Cognitive-Motor Interference in Persons with Parkinson Disease

Tara L. Mclsaac, PhD, PT

Associate Professor of Physical Therapy
A.T. Still University
Arizona School of Health Sciences

October 11, 2014
ACRM - Toronto
Learning Objectives

At the end of this session the participant will be able to:

• Discuss the cognitive and motor deficits seen in Parkinson disease (PD)

• Understand the impact of cognitive and motor deficits in PD on daily activities

• Discuss the basis for cognitive-motor interaction and the possible rationale
Outline

• Parkinson disease: Background
• Changes in Cognition
• Cognitive-Motor Interaction - Theoretical Frameworks
• Evidence of Cognitive-Motor Motor Interference
• Rehabilitation for CMI
Outline

- Parkinson disease: Background
- Changes in Cognition
- Cognitive-Motor Interaction - Theoretical Frameworks
- Evidence of Cognitive-Motor Interference
- Rehabilitation for CMI
Parkinson disease

- 1 to 1.5 million in U.S.
- 6 to 10 million globally
- 60,000 new cases diagnosed each year in U.S.
- Dopaminergic depletion in basal ganglia, disrupts internal balance in basal ganglia activity (Obeso 2008)
  - Clumps of α-synuclein protein, Lewy bodies
- Affects motor and non-motor systems
Cardinal motor signs of PD

- **Tremor, rest & postural**
  - slow frequency (4-6 Hz), supination/pronation

- **Rigidity**

- **Akinesia** (lack of) / **Bradykinesia** (slowed) / **Hypokinesia** (small)

- **Postural instability**
  - retropulsion
  - festination of steps (also speech & thought)
  - freezing of gait (FoG)
The Parkinson’s Complex

Parkinsonism
Substantia Nigra

Pons  Basal Forebrain

Medulla  Amygdala  Hypothalamus

Olfactory Bulb  Spinal Cord (intermediolateral column)

Peripheral Autonomic Nervous System
(heart, intestinal track, bladder)

Neocortex

Olfactory Cortex  Temporal Cortex
Braak’s 6 Stages of Pathology in PD onset up to 10-15 years before symptoms appear
Outline

• Parkinson disease: Background
• Changes in Cognition
• Cognitive-Motor Interaction - Theoretical Frameworks
• Evidence of Cognitive-Motor Interference
• Rehabilitation for CMI
Executive Dysfunction in PD

1. Internal control of attention & action is impaired (Brown & Marsden 1988; Jahanshahi 1995)

2. Self-directed formation of strategies is impaired (Taylor 1986)

3. Set shifting is impaired with dysregulation of top-down and bottom-up attention control (Taylor & Saint-Cyr 1995; Cools 2001, 2009)

4. Planning is impaired with decreased activation of PFC and striatum (Lewis 2003)
Executive Dysfunction in PD

5. Inhibitory control & conflict resolution are impaired, not helped with medication
   - Esp. with more complex tasks, generalized across cog and motor domains (Obeso et al 2011)

   - 12% of variance in CMI on walking speed explained by reduced EF (Brixton test) (Rochester 2008)

Executive Dysfunction in PD

- 18-36% of newly diagnosed PwPD have cognitive impairment (Aarsland 2009; Foltynie 2004)

- Prevalence of Mild Cognitive Impairment (MCI) in nondemented PD is 27% (Litvan 2011, 2012)

- Majority of these (~60%) progress to PD with dementia (PDD) over 4 years, compared with 20% of PD with normal cognition (Williams-Gray 2007)

- PD-MCI predicts development of dementia, which can occur in up to 80% in PwPD over the long term (Aarsland 1996, 2003)
Outline

- Parkinson disease: Background
- Changes in Cognition
- Cognitive-Motor Interaction - Theoretical Frameworks
- Evidence of Cognitive-Motor Interference
- Rehabilitation for CMI
Dual Syndrome Hypothesis

Hypothesis differentiates between 2 Broad Syndromes

1. PD-MCI
   - Tremor-dominant phenotype
   - Fronto-striatal dysfunction
     - Impaired tests of planning, working memory and executive function
     - Respond to dopaminergic dosing but also overdosing effects

2. PD-D
   - Postural Instability/Gait Difficulty (PIGD) phenotype
   - Posterior cortical and temporal lobe dysfunction
     - Early deficits in visuospatial and semantic fluency
     - Rapid cognitive decline to dementia
     - Cholinergic treatment may help

Cognitive Flexibility represented differently in the 2 aspects of EF

1. **Attentional control** (Stroop, TMT, Tower of London, Verbal Fluency, Design Fluency)

