Cognitive Functioning in Movement Disorders

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Definitions

• Cognition
  – Thinking and memory
  – Includes both verbal (language) and nonverbal (spatial) functions

• Dementia
  – Decline in cognitive function without alteration of consciousness (alertness)
  – Impairment (more than normal for age) in memory, plus
    • language, spatial cognition, “executive function” (planning, reasoning, problem-solving)
  – Functional impairment
Causes of Dementia

• CORTICAL
  – Alzheimer’s Disease
  – Frontotemporal Dementia
    • Pick’s Disease
    • Motor-Neuron Disease Inclusion Body Dementia
  – Multi-Infarct Vascular Dementia
  – Dementia with Lewy Bodies

• SUBCORTICAL
  – Huntington’s Disease
  – Parkinson’s Disease
  – Subcortical Vascular Dementia
  – Normal Pressure Hydrocephalus
  – Cerebral HIV Infection

Subcortical Dementia

• Related to damage in structures below the cortex (e.g., basal ganglia, brainstem nuclei, thalamic nuclei, cerebral white matter, cerebellum)

• Has many more causes than cortical dementia
  – Depression
  – Vascular dementia
  – Parkinson’s disease
  – Normal pressure hydrocephalus
  – Huntington’s disease
  – Progressive supranuclear palsy
  – Systemic lupus erythematosus
  – Multiple sclerosis
  – Acquired immune deficiency syndrome
Huntington’s Disease

The tendency to insanity, and sometimes that form of insanity which leads to suicide, is marked. I know of several instances of suicide of people suffering from this form of chorea, or who belonged to families in which the disease existed. As the disease progresses the mind becomes more or less impaired, in many amounting to insanity, while in others mind and body both gradually fail until death relieves them of their sufferings.

Huntington’s Disease

- Insidious onset of abnormal movements in mid-life
  - Involuntary movements, esp. chorea and athetosis
  - Impaired voluntary movements and dystonia
- Subcortical dementia
  - Prominent attention and executive dysfunction
- Emotional/motivational disorder
  - Especially irritability, apathy and depression
- Progresses to death in approximately 15 years
- Autosomal dominant inheritance
Huntington’s Disease

The apparent enlargement of the ventricles seen here is due to atrophy of the head of the caudate from neuronal loss in Huntington’s disease, an autosomal dominant condition characterized clinically by choreiform movements.

Parkinson’s Disease

“...involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forwards, and to pass from a walking to a running pace, the senses and the intellects uninjured.”
20.2 CLA S SYMPTOMS OF LATE-STAGE PARKINSON’S DISEASE, including a stooped and rigid posture, shuffling gait, tremor, a masklike facial appearance, and “pill rolling” (inset). (After Markey, 1986.)

Parkinson’s Disease

- Progressive loss of dopaminergic neurons in substantia nigra
Cognition in Parkinson’s Disease

- Dopamine-producing neurons in the substantia nigra send signals to the striatum, a part of the basal ganglia
- Dopamine-producing neurons in the ventral tegmental area send signals to the frontal lobes
- The striatum and cerebral cortex have reciprocal connections; they send information back and forth
- Different parts of the striatum are connected to different parts of the cortex with specialized functions (visual, motor, executive, motivation)

Extra-Pyramidal Motor System

- Cortex
- Putamen
- Substantia Nigra (compacta)
- Subthalamic Nucleus
- GPe
- GPI
- Thalamus (v.i.m.)
- Globus Pallidus
Parkinson’s Disease

- A syndrome characterized by
  - Slowed mentation (bradyphrenia)
  - Deficits in sustained attention and working memory
  - Forgetfulness
  - Impaired planning and judgment
  - Changes in drives and/or mood states (with apathy, irritability, and depression being most common)

- Because subcortical dementia is often caused by diseases causing movement disorders, can also see
  - Dysarthric speech and psychomotor slowing
  - Problems with motor set acquisition and switching

Subcortical Dementia

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Distinguishing Dementia Syndromes

