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Parkinson's disease and language processing

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EMCL lecture

Internationaal Parkinson Fonds

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

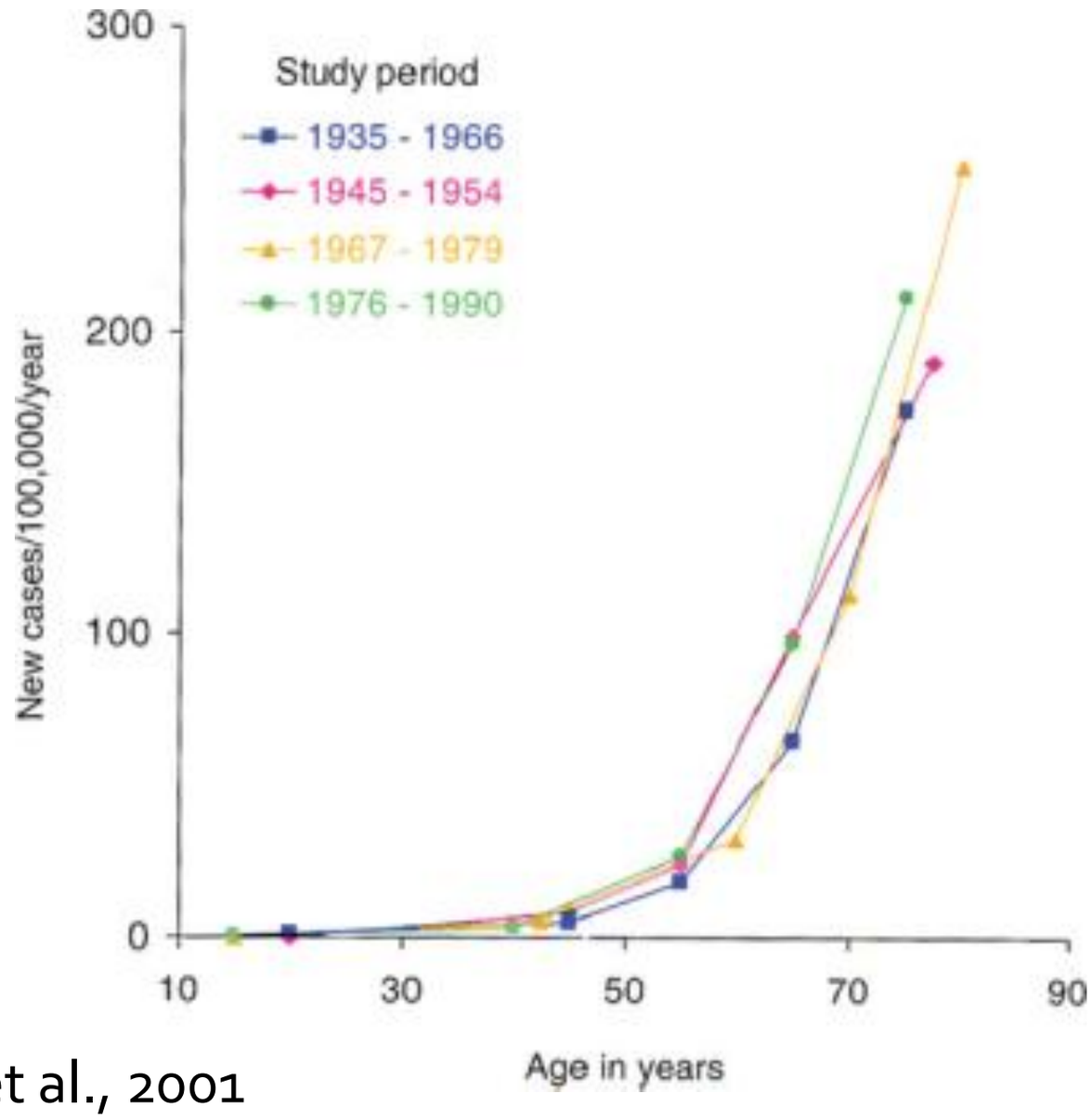
>Second highest prevelance after Alzheimer's disease

>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)