2. **Abstract reasoning** (Sorting, 20 Questions, Word Context, Proverbs)

- 45% of PwPD had impaired performance on \( \geq 1 \) test
- Impaired group performed significantly worse on attentional control than on abstract reasoning tasks

\( N = 34 \) PwPD frontal-type deficits on FAB; 59% H&Y stage 1

Models of Executive Function and Attention Control


2. Multicomponent Model of Working Memory (Baddeley and Hitch 1974)

– Automatic and Controlled processing in both models

• Controlled - Prefrontal cortex (PFC) analogous to ‘central executive’ or SAS – allocating attention

• Automatic - Basal ganglia analogous to ‘contention schedulers’ (Miller and Cohen 2001; Norman and Shallice 1986)
Controlled versus Automatic Processing in PD

Gradient of dopamine depletion in PD: Fronto-striatal loops

Dorsal circuits: planning & WM

Ventral circuits: reward processing and learning

Behavior after withdrawal of DA in PD
Outline

- Parkinson disease: Background
- Changes in Cognition
- Cognitive-Motor Interaction - Theoretical Frameworks
- Evidence of Cognitive-Motor Interference
- Rehabilitation for CMI
Emerging evidence that:
1) cognition predicts mobility declines & falls and 
2) mobility decline & slow gait predict cognitive decline

Fear of Falling is Largest Predictor of Walking Speed – single and dual task

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Predictor</th>
<th>β</th>
<th>P value</th>
<th>Part correlation</th>
<th>R² part correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking speed (single)</td>
<td>Age</td>
<td>-0.198</td>
<td>0.011*</td>
<td>-0.189</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>Sex</td>
<td>0.219</td>
<td>0.004*</td>
<td>0.214</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>UPDRS-III</td>
<td>-0.180</td>
<td>0.027*</td>
<td>-0.165</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>Freezing</td>
<td>-0.071</td>
<td>0.346</td>
<td>-0.069</td>
<td>0.004</td>
</tr>
<tr>
<td></td>
<td>FES</td>
<td>0.390</td>
<td>&lt;0.001*</td>
<td>0.316</td>
<td>0.10</td>
</tr>
<tr>
<td></td>
<td>Brixton</td>
<td>-0.113</td>
<td>0.143</td>
<td>-0.108</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>HADS-D</td>
<td>0.199</td>
<td>0.022*</td>
<td>0.170</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>R² = 0.37; Sig. F Change &lt; 0.001</td>
</tr>
<tr>
<td>Walking speed (dual)</td>
<td>Age</td>
<td>-0.149</td>
<td>0.052</td>
<td>-0.144</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>UPDRS-III</td>
<td>-0.312</td>
<td>0.000*</td>
<td>-0.284</td>
<td>0.08</td>
</tr>
<tr>
<td></td>
<td>Freezing</td>
<td>-0.106</td>
<td>0.168</td>
<td>-0.102</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>FES</td>
<td>0.383</td>
<td>&lt;0.001*</td>
<td>0.308</td>
<td>0.10</td>
</tr>
<tr>
<td></td>
<td>HADS-D</td>
<td>0.216</td>
<td>0.012*</td>
<td>0.187</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>Dopamine</td>
<td>0.212</td>
<td>0.007*</td>
<td>0.202</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>R² = 0.34; Sig. F Change &lt; 0.001</td>
</tr>
<tr>
<td>Interference</td>
<td>UPDRS-III</td>
<td>-0.275</td>
<td>0.002*</td>
<td>-0.275</td>
<td>0.08</td>
</tr>
<tr>
<td></td>
<td>Brixton</td>
<td>0.211</td>
<td>0.015*</td>
<td>0.211</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>R² = 0.12; Sig. F Change &lt; 0.001</td>
</tr>
</tbody>
</table>
Dual Task Cost to Postural Control of Gait is greater for PwPD

Control n=184; PD n=121

Dual task interference on gait and cognitive task of digit span recall

Table 3. Results of the ANCOVA to test for dual-task main effects and dual × task interactions for the whole cohort and the subgroup who performed the dual-task + 1 condition, adjusting for age, sex and order of dual-task presentation. $F (p)$