• CORTICAL
  – Amnesia (memory)
  – Aphasia (language)
  – Agnosia (recognition)
  – Apraxia (purposeful movement)
  – Acalculia (calculations)

• SUBCORTICAL
  – Bradyphrenia (slowed thinking)
  – Impaired attention and concentration
  – Inefficient retrieval from memory
  – Executive dysfunction
    • Impaired formation and disengagement of mental sets
    • Poor planning and forethought

Cognition in Parkinson’s Disease

• Over 50% of PD patients experience some form of cognitive impairment

• Difficulties are typically in:
  – Attention
  – Episodic ("short-term") memory
  – Spatial cognition (perception, navigation, calculation)
  – executive functioning (problem-solving, multi-tasking)
Cognition in Parkinson’s Disease

- It is common to have some word-finding difficulties and trouble multi-tasking even very early on in Parkinson’s.
- Need to distinguish these from normal aging and other neurodegenerative diseases (such as Alzheimer’s disease)
- Later on, some PD patients develop more severe problems with thinking and memory
  - This is what we mean by “dementia”

Three Types of Cognitive Disorder in Parkinson’s Disease

- Uncomplicated PD
  - Mild subcortical cognitive impairment
  - Problems with rapid processing, memory retrieval, and multi-tasking
- Parkinson’s Disease Dementia (PDD)
  - Subcortical-type dementia occurring long after the movement disorder
- Dementia with Lewy Bodies (DLB)
  - Cortical-type dementia at or near onset of movement disorder
  - Typically have AD pathology as well
Prevalence of PDD

- **Prevalence of PD**
  - 500,000 Americans currently believed to have PD
  - Approximately 50,000 additional cases diagnosed each year
- **Prevalence of PDD**
  - Cross-sectional prevalence of dementia ranges from 24% to 40% in patients with PD
- **Risk of developing dementia is 4 to 6 times higher in PD compared with similar age people without PD**
Cognitive Profile in PDD

- Impaired memory retrieval
  - Benefit from external cues
  - Preserved recognition

- Executive dysfunction
  - Conceptual reasoning, problem solving, set shifting
  - Planning and sequencing
  - Behavioral self-regulation

- Attention impairment
  - Long reaction times
  - Diminished vigilance
  - Fluctuations

- Visuospatial deficit
  - Visuospatial analysis and orientation

- Bradyphrenia

There are generally no adverse or beneficial effects of levodopa therapy on cognition in moderate-to-severe Parkinson’s disease patients.
Dementia with Lewy Bodies (DLB)

• Also called:
  – Lewy body dementia (LBD)
  – Cortical Lewy body disease
  – Lewy body variant of Alzheimer’s disease

• Similar in many ways to Alzheimer’s disease

• Distinctive features:
  – fluctuating cognition
  – recurrent visual hallucinations
  – spontaneous parkinsonism early
    • rigidity and bradykinesia
    • frequent falls
  – sensitivity to medications (especially neuroleptics)

• More rapid course?
Dementia with Lewy Bodies (DLB)

- Shares features with Parkinson’s and Alzheimer’s diseases
- Same neuropathology (Lewy bodies) as PD, but extends into the cortex
- Unlike PDD, dementia develops at around the same time as parkinsonism
- On testing, visuospatial impairment is prominent and fluctuating attention is often observed

Pentagon copying is more impaired in dementia with Lewy bodies than in Alzheimer’s disease

T A Ala, I F Hughes, G A Kyrouac, M W Ghobrial, R J Ebde
Criteria for Probable DLB

• Progressive cognitive decline, combined with 2 of 3 “core” features:
  – pronounced “fluctuations” in alertness and attention, such as frequent drowsiness, lethargy, lengthy periods of time spent staring into space, or disorganized speech
  – recurrent visual hallucinations
  – parkinsonian motor symptoms, such as rigidity and the loss of spontaneous movement

• Or 1 core feature with 1 suggestive feature:
  – Severe neuroleptic sensitivity
  – REM sleep behavior disorder
## Cognitive Impairment in Very Mild HD Patients with QNE < 19 and MMSE > 29

