Toward Early Diagnosis and Management of Dementia Using Virtual Reality

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"Demography is destiny"

Auguste Compte
1798-1857
The World in 2050

The next four decades will see dramatic changes in the age structure of the global population. How big those changes will be, when they will happen and where they will be most felt are subjects of much concern. We take a look at some of the projections.

In general, developed countries will have older populations... ...but most people aged 60+ will still live in the developing world.

Map shows the percentage of each area's total population that will be aged 60+ in 2050. It is divided by region, not country.
Aging and Falls

Every 1 second
An older adult falls every second of every day.

Every 20 minutes
An older adult dies from a fall in the US. Many more are injured.

1 in 4
One in four older adults reported a fall in 2014.

#1
Falls are the #1 cause of hip fractures.

$ 31 billion
Annual medical expenses for older adult falls cost over $31 billion, these costs will surge unless preventive measures are adopted.

Dementia Wave is Growing

Prevalence of Dementia in Different Age Groups

Projected Number of Americans Aged 65 and Older with Alzheimer’s Disease

Ziegler & Doblhammer 2009

Alzheimer’s Association Report 2010
Global Economic Impact of Dementia

Cost of Dementia Compared to Company Revenue

Cost of Dementia Compared to National Economies

World Alzheimer Report 2010
Consequences of Dementia

- Cognitive Decline
- Psycho-social Problems
- Motor Deficits
- Motor-cognitive Deficits
- Reduced Physical Activity
- High Fall Risk

Loss of Independence

2. van Gelder, B.M., et al., 2004, Neurology
“We can’t manage what we can’t measure”

Precise and Early Diagnosis of Motor-cognitive Impairment in Older Population is Important

- Early diagnosis = **personalized interventions in early stages**
  1,2

- Early diagnosis = **delay further deteriorative progression** and/or limit the consequences of motor-cognitive impairment, such as increasing risk of falling, decreasing mobility, and loss of independency

2. Amariglio, R.E., et al., 2015, JAMA Neurol
Current modalities to Assess Motor-cognitive Impairment

Subjective to examiner’s skill and experience
- MMSE
- MoCA
- Trail-making test

Too sophisticated, not practical for routine assessment
- MRI
- CSF

1. Cockrell, J.R et al., 2002, Principles and practice of geriatric psychiatry
4. Xekardaki, A., et al., 2015, Radiology
5. Bahureksa, L., et al., 2016, Gerontology
Motor Abnormality is a Predictor of Dementia

Dual-task Deficits Associated with Increased Fall Risk

“Stops walking when talking” is a predictor of falls in older adults

Lundin-Olsson et al (1997), Lancet
What We Need to Know about Dual Task Test

What is Dual Task?

Motor Task + Cognitive Task = Dual Task

Why Dual Task 1?

☑ proved to be a **high efficient to detect** motor-cognitive impairement

☑ allows isolating the **cognitive control component of locomotion**

☑ **exposes cognitive deficits** through the evaluation of activities which simultaneously demand attention resources

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Limitation: Dual Task Walking is Impractical

Timed-Up-and-Go (TUG) Test

3 meters

5-Meter Walk (5MW) Test
A hybrid system to assess motor-cognitive performance

Cognitive Impairment

Motor Impairment

less than 1 min!

Zhou et al (2016), Gerontology
An Alternative System of Dual Task Walking Test

Trial-making Test

Traditional Cognitive Test

Wearable Sensors & Virtual reality

Technology

instrumented trail-making task

Motor-Cognitive Test

iTMT
Instrumented Trail-making Task (iTMT)

human-machine interface installed on a standard laptop

Wearable sensor

Wearable sensor to measure ankle motion in real time
Instrumented Trail-making Task (iTMT)

Simple cognitive challenge

Advanced cognitive challenge

Outcome:
Total time (sec) participant used to complete each iTMT test
Motor planning Error

Outcome:
Ankle reaching speed, m/s
Study Design

Participants

- 10 subject with amnestic mild cognitive impairment (aMCI)$^1$
  - Age: $85.2 \pm 4.6$, BMI: $26.3 \pm 3.7$, 50% male
- 9 subject with Alzheimer's disease$^2$
  - Age: $80.8 \pm 6.6$, BMI: $27.7 \pm 6.4$, 77% male
- 11 age-matched healthy control
  - Age: $80.5 \pm 6.3$, BMI: $23.5 \pm 3.4$, 46% male

Exclusion

- non-ambulatory
- severe gait impairment
- other neurological conditions not associated with cognitive impairment
- clinically significant psychiatric condition or substance abuse

Patients Assessments

Montreal Cognitive Assessment (MoCA):
- Gold Standard
- Cut-off = 25\(^1\)
  - >25 ➔ Intact
  - <25 ➔ Impaired