<table>
<thead>
<tr>
<th>Variable</th>
<th>Dual-task main effect</th>
<th>Group × Dual-task interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Single versus dual-task</td>
<td>Single versus dual-task + 1</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>-----------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>Step velocity (m s$^{-1}$)</td>
<td><strong>26.4 (0.001)</strong></td>
<td><strong>40.3 (0.001)</strong></td>
</tr>
<tr>
<td>Step length (m)</td>
<td><strong>58.8 (0.001)</strong></td>
<td><strong>52.8 (0.001)</strong></td>
</tr>
<tr>
<td>Step time (ms)</td>
<td><strong>14.1 (0.001)</strong></td>
<td><strong>18.1 (0.001)</strong></td>
</tr>
<tr>
<td>Step length variability (m)</td>
<td>2.60 (0.108)</td>
<td><strong>17.0 (0.001)</strong></td>
</tr>
<tr>
<td>Step time variability (ms)</td>
<td>2.76 (0.098)</td>
<td><strong>17.8 (0.001)</strong></td>
</tr>
<tr>
<td>Stance time asymmetry (ms)</td>
<td>1.22 (0.271)</td>
<td>1.16 (0.284)</td>
</tr>
<tr>
<td>Step length asymmetry (m)</td>
<td><strong>6.15 (0.014)</strong></td>
<td><strong>5.15 (0.025)</strong></td>
</tr>
<tr>
<td>Step width (m)</td>
<td>2.43 (0.120)</td>
<td><strong>6.67 (0.011)</strong></td>
</tr>
<tr>
<td>Step width variability (m)</td>
<td>2.34 (0.127)</td>
<td>1.07 (0.304)</td>
</tr>
<tr>
<td>Error rate on digit span (%)</td>
<td><strong>0.731 (0.393)</strong></td>
<td><strong>15.5 (0.001)</strong></td>
</tr>
</tbody>
</table>

Values in bold and italics font indicate statistically significant findings ($p < 0.05$).
Spatiotemporal and Variability Measures of Gait are all Impaired by Dual Tasking


### Table 4.
Descriptive Statistics for Gait Spatiotemporal Measures, Gait Variability Measures, and Dual-Task Cost

<table>
<thead>
<tr>
<th>Variable</th>
<th>Single Task</th>
<th>Dual Task</th>
<th>P</th>
<th>Dual-Task Cost Log_{10} (Dual/Single)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( \bar{X} ) (SD)</td>
<td>Range</td>
<td>( \bar{X} ) (SD)</td>
<td>Range</td>
</tr>
<tr>
<td>Stride time (s)</td>
<td>1.1 (0.1)</td>
<td>0.90 to 1.39</td>
<td>1.3 (0.3)</td>
<td>0.92 to 2.44</td>
</tr>
<tr>
<td>Stride length (m)</td>
<td>1.2 (0.2)</td>
<td>0.52 to 1.46</td>
<td>1.0 (0.2)</td>
<td>0.32 to 1.44</td>
</tr>
<tr>
<td>Step width (m)</td>
<td>0.1 (0.03)</td>
<td>0.03 to 0.13</td>
<td>0.08 (0.03)</td>
<td>0.03 to 0.14</td>
</tr>
<tr>
<td>Swing time (%)</td>
<td>38.2 (2.5)</td>
<td>30.48 to 41.91</td>
<td>35.9 (3.1)</td>
<td>25.65 to 40.37</td>
</tr>
<tr>
<td>Walking speed (m/s)</td>
<td>1.0 (0.2)</td>
<td>0.46 to 1.38</td>
<td>0.9 (0.2)</td>
<td>0.26 to 1.22</td>
</tr>
<tr>
<td>Stride time variability (s)</td>
<td>0.03 (0.02)</td>
<td>0.01 to 0.10</td>
<td>0.08 (0.1)</td>
<td>0.02 to 0.67</td>
</tr>
<tr>
<td>Stride length variability (m)</td>
<td>0.04 (0.02)</td>
<td>0.02 to 0.12</td>
<td>0.05 (0.04)</td>
<td>0.02 to 0.22</td>
</tr>
<tr>
<td>Step width variability (m)</td>
<td>0.4 (0.2)</td>
<td>0.09 to 1.16</td>
<td>0.3 (0.1)</td>
<td>0.10 to 0.78</td>
</tr>
<tr>
<td>Swing time variability (%)</td>
<td>0.04 (0.02)</td>
<td>0.02 to 0.12</td>
<td>0.06 (0.05)</td>
<td>0.02 to 0.28</td>
</tr>
</tbody>
</table>

\* Asterisk denotes significance.

