Motor Biomarkers to predict cognitive decline and dementia

“There is something in the way you walk”

Manuel Montero-Odasso  MD, PhD, FRCPC, AGSF, FGSA

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Director, Gait and Brain Lab, Parkwood Institute
Division of Geriatric Medicine, The University of Western Ontario
Scientist, Lawson Health Research Institute, London ON
Objectives

1. To summarize the current knowledge of the relationship between early motor, mood & cognitive decline in aging and disease.
2. To show the value of the dual-task paradigm to evaluate cognitive and motor relationships.
3. To demonstrate that gait assessment is a complementary window to evaluate brain function.
4. To discuss that gait performance is a motor biomarker that can be used to predict dementia.
What makes a person look old?

- Slow Gait
- Mental Slowing
- Low Mood
Thinking, Feeling, and Moving must be studied together

• Extensive epidemiological evidence supports links between cognition and movement

• Brain networks for movement overlap with networks for cognition

• Thinking, Feeling, and Moving share behavioral and etiological factors that can drive new insights into prevention and treatment

Particularly, to understand the relation with cognitive decline and dementia
### Fig. 1. Models of the relationship between sensory/motor dysfunction and AD. (A) A clinical model. Seminal observations of dysfunction of each sensory/motor modality are documented at the earliest reported stage during the clinical course of AD based on the studies referenced in this review. Parallel progression of these initial sensory or motor dysfunctions to advanced AD dementia raises the question of whether AD may be a heterogeneous disease in origin or a disease with heterogeneous clinical courses. A comprehensive assessment of all relevant sensory and motor measures from the preclinical stage of AD to the advanced dementia stage may help to test this possibility. Future research may also aim to extend these findings to earlier periods of the preclinical AD stage with better sensitivity and specificity by either improving the measurement methodology for detecting sensory and motor changes or by combining sensory/motor measures with other biomarkers, such as cerebrospinal fluid, neuroimaging, and genetic risk factors for AD. (B)
Main Questions

• What are the non-cognitive changes has been associated with developing dementia?

• What are the potential, sensory, motor, behavioral, or sleep, frailty markers that have been shown to serve as potential predictors of dementia?

• Are there prediction models for dementia using these non-cognitive markers?
Outline of this presentation

- Why walking is fundamental
- Gait and Brain Connection
- Predementia syndromes (MCI) and gait
- Walking while talking as a “Brain stress test” to predict dementia
Gait and Brain Connection
...If he was able to keep his body in an upright position, to move his hands in one way and their feet in another. To keep improving his brain and to use his mind as best as possible, he stood a chance of success...

Desmond Morris
“The Naked Ape”
A Zoologist’s Study of the Human Animal. 1967
Bipedalism, Encephalization and Gait

There is a “phylogenetic” Gait and Cognition association

Encephalization

Bipedalism

5 million years

Bipedalism, Encephalization and Gait

It was a fundamental adaptation 1.5 M years before encephalization. Necessary step for encephalization.
Bipedalism, Encephalization and Gait

There is an “ontogenetic” Gait and Cognition decline

80 years

Gait and Cognition
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||§*
Walking is fundamental
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: diabetes on oral agent, HBP

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”
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 Beaufret, MD, PhD, and Jeffrey M. Hausdorff, PhD.

Slow Gait Velocity

Mobility Impairment

Cognitive Impairment

Falls-Fractures

MCI

Dementia

Traditional View

Emerging View

Mild Cognitive Impairment = MCI

- MCI express early problems in “cognition” (pre-dementia state).\textsuperscript{1,2}
- Difficult to characterize who will convert to dementia\textsuperscript{3}
- Gait might provide a window into aspects of brain function in the preclinical onset of dementia

\textsuperscript{2} Dubois B, Albert M. MCI or prodromal dementia? \textit{Lancet Neurol} 2004; 3:246-248-1133
\textsuperscript{3} Petersen RC. \textit{Journal of Internal Medicine} 2004; 256: 183–194
The road to Dementia. Changes before clinical manifestations

Other pathologies: CVD, PD-LBD,
Gait & Brain Study – Overall goals

Can motor biomarkers predict dementia?
### Overall Parkinsonism

<table>
<thead>
<tr>
<th>Study name</th>
<th>Odds ratio</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Z-Value</th>
<th>p-Value</th>
<th>Relative weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caraceni (2007a)</td>
<td>3.170</td>
<td>1.733</td>
<td>5.799</td>
<td>3.744</td>
<td>0.000</td>
<td>40.62</td>
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<tr>
<td>Caraceni (2007b)</td>
<td>8.160</td>
<td>2.477</td>
<td>26.884</td>
<td>4.351</td>
<td>0.001</td>
<td>25.30</td>
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<tr>
<td>Waite (2005)</td>
<td>1.400</td>
<td>0.606</td>
<td>3.233</td>
<td>0.788</td>
<td>0.431</td>
<td>34.07</td>
</tr>
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</table>

