Depression and Cognitive Impairment Impact on Daily Functioning

By Patrick J. Brown, PhD
Clinical Scientist
Division of Geriatric Psychiatry
College of Physicians and Surgeons, Columbia University
New York State Psychiatric Institute

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Genesis of functional impairment

- Ecology of Aging
- Ecology: “…interdependence of one element in a system upon every other element.”

Lawton & Nahemow, 1973
Pathways to functional impairment

Physical Disruption → Functional Impairment → Prognosis

Affective Symptoms → Functional Impairment → Prognosis

Cognitive Dysfunction → Functional Impairment → Prognosis

Prognosis:
- Death
- Assisted Living or NH placement
- Hospitalization

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Physical correlates of function

- **Acute disruptions:**
  - **Metabolic syndrome:** Increased waist circumference, hypertension, BP, etc.
    - Increased risk of mobility disturbance (Penninx et al., 2009)
  - **Stroke:** Level of function post stroke predicts discharge to acute care from inpatient rehab (Chung et al., 2012)
  - **Fractures:** Usual care leads to increased risk of death, nursing home admissions, and decreases in ADLs in hip fracture patients (Singh et al., 2012)

- **Syndromal marker:**
  - **Frailty:** “decreased resiliency and reserves”
    - Increased risk of BADL/IADL impairment, institutionalization, and death (Fried et al., 2001; Bandeen-Roche et al., 2006)
Depression and function

- **Leading cause of disability in the US**
  - 2\textsuperscript{nd} highest cause in world, 50% take short-term disability; Kessler et al. 1999, 2003
  - Increased health care utilization and institutionalization

- **Cyclical relationship:**
  - Baseline depression in nonADL impaired sample predicted incident ADL impairment at follow-up (Bruce et al., 1994)
  - Baseline and incident ADL impairment predicted incident depression (Kennedy et al., 1990)

- **Treatment of depression:**
  - Mixed at best for the improvement of functional impairment in older depressed patients (Heilingenstein et al, 1995; Karp et al., 2009)
Cognitive impairment and function

• Dementia criteria – includes function
  • Clinical Dementia Rating Scale
    • Memory, Orientation, Personal Care, Home and Hobbies, Community Affairs, Judgment and Problem Solving
  • Informant-based interview, largely of function, accurately stages and ‘diagnoses’ dementia (autopsy; Morris, 1993)

• Original MCI criteria:
  • No “substantial interference with work, usual social activities or other activities of daily living.” (Petersen et al, 1999)
  • Studies have shown IADL impairment in MCI stage
    • Episodic memory, Executive function, Processing speed (Wadley et al., 2008; Cahn-Weiner et al., 2000; Pereira et al., 2008; Tomaszewski-Farias et al., 2009)
MCI criteria and function: revisited

• New criteria: “preservation of independence in functional abilities”, “persons with MCI commonly have mild problems performing complex functional tasks…” (Albert et al., 2011)

• We have and continue to publish a line of research consistent with the new MCI criteria and the role that function plays in the dementia process.
## Type of functional impairments in MCI