PD n=35
Different control mechanisms for Temporal and Postural aspects of gait

- Stride length and gait speed (temporal aspects) were associated with processing speed measures.
- Step width variability (postural aspect) was significantly associated with executive function and attention measures.
- These associations were affected differently by dual-tasking – only dual task cost to stride length was associated with processing speed.
- Slowed overall processing may indicate shared system underlying gait and cognition.

For PwPD the ability to change walking as instructed depends on task complexity.
Slower TUG and worse Verbal EF are associated with:

**Verbal Executive Function:**
- Verbal fluency - Word generation (animals)
- Verbal Working Memory – immediate & delayed recall

Timed Up and Go performance and Verbal Executive Function performance predict Quality of Life measures

**Table 3**

<table>
<thead>
<tr>
<th>PDQ-39 Domains</th>
<th>TUG Score (r, P)</th>
<th>EF Score (r, P)</th>
<th>Correlation Coefficients</th>
<th>Regression Model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>TUG Score</td>
<td>EF Score</td>
</tr>
<tr>
<td>Mobility</td>
<td>.37 &lt;.001</td>
<td>−.22 &lt;.001</td>
<td>.26</td>
<td>.27 &lt;.001</td>
</tr>
<tr>
<td>ADL</td>
<td>.27 &lt;.001</td>
<td>−.19 &lt;.001</td>
<td>.16</td>
<td>.19 &lt;.001</td>
</tr>
<tr>
<td>Emotion</td>
<td>.17 &lt;.001</td>
<td>−.10 &lt;.001</td>
<td>.04</td>
<td>.14 &lt;.001</td>
</tr>
<tr>
<td>Stigma</td>
<td>.04 .074</td>
<td>.01 .631</td>
<td>Not entered</td>
<td>Not entered</td>
</tr>
<tr>
<td>Social</td>
<td>.09 &lt;.001</td>
<td>−.07 .003</td>
<td>Not entered</td>
<td>Not entered</td>
</tr>
<tr>
<td>Cognition</td>
<td>.24 &lt;.001</td>
<td>−.24 &lt;.001</td>
<td>.11</td>
<td>.16 &lt;.001</td>
</tr>
<tr>
<td>Communication</td>
<td>.20 &lt;.001</td>
<td>−.18 &lt;.001</td>
<td>.13</td>
<td>.12 &lt;.001</td>
</tr>
<tr>
<td>Pain</td>
<td>.16 &lt;.001</td>
<td>−.01 .534</td>
<td>.05</td>
<td>.13 &lt;.001</td>
</tr>
</tbody>
</table>

Abbreviation: ADL, activities of daily living.

Driving and PD

- Car accidents 2 to 5 times higher for PwPD
- Approach traffic signals more slowly, yet decelerate later and fail to stop before entering the intersection
- Impaired in navigating curves, steering accuracy, speed adaptation, maintaining constant lane position and lane changing
- Increased reaction times to brake and steer
- Greater decline in driving skills with a concurrent auditory task

Cognitive - Motor Dysfunction Impacts Information Processing for Driving

Hierarchy of Risk Factors for driving in PD

N = 55; H&Y stage 2&3.
Rapid Pace Walk
• Cutoff ≥6 s
• Sensitivity 71%
• Specificity 78%

ADL = activities of daily living;
AVLT = Auditory Verbal Learning Test;
BVRT = Benton Visual Retention Task;
CDR = Clinical Dementia Rating Scale;
DMV = Department of Motor Vehicles;
MMSE = Mini-Mental State Examination;
ROCT = Rey-Osterrieth Complex Figure Test;
HVLT = Hopkins Verbal Learning Test;
JOLO = Judgment of Line Orientation;
SDMT = Symbol Digit Modalities Test;
UFOV = Useful Field of View.

Dual Task Costs to Arm task and Foot task differ between PwPD and Controls
Outline

• Parkinson disease: Background
• Changes in Cognition
• Cognitive-Motor Interaction - Theoretical Frameworks
• Evidence of Cognitive-Motor Interference
• Rehabilitation for CMI
Dual task performance improvement greater after Virtual Reality training on Treadmill then TT alone (3x/wk x 6 weeks)
Training improved all aspects of gait, most retained after 1 month