### Tremor

<table>
<thead>
<tr>
<th>Study name</th>
<th>Hazard ratio</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Z-Value</th>
<th>p-Value</th>
<th>Relative weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee (2016)</td>
<td>0.614</td>
<td>0.196</td>
<td>1.349</td>
<td>-1.352</td>
<td>0.176</td>
<td>30.71</td>
</tr>
<tr>
<td>Shih (2014)</td>
<td>0.460</td>
<td>0.171</td>
<td>1.237</td>
<td>-1.528</td>
<td>0.124</td>
<td>30.20</td>
</tr>
<tr>
<td>Thawani (2009)</td>
<td>1.710</td>
<td>0.971</td>
<td>3.012</td>
<td>1.857</td>
<td>0.063</td>
<td>39.08</td>
</tr>
</tbody>
</table>

### Gait Velocity

<table>
<thead>
<tr>
<th>Study name</th>
<th>Hazard ratio</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Z-Value</th>
<th>p-Value</th>
<th>Relative weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Camargo (2016)</td>
<td>2.530</td>
<td>1.113</td>
<td>5.753</td>
<td>2.214</td>
<td>0.027</td>
<td>10.24</td>
</tr>
<tr>
<td>Dumurgier (2016)</td>
<td>2.280</td>
<td>1.758</td>
<td>2.957</td>
<td>6.214</td>
<td>0.000</td>
<td>27.75</td>
</tr>
<tr>
<td>Gray (2013)</td>
<td>1.270</td>
<td>0.967</td>
<td>1.685</td>
<td>1.677</td>
<td>0.098</td>
<td>26.81</td>
</tr>
<tr>
<td>Montero-Odasso (2016)</td>
<td>4.930</td>
<td>1.710</td>
<td>14.212</td>
<td>2.963</td>
<td>0.003</td>
<td>7.00</td>
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<td>Verghez (2014)</td>
<td>1.770</td>
<td>1.380</td>
<td>2.270</td>
<td>4.497</td>
<td>0.000</td>
<td>28.20</td>
</tr>
</tbody>
</table>

From: *Motor function and incident dementia: a systematic review and meta-analysis*  
Recommendations for discussion

Evidence

**Recommendation 1**

There is strong evidence that gait speed is associated with future dementia, in population studies. When gait speed (cut-off gait speed below 0.8m/s) is coupled with cognitive impairment (subjective or objective) the risk is higher. We recommend testing gait speed in primary care clinics in those patients with cognitive complaints/impairments if time/resources are available. GRADE 1B

Note: published protocols on how to assess gait speed with just a stopwatch are available. It is test easy to perform and take, in average 3 minutes to be performed.

**Recommendations for discussion**

Motor

We propose a two step approach

Subjective or Objective Cognitive impairment?

No

Yes

No action

Perform gait speed test

It is not screening, it is case finding

Evidence

Fig. 2. Forest plot of (A) all combined IR for risk of incident dementia; (B) any dementia; (C) Non-AD, and (D) VaD in participants with abnormal gait at baseline, compared with those with normal gait. Square box area is proportional to the sample size of each study; horizontal lines corresponding to the 95% CI; diamond representing the summary value; vertical line corresponding to a RR of 1.00; separation in no difference.
“The Gait and Brain Study”

Population at Risk: MCI

Will develop dementia

40% remains stable after 5 years

60% will develop dementia after 5 years (rate 7-10% year)

Clinical Dementia CDR conversion Clinical Dx

Significance
Early prognosis
Early treatment
Delay disability
Delay placement
Gait & Brain Study - Design and follow-up

**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

- N = 130 (1st wave 2007-2010)
- N = 270 (2nd 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

Gait & Brain Study

- Gait performance
  - Electronic walkway (Zeno Mat® and GAITRite® System)
    - Gait velocity (cm/s)
    - Dual-task gait test

- Cognitive Assessments:
  - MoCA, MMSE, CDR, RAVLT, TMT A/B

- Incident Dementia
  - DSM-IV criteria + when CDR progressed to 1.0 or higher in follow-up

- Analysis
  - Cox proportional hazard models
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
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

Dual task cost

\[ \text{Dual task cost} = \frac{\text{Single gait} - \text{Dual task gait}}{\text{Usual gait}} \times 100 = 30\% \]
Dual-task paradigm - How does it work?