<table>
<thead>
<tr>
<th>FAQ item</th>
<th>Normal ( n = 229 )</th>
<th>aMCI ( n = 394 )</th>
<th>AD ( n = 193 )</th>
<th>Trend test ( z )-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Writing checks, paying bills, or balancing checkbook.</td>
<td>2%</td>
<td>34%</td>
<td>88%</td>
<td>17.97</td>
</tr>
<tr>
<td>2. <strong>Assembling tax records, business affairs, or other papers.</strong></td>
<td>2%</td>
<td>43%</td>
<td>91%</td>
<td>18.47</td>
</tr>
<tr>
<td>3. Shopping alone for clothes, household necessities, or groceries.</td>
<td>&lt; 1%</td>
<td>19%</td>
<td>71%</td>
<td>16.19</td>
</tr>
<tr>
<td>4. <strong>Playing a game of skill such as bridge or chess, working on a hobby.</strong></td>
<td>&lt; 1%</td>
<td>22%</td>
<td>62%</td>
<td>14.27</td>
</tr>
<tr>
<td>5. Heating water, making a cup of coffee, turning off the stove.</td>
<td>0%</td>
<td>8%</td>
<td>28%</td>
<td>9.14</td>
</tr>
<tr>
<td>6. Preparing a balanced meal.</td>
<td>&lt; 1%</td>
<td>20%</td>
<td>65%</td>
<td>14.98</td>
</tr>
<tr>
<td>7. <strong>Keeping track of current events.</strong></td>
<td>&lt; 1%</td>
<td>23%</td>
<td>67%</td>
<td>15.23</td>
</tr>
<tr>
<td>8. Paying attention to and understanding a TV program, book, or magazine.</td>
<td>&lt; 1%</td>
<td>21%</td>
<td>59%</td>
<td>13.83</td>
</tr>
<tr>
<td>9. <strong>Remembering appointments, family occasions, holidays, medications.</strong></td>
<td>4%</td>
<td>55%</td>
<td>91%</td>
<td>18.01</td>
</tr>
<tr>
<td>10. Travelling out of the neighborhood, driving, or arranging to take public transportation.</td>
<td>1%</td>
<td>26%</td>
<td>76%</td>
<td>16.39</td>
</tr>
</tbody>
</table>

- **2-item**
  - 3.5% of Controls, 66% of aMCI, and 96.4% of AD had one deficit (86% of AD had both)

- **Controls vs. aMCI/AD**
  - Sensitivity: 2 vs. 10-item FAQ (.76 vs .81)
  - Specificity: 2 vs. 10-item FAQ (.95 vs .92)

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Brown et al., 2011
Severity of Functional Impairment in older adults with aMCI

Severity Groups:
- No deficits = 0
- Mild severity > 1 and < 4
- Moderate/severe > 5

*p < .0167 (Bonferroni corrected).
(Covariate adjusted means (age, sex, and education; ICV for hippocampal volume)

Brown et al., 2011
Numbers of Functional Impairments

- Denotes a significant difference in post hoc comparisons between no deficits and mild or few;
- Denotes a significant difference in post hoc comparisons between no deficits and moderate/severe or high;
- Denotes a significant difference in post hoc comparisons between mild or few and moderate/severe or high.

No deficits = 0; few deficits ≥ 1 and ≤ 3; high number ≥ 4. \( p < .0167 \) (Bonferroni corrected).

Brown et al., 2011
Neuroanatomical correlates of functional impairment

Means adjusted for age, gender, education, and intracranial volume.

a Denotes a significant difference in post hoc comparisons between no deficits and mild or few;
b Denotes a significant difference in post hoc comparisons between no deficits and moderate/severe or high;
c Denotes a significant difference in post hoc comparisons between mild or few and moderate/severe or high.

$p < .0167$ (Bonferroni corrected).

Brown et al., 2011
Depression and cognitive impairment: Impact on function

- What impacts functional impairment in a combined depressed, cognitively impaired group
  - ADNI has low comorbidity, no depressive symptoms
  - 3,117 patients with aMCI and nonaMCI from baseline NACC
    - The amnestic group was older, more educated, more functionally impaired, less independent, and had fewer ischemic problems than the nonaMCI group (p < .01)
    - The nonamnestic group had better memory but poorer executive function

