Cognitive Impairment: Is there an association with falls?

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Objectives

- To be able to describe the association between cognition and falls
- To be aware of the theories of how cognition may contribute to falls
- To understand how neuroimaging can predict falls
- To be aware of the non-pharmacologic cognitive interventions to reduce falls
- To be aware of the trials using pharmacotherapy to prevent falls in cognitive impairment
- To be aware of the potential role for computerized cognitive training in preventing falls
Epidemiology of Falls

- Falls at least 1/yr (or more)
  - 1/3 community-living adults >65 each year
  - 50% > age 85
  - 80% with neurologic disease
    - Parkinson’s Disease
    - Multiple Sclerosis
    - Stroke
Cognitive Impairment

- 60% with cognitive impairment fall yearly
  - 2x baseline
- Up to 80% with dementia
  - (despite intact motor function)
- Gait alteration may predict Alzheimer's Disease 6-10 years later
  - ?share neural networks
  - ?gait as biomarker for cognitive decline
Mini Mental Status Examination

- Inconsistent data re: MMSE
- Only associated with certain cognitive domains

| Table 3 |
|------------------|-------------|-----------------|--------|
| Logistic Regression Model Estimates for Falls based on MMSE Domain errors in 618 Subjects, 35.7% of whom experienced falls in the most recent 12 months |

<table>
<thead>
<tr>
<th>MMSE Domain</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval (Lower - Upper)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orientation to Place</td>
<td>1.81</td>
<td>1.19 – 2.76</td>
<td>0.006</td>
</tr>
<tr>
<td>Visual Construction</td>
<td>1.67</td>
<td>1.01 – 2.74</td>
<td>0.044</td>
</tr>
</tbody>
</table>

Ramirez et al 2010 Ethn Dis
Executive Function

- Set of higher order cognitive processes
  - Control, integrate, organize, maintain other cognitive abilities
  - Ex. Task planning, problem solving, sensory integration, judgment and reasoning
- Not tested on the MMSE
- Older adults with 2 or more falls
  - Lower EF testing
  - Similar memory scores

Hausdorff et al. Exp Aging Res. 2006
Executive Function

- Baseline EF scores associated with falls in prospective study

Mirelman et al 2012
Attention

- Subset of Executive Function
  - Need to select preferred stimulus while ignoring unnecessary and irrelevant stimuli
    - Selective
      - filtering and suppression
    - Sustained
      - maintain attention over time
    - Divided
      - Ability to carry out multiple tasks at same time
    - Alternating
      - Rapid shifting from one task to another
"May I have your undivided attention, or at the very least, your divided attention?"
Attention - Dual Task

- Paradigms to measure cognitive abilities on gait
  - Ex. Walk and carry water
  - Walk and count backward from 30 by 3’s
- With decreased attention – one of gait or secondary task will deteriorate when performed simultaneously
- DT effects larger in fallers
  - Also larger in patients with stroke, AD, PD
Attention - Dual Task

- Those with reduced EF had more:
  - Stride length variability
  - Postural instability (medio-lateral trunk sway)
  - Gait variability
Reaction Time

- An index of speed of information processing
- Becomes longer with age
- Slow reaction times associated with increased risk of falling

- Fall can be seen as loss of balance with incomplete or late recovery
Depression

- Several studies have shown link to falls
- Severity of depression linked to rate of falls
  - Eggermont et al, 2012
- Prospectively, depression increases odds ratio of falls
  - 1.32-2.2 (Ku et al 2012)
- Depression associated with increased risk of fracture
  - 40-185% increase in distal radial fracture
    - Hwang et al 2011
Theories: Executive function and Falls

- Awareness of one’s environment may modulate posture control, gait and mitigate falls risk
  - Anticipate hazards
  - Plan ahead

- Judgment may also play an important role in the assessment, planning, response to a given situation and choice of the gait pattern
  - Ex.. fast or cautious

- Community dwelling fallers with Executive Dysfunction:
  - Overestimate reach capacity by 16%
  - $c/w$ 2% with no EF deficits