Brain areas activated while...

Walking (Single task)

Cognitive task (Single task)

Shared resources (Dual-task)

Pashler H. Psychol Bull. 1994
Stride time is a fine parameter of cortical control of gait
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.

Association of Dual-Task Gait With Incident Dementia in Mild Cognitive Impairment
Results From the Gait and Brain Study

Manuel M. Montero-Odasso, MD, PhD, FRCPC; Yanina Sarquis-Adamson, PhD; Mark Speechley, PhD; Michael J. Borrie, MBBS, FRCPC; Vladimir C. Hachinski, MD, DPhil, FRCPC; Jennie Wells, MD, FRCPC; Patricia M. Riccio, MD; Marcelo Schapira, MD; Ervin Sejdic, PhD; Richard M. Camicioli, MD, FRCPC; Robert Bartha, PhD; William E. McIlroy, PhD; Susan Muir-Hunter, PT, PhD
Gait & Brain Study - Design and follow-up

Design and Participants:
• Ongoing cohort
• Seniors with SCI & MCI, >65 y/o, no frailty, no dementia at baseline, able to ambulate independently
Mean follow-up: 24 months
Bi annual assessments:
• Battery of Cognitive test
• Gait, Balance, Blood tests, MRI

To be included in this study, participants had to:
- Have at least 2 assessment visits
- Fulfill MCI criteria

Total Since 2007
N = 400

N = 130
(1st wave 2007 - 2010)

N = 210
(2nd wave 2010 - ongoing)

N = 47 progressed to dementia
N = 60 drop out
N = 6 deceased

N = 250 in follow-up

From: Association of Dual-Task Gait With Incident Dementia in Mild Cognitive Impairment: Results From the Gait and Brain Study


Cumulative Hazard Ratio for Progression to Dementia for Low and High Dual-Task Cost in Gait Velocity (n = 112) A, Dual-task gait cost (DTC) while counting backward. B, While performing serial sevens subtractions. C, While naming animals.
Figure 2. Risk of Dementia Stratified By Gait Velocity (centimeters per second) Quartiles in 3 Dual-Tasks Conditions

A. Gait velocity, counting

B. Gait velocity, serial sevens

C. Gait velocity, naming animals

The 3 dual-tasks conditions are counting backward (A), serial sevens subtractions (B), and naming animals (C).
Proposal that Dual-Task gait (dark red) can be an early biomarker for Dementia progression before cognitive and brain structural changes happen.

*Adapted from Jack et al model. Lancet Neurology 2010*
Gait & Brain Study –

Trajectories of decline gait and cognition
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 Sejdic, PhD,## Louis Bherer, PhD,## Howard Chertkow, MD,## and The Canadian Gait and Cognition Network
**Recommendation 1**

There is strong evidence that gait speed is associated with future dementia, in population studies. When gait speed (cut-off gait speed below 0.8 m/s) is coupled with cognitive impairment (subjective or objective) the risk is higher. We recommend testing gait speed in primary care clinics in those patients with cognitive complaints/impairments if time/resources are available.

**GRADE 1B**

Note: published protocols on how to assess gait speed with just a stopwatch are available. It is easy to perform and takes, on average, 3 minutes to be performed.

**Recommendations for discussion**

Motor

We propose a two-step approach

- **Subjective or Objective Cognitive Impairment?**
  - No
    - No action
  - Yes
    - Perform gait speed test

It is not screening, it is case finding

Evidence

**Table 2. Risk of Progression to Dementia According to Motor Decline, Cognitive Decline, and Motor and Cognitive Decline**