Brown et al., 2012
# Sample characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total MCI N = 3117</th>
<th>aMCI n = 2488</th>
<th>nonaMCI n = 629</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>74.37 (9.37)</td>
<td>74.83 (9.33)</td>
<td>72.57 (9.33)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Education</td>
<td>14.91 (3.34)</td>
<td>14.97 (3.30)</td>
<td>14.67 (3.45)</td>
<td>.045</td>
</tr>
<tr>
<td>M/F (F)</td>
<td>1407/1710 (54.9%)</td>
<td>1132/1356 (54.5%)</td>
<td>275/354 (56.3%)</td>
<td>.423</td>
</tr>
<tr>
<td>MMSE</td>
<td>27.27 (2.32)</td>
<td>27.14 (2.35)</td>
<td>27.80 (2.13)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Logical Mem Del</td>
<td>7.04 (4.76)</td>
<td>6.32 (4.61)</td>
<td>9.90 (4.21)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Trails A (sec)</td>
<td>45.16 (23.48)</td>
<td>45.13 (23.76)</td>
<td>45.30 (22.32)</td>
<td>.869</td>
</tr>
<tr>
<td>Trails B (sec)</td>
<td>142.66 (80.34)</td>
<td>140.41 (78.92)</td>
<td>151.57 (85.19)</td>
<td>.003</td>
</tr>
<tr>
<td>Digit Symbol</td>
<td>36.90 (12.27)</td>
<td>37.02 (12.34)</td>
<td>36.43 (12.01)</td>
<td>.279</td>
</tr>
<tr>
<td>CDR sum of boxes</td>
<td>1.28 (1.13)</td>
<td>1.33 (1.11)</td>
<td>1.11 (1.20)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Mean</td>
<td>1.00 (0/9)</td>
<td>1.00 (0/8)</td>
<td>0.50 (0/9)</td>
<td></td>
</tr>
<tr>
<td>Median (min/max)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GDS</td>
<td>2.49 (2.70)</td>
<td>2.44 (2.62)</td>
<td>2.65 (2.98)</td>
<td>.116</td>
</tr>
<tr>
<td>GDS ≥ 5, % (n)</td>
<td>17.3% (538)</td>
<td>16.6% (414)</td>
<td>19.7% (124)</td>
<td>.068</td>
</tr>
<tr>
<td>FAQ</td>
<td>3.31 (4.97)</td>
<td>3.46 (5.04)</td>
<td>2.71 (4.66)</td>
<td>.002</td>
</tr>
</tbody>
</table>

*Brown et al., 2012*
The relationship of depression, cognitive impairment, and function

Path analysis conducted in MPlus, model includes probit regression coefficients and SEs, and Function as a latent outcome variable. Covariates include age, gender, education, Hachinski and, in each model with Trails B, Trails A

* p < .001; ** p < .0001

Brown et al., 2012
Depression, cognitive impairment, and function in nonaMCI elders

Path analysis conducted in MPlus, model includes probit regression coefficients and SEs, and Function as a latent outcome variable. Covariates include age, gender, education, Hachinski and, in each model with Trails B, Trails A

GDS

\[ .219 (.039)** \]

Digit Symbol

\[ -.314 (.036)** \]

\[ -.200 (.050)** \]

Trails B

Function

Mediation:
- 29% of direct effect of Trails B (after controlling for Trails A) on Fx attributed to Digit Symbol

Brown et al., 2012

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Conclusions:
What we know about functional deficits in MCI?

- Subtle functional deficits occur early in the MCI stage
  - Marker for disease progression:
    - Early fx deficits are associated with deficits in episodic memory and processing speed
    - Fx deficits are associated with medial temporal atrophy
  - Clinical utility: Clinicians can assess specific informant-reported deficits commonly observed in the MCI stage
    - Medication management, remembering appointments, and managing one’s finances.
    - Mindful that the impairment is a “change” from premorbid fx
  - Depression appears to have a direct and indirect effect on function in cognitively impaired individuals
    - Slowing plays an important role in impaired daily activities
Clinical Disease Stage for Dementia

Abnormal

- Amyloid-β (CSF/PET)
- Synaptic dysfunction (FDG-PET/fMRI)
- Tau-mediated neuronal injury (CSF)
- Brain structure (volumetric MRI)
- Cognition
- Clinical function

Clinical Disease Stage

Normal → Preclinical → MCI → Dementia

Sperling et al., 2011
Future Directions

Despite its utility, how will research on function contribute to the field as the focus turns towards “the silent years” of the dementia process?

- Improvements in assessment may play a role
  - Increased breathe of assessment with deficits statistically shown to load on a specific cognitive domain
    - ECog; Farias, 2008
  - Performance measures
    - UPSA (Goldberg’s group)
  - Technological advances:
    - Will improved technology identify subtle deficits in these “silent years” to expand the role of clinical measures as neuropathological techniques continue to advance?
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