 2500 older adults ranging from normal aging to SCI and MCI, and neurodegenerative diseases (PD, FTD, AD)

Since 2017  Conducting a nation-wide clinical trial to improve gait and cognition