<table>
<thead>
<tr>
<th>Decline Pattern</th>
<th>Unadjusted</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor intermittent</td>
<td>2.60 (0.89-7.60)</td>
<td>0.8</td>
<td>3.52 (1.14-10.84)</td>
<td>0.03</td>
<td>2.72 (0.80-9.24)</td>
</tr>
<tr>
<td>Sustained</td>
<td>7.02 (2.42-20.35) &lt; 0.001</td>
<td>6.21 (2.08-16.01)</td>
<td>0.001</td>
<td>5.70 (1.91-17.01)</td>
<td>0.002</td>
</tr>
<tr>
<td>Cognitive intermittent</td>
<td>1.30 (0.44-3.82)</td>
<td>0.63</td>
<td>1.20 (0.40-3.36)</td>
<td>0.75</td>
<td>1.31 (0.44-3.87)</td>
</tr>
<tr>
<td>Sustained</td>
<td>5.03 (1.23-2.48)</td>
<td>0.02</td>
<td>2.70 (1.11-5.33)</td>
<td>0.03</td>
<td>2.52 (0.84-6.01)</td>
</tr>
<tr>
<td>Combined intermittent purity motor</td>
<td>2.25 (0.63-6.46)</td>
<td>0.23</td>
<td>3.77 (0.96-14.51)</td>
<td>0.06</td>
<td>5.41 (0.98-29.91)</td>
</tr>
<tr>
<td>Pure cognitive</td>
<td>0.97 (0.18-5.30)</td>
<td>0.97</td>
<td>0.79 (0.14-4.53)</td>
<td>0.79</td>
<td>1.35 (0.21-8.47)</td>
</tr>
<tr>
<td>Motor and cognitive</td>
<td>5.39 (1.69-16.88)</td>
<td>0.004</td>
<td>5.41 (1.69-17.00)</td>
<td>0.004</td>
<td>6.28 (1.76-22.25)</td>
</tr>
</tbody>
</table>

No decline is the reference category.

*Model 1 adjusted for baseline Montreal Cognitive Assessment (MoCA) score; Model 2 adjusted for age, sex, baseline MoCA score; Model 3 adjusted for age, sex, baseline comorbidities, baseline MoCA score; Model 4: adjusted for age, sex, baseline comorbidities, baseline MoCA score, time-dependent covariate (comorbidities developed during follow-up).

*Model 1 adjusted for baseline gait velocity; Model 2 adjusted for age, sex, baseline gait velocity; Model 3 adjusted for age, sex, comorbidities, baseline gait velocity; Model 4 adjusted for age, sex, baseline comorbidities, baseline gait velocity, time-dependent covariate.

*Model 1 adjusted for baseline MoCA score, baseline gait velocity; Model 2 adjusted for age, sex, baseline MoCA score, baseline gait velocity; Model 3 adjusted for age, sex, baseline MoCA score, baseline gait velocity, time-dependent covariate; Model 4 adjusted for age, sex, baseline comorbidities, baseline MoCA score, baseline gait velocity, time-dependent covariate.
Walking is cognitively demanding!
Summary, so far!

- Gait is cognitive and can be a motor marker of 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.
What is the underlying mechanism of gait-cognitive relation and dysfunction?
What do these symptoms have in common? They rely in similar brain regions and networks.

- **Cortical**
  - Goal direct system: must reach the goal and avoid impeding objects
  - Regulates propulsion and navigation

- **Subcortical**
  - Motor system
    - 1-Basal ganglia & Brain stem Level
    - Generates propulsive movement
    - 2-Spinal Level: Central Pattern Generator (CPG)
  - Provides cadence and rhythm

- **Spinal**
  - Postural system and peripheral limbs
    - 1-Muscle and Joints
    - 2-Vestibular
    - 3-Ocular
  - Helps to position center of gravity
  - Provides propulsion

- **Gait**

---

Fig. 3. Potential mechanism affecting the common brain structures and networks that regulate gait control and cognitive performance. Adapted from Montero-Odasso et al. [5].
Contribution of Brain Imaging to the Understanding Of Gait Disorders in Alzheimer’s Disease: A Systematic Review

Cédric Annweiler, MD, PhD, Olivier Beauchet, MD, PhD, Sébastien Celle, MS, Frédéric Roche, MD, PhD, Thierry Annweiler, MD, BS, Gilles Allali, MD, PhD, Robert Bartha, PhD, and Manuel Montero-Odasso, MD, PhD; On behalf of the WALK Team (Working group Angers-London for Knowledge)

Abstract
Although gait disorders are common in Alzheimer’s disease (AD), determining which brain structures and related lesions are specifically involved is a goal yet to be reached. Our objective was to systematically review all published data that examined associations between gait disorders and brain imaging in AD. Of 486 selected studies, 4 observational studies met the selection criteria. The number of participants ranged from 2 to 61 community dwellers (29%-100% female) with prodromal or dementia-stage AD. Quantitative gait disorders (ie, slower gait velocity explained by shorter stride length) were associated with white matter lesions, mainly in the medial frontal lobes and basal ganglia. The nigrostriatal dopamine system was unaffected. Qualitative gait disorders (ie, higher stride length variability) correlated with lower hippocampal volume and function. Gait disorders in AD could be explained by a high burden of age-related subcortical hyperintensities on the frontal–subcortical circuits (nonspecific) together with hippocampal atrophy and hypometabolism (specific).
Vascular burden as a substrate for higher-level gait disorders in older adults. A review of brain mapping literature.

