Language impairment and improvement in Parkinson’s disease: what, when, and why

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Introduction

- Parkinson’s Disease (PD) is a progressive disease involving the degeneration of dopaminergic neurons in the basal ganglia.
- Studies have found deficits in language processing in PD, especially in rule-governed grammar; but findings are mixed.

Purpose of study

- Comprehensive examination of the nature and extent of language dysfunction in PD, in particular grammar, by testing multiple aspects of language within subjects: morphology, syntax, lexical processing.
- Expansion of the literature beyond the usual investigation of English-speaking subjects, in Farsi-speaking patients and healthy controls.
- Only patients with moderate-to-severe PD, whose dependencies may extend to fronto-basal ganglia circuits implicated in language.
- Testing whether sex (male vs. female) modulates grammar dysfunction in PD, since females may rely less on basal ganglia-circuits for aspects of grammar.

Previous research on language in PD

- Morphology
  - Initial study from 1997: Patients with advanced PD (high hypokinesia) impaired at producing rule-governed past tense forms (regulars, e.g., walked; and novel verbs, e.g., ‘sleeping’, relative to stored past tense forms (irregular, e.g., slept).
  - Correlation between right-side hypokinesia and performance with novel and existing regular (but not irregular) verbs favored findings since then (2013), though often no group-by-verb-type analyses, and PD patients not advanced.
- Syntax
  - Several studies have found impairment in PD patients in syntactic comprehension compared to controls (2013), but seeRefs. (2012).
  - Fewer studies investigating productions (2018), or judgment (2016).
- Lexical Processing
  - Knowledge of commonly manipulated objects (e.g., ‘hammer’) should rely on motor skills (2014) and conceptual/semantic knowledge (2015) of deactivation.
  - Knowledge of non-manipulated objects (e.g., ‘elephant’) should rely only on deactivation (2013).
  - No study directly comparing PD patients and controls at naming of manipulated vs. non-manipulated objects.
  - Previous work suggests greater impairment of action verbs versus object nouns in PD (2011).

Research Question

How do PD patients perform, within-subjects, on morphological, syntactic, and lexical processing?

Declarative/Procedural (DP) model:

- Learning, storing, and processing of language depends on:
  - Procedural memory (fronto-basal ganglia circuits and dopamine).
  - Rule-governed combination in grammar (in morphology, syntax).
- Declarative memory (hippocampus and other medial temporal lobe structures):
  - Idiosyncratic aspects of language (simple words, irregular morphologies).
  - Can also subserve grammar (e.g., storing complex forms like ‘walked’ as chunks).

Predictions:

- PD patients should show impairments, compared to normal controls (NC), at rule-governed grammar: syntactic processing and regular morphology.
- The grammatical impairments may be more apparent in male than female PD patients, especially for regular morphological forms, which females tend to memorize in declarative memory (due to a female advantage at declarative memory).
- Right-side hypokinesia, which reflects left basal ganglia degeneration, should predict the degree of grammatical impairment.
- Time since last levodopa medication may predict grammatical processing.
- PD patients should show impairments at naming manipulated but not non-manipulated objects.

Methods

Participants

80 native Farsi speakers, 40 with moderate-to-severe PD and 40 normal controls, matched on various factors:

<table>
<thead>
<tr>
<th>PD (n=40)</th>
<th>NC (n=40)</th>
<th>Comparison</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>58.0 (10.3)</td>
<td>59.5 (11.6)</td>
</tr>
<tr>
<td>Education (years)</td>
<td>10.8 (2.7)</td>
<td>10.5 (3.7)</td>
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<tr>
<td>Handedness</td>
<td>3.70 (1.3)</td>
<td>3.72 (1.5)</td>
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<tr>
<td>MMSE</td>
<td>27.4 (1.1)</td>
<td>27.7 (1.1)</td>
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<tr>
<td>Disease stage (FTD)</td>
<td>8.9 (1.7)</td>
<td>8.9 (1.6)</td>
</tr>
<tr>
<td>Time since levodopa (years)</td>
<td>6.5 (2.2)</td>
<td>8.5 (2.3)</td>
</tr>
</tbody>
</table>

Morphology

3-way interaction between group, sex, and verb type: F(2, 37) = 5.83, p = 0.003

<table>
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<tr>
<th>Regular verbs:</th>
<th>Regular novel verbs:</th>
<th>Irregular novel verbs:</th>
</tr>
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<tbody>
<tr>
<td>- group-by-sex interaction: F(3, 8) = 10.76, p = 0.001: more pronounced impairment in males with PD than females with PD</td>
<td>- no group-by-sex interaction: F(1, 21) = 0.79, p = 0.47: main effect of group (impairment in PD patients) across sex</td>
<td>- Irregular: F(3, 28) = 50.96, p = 0.001; Novel: F(3, 28) = 55.30, p &lt; 0.001</td>
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Correlations:

- Role of hypokinesia: Correlations between verb production accuracy and right-side hypokinesia:
  - Regular: r(18) = 0.50, p = 0.001
  - Regular: r(18) = 0.34, p = 0.03
  - Irregular: r(18) = 0.18, p = 0.35
- Role of levodopa: Correlations between verb production accuracy and time since last levodopa medication:
  - Regular: r(18) = -0.65, p = 0.001
  - Regular: r(18) = -0.82, p = 0.001
  - Irregular: r(18) = -0.11, p = 0.47

Syntax

- Lower accuracy for PD patients: F(3, 28) = 64.32, p < 0.001: no effect of sex or sentence-type.
- No correlations with hypokinesia or time since last levodopa medication

Lexical Processing

- Lower accuracy for PD patients who are NCs at naming manipulated objects: F(3, 28) = 7.33, p < 0.001: no effects of sex.
- No correlations with hypokinesia or time since last levodopa medication

Summary

- Regular morphology impaired in PD, but modulated by sex: deficit more pronounced in males.
- Right-side hypokinesia correlates with regular but not irregular morphology.
- Time since last levodopa medication correlates with regulars but not irregulars.
- Syntactic comprehension and judgment impaired in PD; not affected by sex, hypokinesia, or levodopa.
- Phonological impairment but not non-manipulated objects impaired in PD.

Implications

- Grammatical processing impaired in moderate-to-severe PD, across syntax and morph.
- Grammar less impaired in females in morphological: consistent with independent evidence that females tend to memorize regulars.
- Rule-governed morphology depends on left basal ganglia motor circuits and dopamine.
- Syntactic processing may not depend on left basal ganglia motor circuits and dopamine: different mechanisms at work (e.g., working memory).-
- Grammatical impairments in PD found beyond English.
- Knowledge of manipulated objects affected in moderate-to-severe PD.

Conclusions

- Language is impaired in PD – at least in patients with moderate-to-severe disease progression.
- Grammar is particularly affected, with no apparent purely lexical deficits.
- The morphological impairments are modulated by various factors, which also interact.
  - These factors include aspect of language (morphology vs. syntax), right-side hypokinesia, effects left caudate basal ganglia degeneration, time since last levodopa medication, sex, and PD severity.
- The evidence indicates a role for dopamine in aspects of grammar in PD.
- The results are consistent with the predictions of the declarative/procedural model.

References


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