Parkinson’s disease and language processing

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EMCL lecture
Part 1: introduction to Parkinson’s disease (PD)
  - Neuropathology
  - Motor symptoms
  - Cognitive symptoms

Part 2: language processing impairments in PD?
  - The results of my experiments
Parkinson’s disease
Second highest prevalence after Alzheimer’s disease

men = women (≥ 50)
>European population

- Incidence 0.3 per 1000 persons aged 55-65
- Incidence 4.4 per 1000 persons aged 85 and older

(de Lau et al., 2004)

Rocca et al., 2001
> Neurodegenerative

> Progressive
AN ESSAY ON THE SHAKING PALSY.

BY JAMES PARKINSON, MEMBER OF THE ROYAL COLLEGE OF PHYSICIANS.

LONDON: PRINTED BY W. BAILLIE AND SONS, FOR SHEPHERD, NEELY, AND JONES, PATERNOSTER ROW. 1817.
James Parkinson describes a disease of the central nervous system in 6 patients

“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 intellects being uninjured”
Major neuro-pathological feature in PD:
progressive degeneration of dopamine producing neurons in the substantia nigra pars compacta (SNc) and ventral tegmental area (VTA)
Cut section of the midbrain where a portion of the substantia nigra is visible.

Substantia nigra

Diminished substantia nigra as seen in Parkinson’s disease.
Cause
The basal ganglia
Motor en premotor cortex

Dorsolateral Prefrontal cortex
Cortico-striato-cortical circuits
PD pathology
SUMMARY NEUROPATHOLOGY

> The cells of the Substantia Nigra degenerate

> Consequence: a decreased amount of dopamine

- Dysfunctioning of the striatum
- Dysfunctioning of the areas connected to the striatum (fronto-striatal circuits), for example:
  - Motor and premotor cortex
  - Dorsolateral prefrontal cortex
Cardinal motor symptoms
1. Resting tremor
2. Rigidity
3. Akinesia/bradykinesia/hypokinesia

Secondary motor symptoms
1. Freezing
2. Masked face
3. Hypokinetic dysarthria
4. Hypophonia
5. Dysphagia
6. …
Clinical appearance:

- Difficulties arising from chair
- Difficulties walking: slow and with short steps
- Difficulties turning in bed
- Monotone speech
- Drooling
>Movie clip: The Unknown Mr Parkinson
## Non-motor symptoms

<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>% affected after 15 years</th>
<th>% affected after 20 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Falls</td>
<td>81</td>
<td>87</td>
</tr>
<tr>
<td>Fractures</td>
<td>24</td>
<td>35</td>
</tr>
<tr>
<td>Freezing of gait</td>
<td>N/A</td>
<td>81</td>
</tr>
<tr>
<td>Choking</td>
<td>50</td>
<td>48</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>N/A</td>
<td>50</td>
</tr>
<tr>
<td>Urinary incontinence</td>
<td>41</td>
<td>71</td>
</tr>
<tr>
<td>Symptomatic orthostasis</td>
<td>35</td>
<td>48</td>
</tr>
<tr>
<td>Excessive daytime sleepiness</td>
<td>N/A</td>
<td>70</td>
</tr>
<tr>
<td><strong>Depression</strong></td>
<td><strong>50</strong></td>
<td><strong>N/A</strong></td>
</tr>
<tr>
<td>Hallucinations</td>
<td>50</td>
<td>74</td>
</tr>
<tr>
<td><strong>Cognitive decline</strong></td>
<td><strong>84</strong></td>
<td><strong>N/A</strong></td>
</tr>
<tr>
<td><strong>Dementia</strong></td>
<td><strong>48</strong></td>
<td><strong>83</strong></td>
</tr>
<tr>
<td>Employed</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Living in an aged care facility</td>
<td>40</td>
<td>48</td>
</tr>
<tr>
<td>Motor complications</td>
<td>95</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Hely et al., 2005; Hely et al., 2008
Muslimovic et al., 2005

The bar chart illustrates the percentage of impairments in various cognitive functions. The x-axis represents different cognitive functions: psychomotor speed, language, memory, attention/executive functions, and visuospatial skills. The y-axis shows the percentage of impairments ranging from 0 to 100.

- Psychomotor speed shows moderate impairments around 50%.
- Language impairments are relatively low, around 20%.
- Memory impairments are also moderate, around 40%.
- Attention/executive functions show the highest impairments, reaching approximately 90%.
- Visuospatial skills have significant impairments close to 60%.