Other Theories

- Judgment in the planning stages of motor activities may be impaired
  - Leads to instability
- Reduced EF causes less effective compensation for age- or disease-associated changes in gait and balance
Cycles of Life

Idyllic Youth

Awkward Adolescence

Experimental Phase

Courtship

Parenthood

Midlife Crisis

Retirement

Eccentric Old Age

Grant Snider
Neuroimaging and Falls

- White matter changes
  - Postural instability
  - Gait disturbances
  - Falls
Neuroimaging and Falls

- Ventricular enlargement/white matter hyperintensity
  - Functional impairment
  - Decline of gait speed

- Less association with Memory/Hippocampal volume and falls
Neuroimaging and Falls

- Fallers had more gray matter loss
  - Areas associated with controlling behaviours with spatial and sensory guidance

Makizako et al 2013
Role of Cognitive Pharmacotherapy

- Methylphenidate and amphetamines designed to increase attention and EF

Ben-Itzhak et al 2008
Parkinson’s Disease and Falls

- Acetylcholinesterase hydrolysis rates lower in PD fallers vs PD non-fallers
- No difference in dopaminergic nerve density
Acetylcholinesterase Inhibitors in PD

- Randomized, cross-over, double blind study

Chung et al 2010
Acetylcholinesterase Inhibitors

- Pilot study in Alzheimer’s Disease

Montero-Odasso et al 2009
Acetylcholinesterase Inhibitors

- Galantamine up to 16mg/day
  - PD
    - less freezing, improvement of gait, less falls (UPDRS scores)
    - Better cognitive scores
      - Litvinenko et al Neurosci Behav Physiol. 2008
  - Mild/Moderate AD
    - Dual-task effects on stride time improved
Vascular Dementia and Dopamine

- Subcortical vascular encephalopathy
  - Most common form of vascular dementia
  - Deficits include frontal and executive function
- Studies showing inconsistent role for Levodopa in improving mobility
- Amantidine
  - Enhanced release of endogenous dopamine
  - Measures of gait performance increased
Vitamin D

- Evidence of reduced risk of falls
- No benefit for falls seen in recent Cochrane review
  - Unless Vitamin D deficient
- ?Effects on cognition
Cognitive Training

- Double blind, randomized control
- 23 patients
- BERG <52 or gait speed <1.1 m/sec
- MMSE <24 excluded

3 Groups:
- Balance training
- Dual Task - Balance training + cognitive tasks (naming objects, remembering numbers)
  - Fixed Priority: Focused on Balance
  - Variable Priority: Alternatively focused on balance and cognitive tasks
- All groups showed improvement in Single Task gait speed
- Only variable priority maintained improvement at 12-week follow-up
Dual Task Training in AD

- Similar results in an RCT, 61 patients with mild-moderate AD
- DT training led to increased performance on DT tasks vs exercise alone
  - DT tasks were calculation exercises
    - (ex. Serial 3’s backwards)
- First Class II evidence of DT treatment in cognitive impairment

Schwenk et al 2010
Computerized Cognitive Training

- Games ‘played’ on the computer
  - 20 older adults assigned to control or computer based DT training (while seated)
  - Effect on postural control

Li et al. 2010
Computerized Cognitive Training

- Pilot study:
  - 24 sedentary adults randomly assigned to computerized training or wait list

Vergheese et al 2010
Virtual Treadmill Training

- 20 patients with Parkinson’s Disease
- Treadmill training for 18 sessions with virtual obstacles
- Dual-task gait variability, Trails A and B, and functional performance measures improved

Mirelman et al 2011
Conclusions

• Some domains of cognition are strongly associated with risk of falls
  ◦ Especially executive function, attention

• Cognitive interventions have effects that carry over to physical function

• By identifying fallers with cognitive impairment, may be able to target non-pharmacologic cognitive therapies to prevent falls

• Not all medications may be bad in falls
  • Consider mental and cognitive well-being
  • Much more work to be done – data very preliminary