Means (+ SD)

<table>
<thead>
<tr>
<th></th>
<th>Huntington’s (N=17)</th>
<th>Normal (N=110)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>49.68 (11.09)</td>
<td>37.07 (9.62)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Quantified Neurologic Exam</strong></td>
<td>13.92 (4.00)</td>
<td>2.44 (2.39)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td>15.06 (3.13)</td>
<td>15.05 (2.54)</td>
<td>.99</td>
</tr>
<tr>
<td><strong>Mini-Mental State Exam</strong></td>
<td>29.47 (0.51)</td>
<td>29.60 (0.49)</td>
<td>.61</td>
</tr>
<tr>
<td><strong>Est. WAIS-R I.Q. (2-subtest)</strong></td>
<td>110.06 (14.16)</td>
<td>108.68 (10.58)</td>
<td>.56</td>
</tr>
<tr>
<td><strong>Brief Test of Attention</strong></td>
<td>14.35 (3.14)</td>
<td>17.13 (2.90)</td>
<td>.001*</td>
</tr>
<tr>
<td><strong>Hopkins Verbal Learning Test, delayed recall</strong></td>
<td>9.80 (1.40)</td>
<td>11.42 (1.00)</td>
<td>.022*</td>
</tr>
<tr>
<td><strong>Hopkins Verbal Learning Test, recognition discrimination</strong></td>
<td>10.71 (1.26)</td>
<td>11.53 (0.75)</td>
<td>.002*</td>
</tr>
<tr>
<td><strong>Trail Making Test, part A</strong></td>
<td>38.12 (20.54)</td>
<td>24.59 (8.31)</td>
<td>.001*</td>
</tr>
<tr>
<td><strong>Trail Making Test, part B</strong></td>
<td>91.06 (39.30)</td>
<td>58.21 (18.83)</td>
<td>.001*</td>
</tr>
<tr>
<td><strong>Stroop word reading T-score</strong></td>
<td>42.35 (8.24)</td>
<td>48.35 (7.42)</td>
<td>.001*</td>
</tr>
<tr>
<td><strong>Stroop color naming T-score</strong></td>
<td>42.35 (8.82)</td>
<td>47.51 (7.90)</td>
<td>.016*</td>
</tr>
<tr>
<td><strong>Stroop color-word T-score</strong></td>
<td>42.88 (6.32)</td>
<td>49.15 (7.56)</td>
<td>.006*</td>
</tr>
<tr>
<td><strong>Stroop interference T-score</strong></td>
<td>48.59 (6.78)</td>
<td>50.13 (6.70)</td>
<td>.862*</td>
</tr>
</tbody>
</table>

*Age covaried
Hopkins Verbal Learning Test-Revised in Neurodegenerative Disorders
education-adjusted means ± SEs

NUMBER RECALLED

TRIAL

Alzheimer’s (N=143)
Old Normal (N=102)
Parkinson’s (N=114)
Middle-Age Normal (N=62)
Huntington’s (N=90)
Young Normal (N=38)

Hits minus False-Positives

Alzheimer’s (N=143)  Old Normal (N=102)  Parkinson’s (N=114)  Middle-Age Normal (N=62)  Huntington’s (N=90)  Young Normal (N=38)
The Hopkins Board
A Culture-Fair Test of Verbal and Spatial Learning and Memory

- **Naming**
  - “What are these?”

- **Learning**
  - “Try to remember where I place these pictures.”

- **20’ Delayed Recall of Items**
  - “What were those pictures?”

- **20’ Delayed Recall of Locations**
  - “Where were they?”

[Diagram of the Hopkins Board with nine squares containing various images: a tree, an eye, a bowl, a foot, a flower, an ear, the sun, a nose, and a hand.]
The Hopkins Board
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- Naming
  - “What are these?”
- Learning
  - “Try to remember where I place these pictures.”
- 20’ Delayed Recall of Items
  - “What were those pictures?”
- 20’ Delayed Recall of Locations
  - “Where were they?”