The data highlights the severe impairments in attention/executive functions compared to other domains.
Executive dysfunction
Visuospatial dysfunction
Memory dysfunction

Visuospatial and memory dysfunctions are secondary to executive dysfunction in PD (Pillon et al., 2003; Higginson et al., 2003)

Language impairments?
Executive functions

> Controlled processing (SAS)
> Crucial for the guiding, directing and management of cognition, emotion and behavior (Strauss, Sherman, Spreen, 2006)
> Planning and regulation of behavior of complex everyday tasks
> New situations / tasks
Blanket term
- Cognitive flexibility
- Inhibition
- Working memory
- Prospective memory
- Planning
- Motivation / Effort
- Monitoring
Executive functions: model
Koerts, Leenders & Brouwer (2009)
Study on language and cognition in Dutch speaking PD patients
General background

>Linguistic impairments in PD patients without dementia

>PD disrupts both language production and comprehension

>PD can compromise most aspects of language processing:
  ▪ Morphosyntax
  ▪ Lexical-semantic
  ▪ Discourse or higher level language abilities
General background

> Debate regarding the nature of the deficit

- Deficit in **language-specific resources** in PD (e.g., Lieberman et al., 1990, 1992; Natsopoulous et al., 1991, 1993; Ullman, 1997)

- Deficit in **cognitive resource system** in PD (e.g., Geyer and Grossman, 1994; Grossman et al., 1992, 1994)

> How are the basal ganglia involved in language processing?
Theories on the involvement of the BG in language processing

1. Lieberman: BG are ‘sequencing engine’ that can reiterate ‘motor patterns generators’ as well as ‘cognitive patterns generators’

2. Ullman: declarative-procedural hypothesis: BG and frontal cortex together constitute the procedural memory system that regulates morphosyntactic aspects of language
Theories on the involvement of the BG in language processing
3. Longworth et al.: domain general inhibitory role of the basal ganglia
4. Friederici & Kotz: role in the late syntactic integration processes (ERP studies)
EXPERIMENTS in PD and HC
> Exp. 1: Sentence comprehension task
> Exp. 2: Verb production task
> Exp. 3: Reading sentences with and without grammatical errors (fMRI)

> Standard neuropsychological tasks
  - Attention (visual, auditory and divided)
  - Working memory (digit span, word span)
  - Set switching (Trail Making Test A/B & Odd Man out)
  - Inhibition (Stroop Color Word Test)
  - Verbal fluency (Letter, Semantic & Action)
  - Abstract sequencing task (Lelekov et al., 2000)
> Subjects:

1. Sentence comprehension & verb production experiment
   > 28 patients with PD (mean age 61.39)
   > 28 healthy subjects (mean age 62.93)

2. fMRI experiment
   > 15 patients with PD (mean age 61.73)
   > 15 healthy subjects (mean age 57.33)
Sentence Comprehension
> Deficit in comprehension of complex syntactic structures: non-canonical constructions such as passives, sentences with center embedded clauses

> Off-line tasks: sentence picture matching or grammaticality judgement tasks

> On-line tasks: priming studies, eyetracking studies, word detection tasks
Total of 80 items

Het paard schopt de koe
The horse kicks the cow

De koe wordt door het paard geschopt
The cow is by the horse kicked
2x2x2 design

e.g. *Short Active*
De vrouw draagt de man.

e.g. *Long Active*
De *goed getrainde* vrouw *met het korte haar* draagt de *sterk vermagerde* man *met de scheiding in het haar.*
Conclusions:

> Identical pattern of errors in both groups
  - Main effect of matching
  - Main effect of syntactic complexity
  - No length effect
  - Matching x length effect
  - Matching x length x syntactic complexity
Conclusions:

> Correlation total score and visual attention
> Correlation passives and
>  - set-switching (Hochstadt et al., 2006; 2009)
>  - digit span backward
>  - inhibition (trend)
> PD patients: no specific morphosyntactic disturbance in comprehension such as in agrammatic patients → limits in set-switching and working memory are responsible
>Coffee break?
Verb production
Ullman et al., 1997

Sentence completion task (past tense)

Conclusion: PD suppression of motor activity and grammatical rule application

Ullman et al. (1997) and Ullman (2001):

- Temporal lobe → declarative memory (mental lexicon)
- Frontal-basal ganglia circuit → procedural memory system (grammar)

Contradiction: Longworth et al. (2005) among found no replication of Ullman’s findings
The boy reads a book.