Table 2. Training Effects on Gait Measures

<table>
<thead>
<tr>
<th>Test Condition</th>
<th>Pretraining</th>
<th>Posttraining</th>
<th>Follow-Up</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual gait</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Speed (m/s)</td>
<td>1.16 ± 0.18</td>
<td>1.26 ± 0.20*</td>
<td>1.28 ± 0.19†</td>
<td>.006</td>
</tr>
<tr>
<td>Stride time (s)</td>
<td>1.08 ± 0.07</td>
<td>1.04 ± 0.05*</td>
<td>1.04 ± 0.09</td>
<td>.021</td>
</tr>
<tr>
<td>Stride length (cm)</td>
<td>123.08 ± 17.22</td>
<td>129.78 ± 18.20*</td>
<td>133.18 ± 15.65†</td>
<td>.043</td>
</tr>
<tr>
<td>Dual-task gait</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Speed (m/s)</td>
<td>1.01 ± 0.23</td>
<td>1.17 ± 0.15*</td>
<td>1.13 ± 0.17</td>
<td>.032</td>
</tr>
<tr>
<td>Stride time (s)</td>
<td>1.15 ± 0.11</td>
<td>1.10 ± 0.07*</td>
<td>1.08 ± 0.09†</td>
<td>.016</td>
</tr>
<tr>
<td>Stride length (cm)</td>
<td>113.07 ± 23.70</td>
<td>121.31 ± 24.21</td>
<td>126.32 ± 15.88†</td>
<td>.046</td>
</tr>
<tr>
<td>Gait during endurance testing</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Speed (m/s)</td>
<td>1.01 ± 0.18</td>
<td>1.16 ± 0.18*</td>
<td>1.13 ± 0.16†</td>
<td>.004</td>
</tr>
<tr>
<td>Stride time (s)</td>
<td>1.13 ± 0.24</td>
<td>1.04 ± 0.07*</td>
<td>1.06 ± 0.13</td>
<td>.246</td>
</tr>
<tr>
<td>Obstacle negotiation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Speed (m/s)</td>
<td>0.96 ± 0.19</td>
<td>1.17 ± 0.22*</td>
<td>1.17 ± 0.20†</td>
<td>.001</td>
</tr>
<tr>
<td>Stride time (s)</td>
<td>1.10 ± 0.09</td>
<td>1.05 ± 0.07*</td>
<td>1.06 ± 0.10</td>
<td>.232</td>
</tr>
<tr>
<td>Stride length (cm)</td>
<td>147.97 ± 16.97</td>
<td>160.66 ± 17.79*</td>
<td>161.46 ± 17.47†</td>
<td>.019</td>
</tr>
</tbody>
</table>

Notes: p Values in the right column are for the overall repeated measures analysis of variance models.
* Significant immediate effects at posttraining.
† Significant retention effects as compared with baseline evaluation analyzed in post hoc analysis.
Training improved cognitive tasks and reduced dual task cost by 56% - Clinical improvements retained

Table 3. Training Effects on Cognitive and Clinical Measures

<table>
<thead>
<tr>
<th></th>
<th>Pretraining</th>
<th>Posttraining</th>
<th>Follow-Up</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cognitive</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of errors made during serial subtraction</td>
<td>1.5 ± 1.8</td>
<td>1.0 ± 1.2</td>
<td>0.8 ± 1.2</td>
<td>.16</td>
</tr>
<tr>
<td>Dual-task cost</td>
<td>13.9 ± 14.8</td>
<td>6.9 ± 8.4*</td>
<td>12.8 ± 7.6</td>
<td>.05</td>
</tr>
<tr>
<td>Trail Making Test A (s)</td>
<td>69.0 ± 15.9</td>
<td>57.2 ± 11.9*</td>
<td>—</td>
<td>.003</td>
</tr>
<tr>
<td>Trail Making Test B (s)</td>
<td>141.4 ± 34.9</td>
<td>120.4 ± 18.2*</td>
<td>—</td>
<td>.05</td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UPDRS motor — part III</td>
<td>26.5 ± 7.6</td>
<td>23.5 ± 6.6*</td>
<td>24.7 ± 7.1†</td>
<td>.02</td>
</tr>
<tr>
<td>Four Square Step Test (s)</td>
<td>13.3 ± 2.5</td>
<td>11.6 ± 1.6*</td>
<td>11.9 ± 1.6†</td>
<td>.009</td>
</tr>
<tr>
<td>Quality of life (PDQ-39)</td>
<td>27.4 ± 15.9</td>
<td>19.4 ± 13.6*</td>
<td>23.6 ± 14.5</td>
<td>.04</td>
</tr>
</tbody>
</table>

Notes: p Values in the right column are for the overall repeated measures analysis of variance models. PDQ = Parkinson’s disease quality of life questionnaire; UPDRS = Unified Parkinson’s Disease Rating Scale.
* Significant immediate effects at posttraining.
† Significant retention effects as compared with baseline evaluation as analyzed in post hoc analysis.

Thank you