Learning Spatial Locations in Dementia
Brandt et al. (2005)
The Hopkins Board
A Culture-Fair Test of Verbal and Spatial Learning and Memory

- Naming
  - “What are these?”
- Learning
  - “Try to remember where I place these pictures.”
- 20’ Delayed Recall of Items
  - “What were those pictures?”
- 20’ Delayed Recall of Locations
  - “Where were they?”

Verbal and Spatial Memory in Dementia
Brandt et al. (2005)
Discrimination of AD, HD and PD Using the HVLT-R and the Hopkins Board

- Age, education, and MMSE scores were entered first
- Then 3 HVLT-R variables and 5 HB variables allowed to enter stepwise (to minimize Wilk’s lambda)
- Criterion for entry was $F < .05$; criterion for removal was $F > .10$
- Five variables were entered and retained:
  - HB delayed item recall, HVLT-R delayed recall, HB naming, HB trials to criterion, and HVLT-R sum of immediate recall trials (in that order)

<table>
<thead>
<tr>
<th>Step</th>
<th>Variable</th>
<th>Standardized canonical coefficients (Function 1)</th>
<th>Standardized canonical coefficients (Function 2)</th>
<th>Wilk's Lambda</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>HB delayed recall of items</td>
<td>0.634</td>
<td>0.148</td>
<td>0.542</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>2</td>
<td>Age (years)</td>
<td>-0.329</td>
<td>0.091</td>
<td>0.235</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>3</td>
<td>HVLT-R delayed recall</td>
<td>0.525</td>
<td>0.250</td>
<td>0.217</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>4</td>
<td>Education (years)</td>
<td>0.150</td>
<td>0.043</td>
<td>0.117</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>5</td>
<td>HVLT-R total learning</td>
<td>-0.256</td>
<td>0.040</td>
<td>0.211</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>
Scatterplot of AD, HD and PD Cases on Two Canonical Discriminant Functions

Discrimination of AD, HD and PD Using the HVLT-R and the Hopkins Board

<table>
<thead>
<tr>
<th>Original Sample</th>
<th>Predicted Group Membership</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alzheimer</td>
<td>122 (90.4%)</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Huntington</td>
<td>2</td>
<td>42 (66.7%)</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>Parkinson</td>
<td>6</td>
<td>10</td>
<td>59 (78.7%)</td>
</tr>
</tbody>
</table>

Cross-Validation (hold-one-out)

|                 | Alzheimer                  | 122 (90.4%) | 4 | 9 |
|                 | Huntington                 | 3 | 38 (60.3%) | 22 |
|                 | Parkinson                  | 8 | 14 | 53 (70.7%) |

81.7% of original grouped cases correctly classified
Cholinesterase Inhibitors for Parkinson's Disease Dementia

Cochrane Database of Systematic Reviews, 2007

- Rivastigmine appears to improve cognition and activities of daily living in patients with PDD.
- This results in clinically meaningful benefit in about 15% of cases.
Training of executive functions in Parkinson’s disease

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d Institute of Radiology, University of Gießen, Germany
e Department of Neurology, Jacobs-Lysholm University of Gießen, Germany

Abstract

Cognitive disturbances are common in Parkinson’s disease (PD). Examination of cognitive function often reveals deficits in executive functions, including maintenance and inhibition of attention, flexibility in thinking, and planning. The involvement of the dopaminergic system in cognitive executive functions has been suggested by numerous studies. The aim of the present study was to analyze the effect of cognitive training on cognitive performance of PD-patients (N = 26). Half of the patients participated in a cognitive training regimen, while the other patients only received standard treatment. The outcome showed improved performance of the group with cognitive treatment in two executive tasks after the training period, while no improvement was seen in the standard treatment group. The results indicate that specific training is required for improvement of executive functions, while general rehabilitation is not sufficient. Thus, PD-patients might benefit from a short-term cognitive executive function training program that is tailored to the individual patient’s needs.

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