— **Objective:**
  - To determine the distribution of WMH
  - is associated with gait disorders

— **Methods:**
  - Medline literature review

— **Results:**
  - $n = 21$ manuscripts
  - GV associated with WMH on the corticospinal tract
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  ▪ GV associated with WMH on the corticospinal tract
Watershed Areas of the Brain

Wong, HH et al, Stroke 2001; ooo = watershed
Findings in our cohort
Slow gait in MCI is associated with ventricular enlargement: results from the Gait and Brain Study

C. Annweiler · O. Beauchet · R. Bartha · M. Montero-Odasso

Structural imaging

Brain ventricular volume

Gait Velocity
Motor cortex and gait in mild cognitive impairment: a magnetic resonance spectroscopy and volumetric imaging study

Cédric Annweiler,1,2,3,4 Olivier Beauchet,4 Robert Bartha,3 Jennie L. Wells,1 Michael J. Borrie,1 Vladimir Hachinski5 and Manuel Montero-Odasso1,2

- PMC neurochemistry: proton MR spectroscopy
  - NAA/Cr: neuron health/function (NAA/Cr<1.17)
  - Cho/Cr: inflammation (Cho/Cr>0.58)

Figure 1. The spectroscopy voxel placed in the right motor cortex is outlined in yellow on sagittal (left), axial (middle), and coronal (right) images.

Figure 2. Representative 1H-MRS data from the motor cortex in one subject.
Volume of the entorhinal cortex and the onset of dementia

Findings in MCI participants that converted to dementia

The relationship between gait and cognition in MCI older adults may be explained by atrophy of the entorhinal cortex, and it may predict future onset of dementia.

Findings in our cohort

- Smaller entorhinal cortex was associated with worst dual-task gait and future onset of dementia.

\[
y = -0.0139x + 32.428 \\
R^2 = 0.2597
\]

Volume in the entorhinal cortex (mm\(^3\))

Velocity dual-task cost (%)

Counting backwards

\[
y = -0.0152x + 46.111 \\
R^2 = 0.1455
\]

Volume in the entorhinal cortex (mm\(^3\))

Velocity dual-task cost (%)

Serial sevens

Entorhinal cortex atrophy precedes hippocampal atrophy in SMI, MCI, and AD. (Pennanen, 2004; Jessen, 2006)

Entorhinal cortex plays an important role in dual-tasking gait (working memory and attention) and its atrophy may lead to progression to dementia.
Gait and cognition: Is there a relationship?

• Which functions and areas of the brain are involved?

  ...attention, executive function, and memory

• Which variables of gait are most affected?

  ...gait variability

• What are the common underlying factors?

  ...vascular risk factors
Is Gait a motor biomarker that can predict dementia?
Proposal that Dual-Task gait (dark red) can be an early biomarker for Dementia progression before cognitive and brain structural changes happen.

*Adapted from Jack et al model. Lancet Neurology 2010*
Conclusions

Preclinical condition → Neurodegeneration → Aging → Hypertension and vascular mechanisms

Early clinical presentation → Impaired dual-task gait performance → Progression to dementia

Final outcome
Conclusions

- A high dual-task cost was associated with an increased risk of dementia by 3.8 times.

- Combining a simple measure (gait velocity) with a cognitive task (counting, naming animals) is superior than solely slow gait to detect risk for dementia.

- Dual-task test is easy to perform, low tech, and economical.

- Results are in agreement with:
  - “Motor signature” of cognitive decline
  - “Motoric Cognitive Risk” syndrome
Conclusions

- Dual-task gait is an early clinical marker of progression to dementia can be used in screening patients with MCI who could benefit the most from additional testing.

- Can identify high-risk individuals with MCI to plan frequency of follow-up visits to monitor function.

Key Points

**Question** Can dual-task gait testing (assessing gait while performing a challenging cognitive task) identify patients with mild cognitive impairment at risk of progression to dementia?

**Findings** In this cohort study of 112 older adults with mild cognitive impairment with up to 6 years of follow-up, poor performance in dual-task gait testing was significantly associated with a 2- to 3-fold risk of dementia incidence independent of age, sex, education, comorbidities, and baseline cognition.

**Meaning** Dual-task gait testing may serve clinicians to detect patients with mild cognitive impairment at higher risk of progression to dementia, allowing for optimization of further biomarker testing and initiation of early interventions.
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