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

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Introduction

- Parkinson's Disease (PD): 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: examination of *Farsi*, in Farsi-speaking patients and healthy controls
- only patients with *moderate-to-severe PD*, whose degeneration may extend to frontal/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[1]:
  - Patients with advanced PD (high hypokinesia) impaired at producing rule-governed past-tense forms (regulars, e.g., *walked*, and novel verbs, e.g., *plagged*), relative to stored past-tense forms (irregulars, e.g., *kept*)
  - Correlation between right-side hypokinesia and performance with novel and existing regular (but not irregular) verbs
- Mixed findings since then[2,3,4,5,6,7], 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[8,9,10]; but see Refs[7,10]
- Fewer studies investigating production[11,12,13,14] or judgment[15,16,17]

Lexical Processing

- Knowledge of commonly manipulated objects (e.g., *hammer*) should rely on motor-skill knowledge (→ procedural memory) and conceptual/semantic knowledge (→ declarative memory)[18]
- Knowledge of non-manipulated objects (e.g., *elephant*) should rely only on declarative memory.[18]
- 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 [19,20,21]

Research Question

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

Declarative/Procedural (DP) model:

- learning, storage, and processing of language depends on:
  - Procedural memory (frontal/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 morphology); 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[22] and 40 normal controls, matched on various factors:

	PD (n = 40)		NC (n = 40)		Comparison
	Males	Females	Males	Females	
Age (years)	63.8 (10.2)	59.3 (7.1)	59.9 (5.8)	59.1 (5.4)	$F(3,76) = 1.78$, $p = 0.15$
Education (years)	10.8 (2.7)	10.5 (3.7)	11.1 (3.6)	12.0 (3.0)	$F(3,76) = 0.79$, $p = 0.50$
Handedness	70.0 (0.1)	72.0 (0.1)	69.0 (0.1)	70.0 (0.1)	$F(3,76) = 0.18$, p =0.90
MMSE	27.6 (1.0)	27.7 (1.1)	27.2 (1.1)	27.7 (0.8)	$F(3,76) = 0.56$, p =0.64
Disease stage[22]	3.4 (0.5)	3.2 (0.4)	N/A	N/A	$t(38) = 0.88$, p =0.45
Right-side hypokinesia	8.9 (2.1)	7.9 (1.6)	N/A	N/A	$t(38) = 1.55$, $p = 0.13$
Time since levodopa (hours)	6.5 (2.2)	6.8 (2.3)	N/A	N/A	$t(38) = -0.425$, p = 0.67

Tasks and Materials

Morphology

Past-tense production, given visually presented stems, of 23 existing regular (e.g., *kesh-keshid* 'pull-pulled'), 23 existing irregular (e.g., *frush-frukht* 'sell-sold'), and 23 novel regular (e.g., *gash-gashid*) Farsi verb forms (matched for syllable count, letter count, and surface-form frequency; all *p*s > .1).

Syntax (from Farsi Bilingual Aphasia Test[23])

1) Comprehension of auditorily presented negative (n = 10), subject-topicalized (n = 10), and object-topicalized (n = 10) sentences assessed using a picture-selection task.
2) Grammaticality judgment of 20 auditorily presented sentences (14 correct, 6 incorrect). All violations were (person, number, case, or voice) agreement errors.

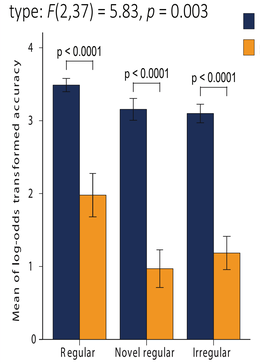
Lexical Processing

Picture naming of 30 objects that are commonly manipulated (e.g., *chakkosh* 'hammer') and 30 that are not (e.g., *fil* 'elephant'), matched on syllable count, letter count, and surface form frequency; all *p*s > .1.

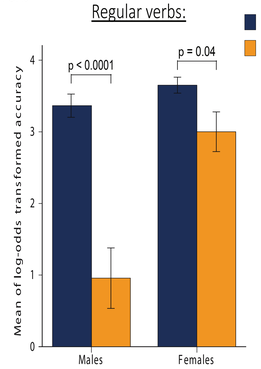
Results

Morphology

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



Regular verbs:



Regular verbs:
- group-by-sex interaction [$F(1,38) = 10.76$, $p = 0.001$]: more pronounced impairment in males with PD than females with PD

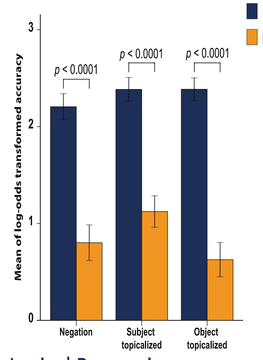
Irregular and novel verbs (not pictured):
- no group-by-sex interaction [irregulars: $F(1,38) = 2.97$, $p = 0.08$; novels: $F(1,38) = 0.50$, $p = 0.47$]
- main effect of group (impairment in PD patients) across sex [irregulars: $F(1,38) = 59.86$, $p < 0.001$; novels: $F(1,38) = 55.30$, $p < 0.001$]

Correlations:

Role of hypokinesia: Correlations between verb production accuracy and right-side hypokinesia:
- Regular: $r(38) = -0.50$, $p = 0.001$
- Novel: $r(38) = -0.34$, $p = 0.03$
- Irregular: $r(38) = -0.18$, $p = 0.25$

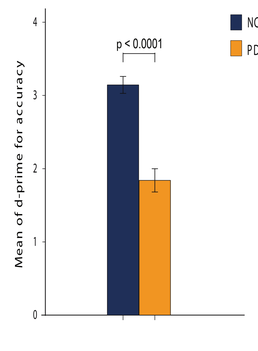
Role of levodopa: Correlations between verb production accuracy and time since last levodopa medication:
- Regular: $r(38) = -0.85$, $p < 0.0001$
- Novel: $r(38) = -0.62$, $p < 0.0001$
- Irregular: $r(38) = -0.11$, $p = 0.47$

Syntax

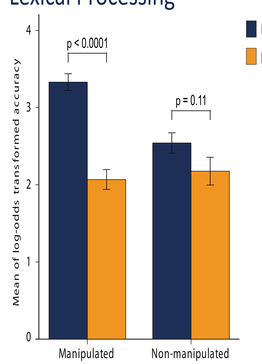


Syntactic Comprehension:
- Lower accuracy for PD patients [$F(1,38) = 64.32$, $p < 0.0001$]; no effects of sex or sentence type.
- No correlations with hypokinesia or time since last levodopa medication

Syntactic Judgment:
- Lower accuracy for PD patients [$F(1,38) = 73.66$, $p < 0.0001$]; no effects of sex.
- No correlations with hypokinesia or time since last levodopa medication



Lexical Processing



Group-by-object-type interaction [$F(1,38) = 23.68$, $p < 0.0001$]:
- Lower accuracy for PD patients than NCs at naming manipulated objects [$t(78) = -7.43$, $p < 0.0001$]
- No group difference for non-manipulated objects [$t(78) = -1.64$, $p = 0.11$]
- No correlations with hypokinesia or time since last levodopa medication

Discussion

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
- Naming manipulated but not non-manipulated objects impaired in PD

Implications

- Grammatical processing impaired in moderate-to-severe PD, across syntax and morphology
- Grammar less impaired in females in morphology: 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 grammatical impairments are modulated by various factors, which also interact.
- These factors include aspect of language (morphology vs. syntax), right-side hypokinesia (reflecting left basal ganglia degeneration), time since last levodopa medication, and sex of the PD patient (male vs. female).
- 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

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