The boy read yesterday a book.
ceived = matrix

ase = matrix + embedded

de jongen leest een boek. it is de jongen die een boek leest.

he boy reads a book. his is the boy who a book reads.
Statistical analysis:
> Mokken-model (Mokken, 1971) : 45 item scale
> Influence of linguistic variables?
> Error analysis
> Correlation between the verb production scale and cognitive measures/clinical characteristics
The PD-patients scored significantly lower on the ability-scale than the healthy control group.

Dutch speaking patients do have deficits in the production of verbs in sentence context!
Effect of linguistic variables

1. base position < derived position (length)
2. present < past tense
3. intransitive < transitive verbs
Error analysis: overuse the past tense

Table 3 – PD patients’ error percentages above the cut-off score for production of past tense when a present tense is required.

<table>
<thead>
<tr>
<th>Target</th>
<th>Number of analyzable items</th>
<th>Cut-off score in %</th>
<th>Errors in %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present tense</td>
<td>31</td>
<td>1.61</td>
<td>13.59</td>
</tr>
<tr>
<td>Base position</td>
<td>16</td>
<td>3.13</td>
<td>18.75</td>
</tr>
<tr>
<td>Derived position</td>
<td>15</td>
<td>3.33</td>
<td>8.10</td>
</tr>
<tr>
<td>Regular</td>
<td>15</td>
<td>3.33</td>
<td>12.38</td>
</tr>
<tr>
<td>Irregular</td>
<td>16</td>
<td>3.13</td>
<td>14.73</td>
</tr>
</tbody>
</table>

Stuck in set perseverations
Correlation between 45 item scale

- set-switching
- digit span backward (compensation)
Conclusions

> Working memory overload and set switching impairments can lead to verb production deficits in PD
fMRI experiment
Background

> ERP-violation studies: intact ELAN (automatic), but absent/reduced P600 (controlled) (Kotz et al., 2002; Friederici et al., 2003)

> fMRI-study: comparable performance patterns on a sentence comprehension task, but PD patients different activation patterns compared to HC subjects (Grossman et al., 2003)
fMRI Methods: Materials:
> Sentences: 2x3 factorial design
  ▪ Canonicity (active vs. passive)
  ▪ Grammaticality (no-violation, subject-verb-agreement violation vs. argument-structure violation)
> Visual control condition: consonant strings
e.g.: Vm gthsv/ kcrtf/ pg btcpkh/ bcpfhsvhn
### Materials

<table>
<thead>
<tr>
<th>Gram.</th>
<th>Canonicity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Active</td>
</tr>
<tr>
<td>N</td>
<td>De juwelier/ heeft/ de poelier/ getipt.</td>
</tr>
<tr>
<td></td>
<td>The jeweler has the poulterer tipped off.</td>
</tr>
<tr>
<td>I</td>
<td>De juwelier/ heeft/ de poelier/ tipt.</td>
</tr>
<tr>
<td></td>
<td>The jeweler has the poulterer tips off.</td>
</tr>
<tr>
<td>VA</td>
<td>De juwelier/ heeft/ de poelier/ geoproest.</td>
</tr>
<tr>
<td></td>
<td>The jeweler has the poulterer snorted.</td>
</tr>
<tr>
<td>C</td>
<td>Vm gths/ kcrf/ pg btcpkh/ bcpfhsvhn.</td>
</tr>
</tbody>
</table>
Mixed blocked/event related design
> 4 runs (11 min per run): 6 visual control blocks, 5 sentence blocks

Sentence block

* *
* *
* *

Visual control block

cue

240 target sentences
90 fillers
120 consonant strings
> Whole brain analyses
> Region of interest analyses:
  ▪ BA 44
  ▪ BA 45
  ▪ BA 47
  ▪ Nucleus Caudatus
  ▪ Putamen
  ▪ Pallidum
Canonicity (A>P) effect only in HC
Main effect of canonicity
(P>A)

Left anterior prefrontal cortex
(BA 10)
Conclusions

> PD patients fail to exploit sequential syntactic information word order (A vs P) → lose capacity to use heuristics

> Increased recruitment of PFC (BA 10) during reading of P vs A = cortical compensatory mechanism (working memory strategy)

> Disproportionate focus on the inflectional violation in PD (visual features of stimulus?)
Thank you for your attention!