Trail-making Test A&B (TMT A&B):
- Gold Standard
- Partially Included in MoCA and many other tests
- Sensitive to a variety of neurological impairments

Dual Task Walking Test:
- Primary task: motor
- Secondary task: cognitive

\[ DT_{cost} = SV_{single} - SV_{dual} \]

Statistical Analysis

• **Test-retest reliability**
  o Intra-class correlation and absolute agreement model (ICC (1,1))

• **Analysis of covariance for between groups difference**
  o Compare difference between sample groups for the average completion time of iTMT tests
  o Adjusted for age, BMI, and education level

• **Post hoc analysis for pairwise comparison**
  o Sidak adjustment

• **Agreement with traditional tools**
  o Spearman’s correlation coefficients
Feasibility and Reliability of iTMT

Feasibility
All participants finished all of the three iTMT test, including an Alzheimer’s patient with MoCA score 8

Reliability
Intra-class correlation
- \(iTMT_{\text{fixed}}\) (Simple): 0.742
- \(iTMT_{\text{random}}\) (Medium): 0.836
- \(iTMT_{\text{number-letter}}\) (Advanced): 0.826
Participants Demographic and Clinical Exam Data

<table>
<thead>
<tr>
<th>Variable</th>
<th>Healthy (n = 11)</th>
<th>aMCI (n = 10)</th>
<th>AD (n = 9)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (mean±SD)</td>
<td>80.5±6.3</td>
<td>85.2±4.6</td>
<td>80.8±6.6</td>
<td>0.152</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>6.0 (54.5)</td>
<td>5.0 (50.0)</td>
<td>2.0 (22.2)</td>
<td>0.305</td>
</tr>
<tr>
<td>Height, cm (mean±SD)</td>
<td>168.9±9.5</td>
<td>161.0±10.6</td>
<td>172.5±10.7</td>
<td>0.058</td>
</tr>
<tr>
<td>Body mass, kg (mean±SD)</td>
<td>67.6±14.0</td>
<td>69.4±10.7</td>
<td>83.9±25.7</td>
<td>0.112</td>
</tr>
<tr>
<td>BMI, kg/m² (mean±SD)</td>
<td>23.5±3.4</td>
<td>26.3±3.7</td>
<td>27.7±6.4</td>
<td>0.130</td>
</tr>
<tr>
<td>Education level, years (mean±SD)</td>
<td>15.2±3.0</td>
<td>13.8±2.3</td>
<td>14.6±1.8</td>
<td>0.451</td>
</tr>
<tr>
<td>MoCA score, 0-30 (mean±SD)</td>
<td>27.7±1.8</td>
<td>23.3±2.9</td>
<td>16.6±4.5</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>TMT A, s (mean±SD)</td>
<td>34.8±10.5</td>
<td>54.8±12.9</td>
<td>68.8±25.5</td>
<td>0.001*</td>
</tr>
<tr>
<td>TMT B, s (mean±SD)</td>
<td>77.7±32.9</td>
<td>164.3±70.2</td>
<td>278.0±157.5</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>
iTMT is Sensitive to Separate Healthy, aMCI, and AD

Difference Between

- Healthy---aMCI: 31%
  \[ p = 0.327, \text{Cohen's } d \text{ effect size } d = 0.78 \]
- Healthy---AD: 62%
  \[ p = 0.002, d = 1.57 \]
- aMCI--AD: 45%
  \[ p = 0.022, d = 1.12 \]

**Effect size d**
- Large = 0.80
- Medium = 0.50
- Small = 0.20
A Large Effect Size was Observed for Cognitive Impairment Identification using iTMT

- MoCA (cut-off = 25):
  - Cognitive Intact
  - Cognitive Impaired

- 45% difference:
  - $p = 0.038$
  - Cohen’s $d$ effect size = 1.01

Effect size $d$

- Large = 0.80
- Medium = 0.50
- Small = 0.20
iTMT vs. Traditional Cognitive Assessments

iTMT has fair-to-good agreement with MoCA, TMT A and B
iTMT vs. Dual Task Walking

iTMT has good correlation with dual task cost

No noticeable correlation was observed between traditional cognitive assessments and dual task walking
Motor-Planning Error is an indicator of frailty

iTMT Parameters for Nonfrail and Frail Subjects
Conclusions – iTMT is Practical and Sensitive to Identify Motor-cognitive Impairment

- Objective & low cost
- Quick (takes less than 1 minute)
- Practical (easy of use and administration, no walking test)
- Sensitive (identify cognitive impairment with large effect size)
- Assess simultaneously motor & cognitive performance
Limitations and Future Study

- Small sample size

**Future directions:**

- Using virtual reality based on dual task method as an intervention program.

Schwenk et al (2017), JRRD
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Thank you!

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