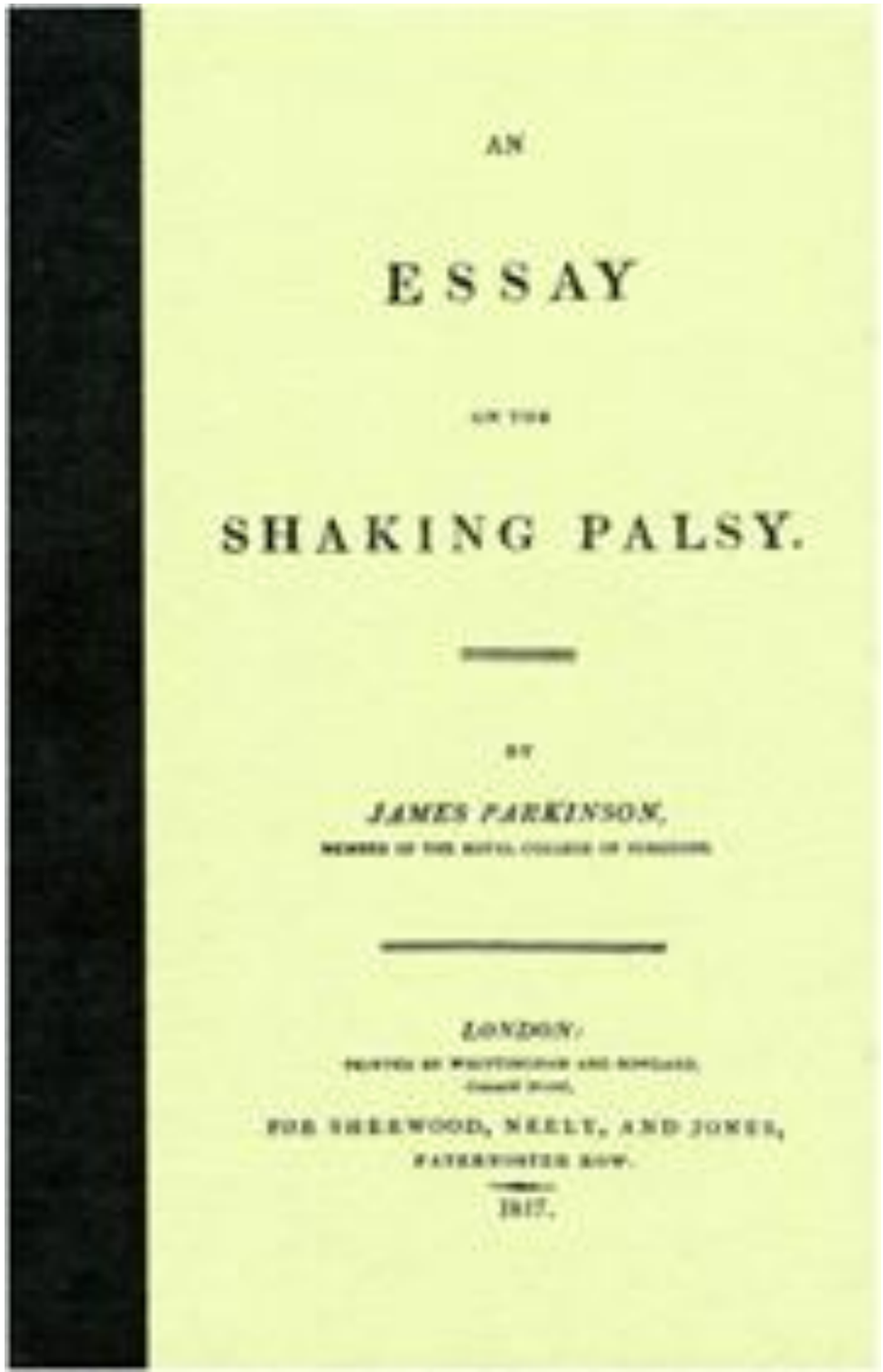


Rocca et al., 2001

>Neurodegenerative

>Progressive

History



AN

ESSAY

ON THE

SHAKING PALSY.

BY

JAMES PARKINSON,

MEMBER OF THE ROYAL COLLEGE OF SURGEONS.

LONDON:

PRINTED BY WHITTINGHAM AND ROWLAND,

Cannon Street,

FOR SHERWOOD, NEELY, AND JONES,

PATERNOSTER ROW.

1817.

History

>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"*

Cause

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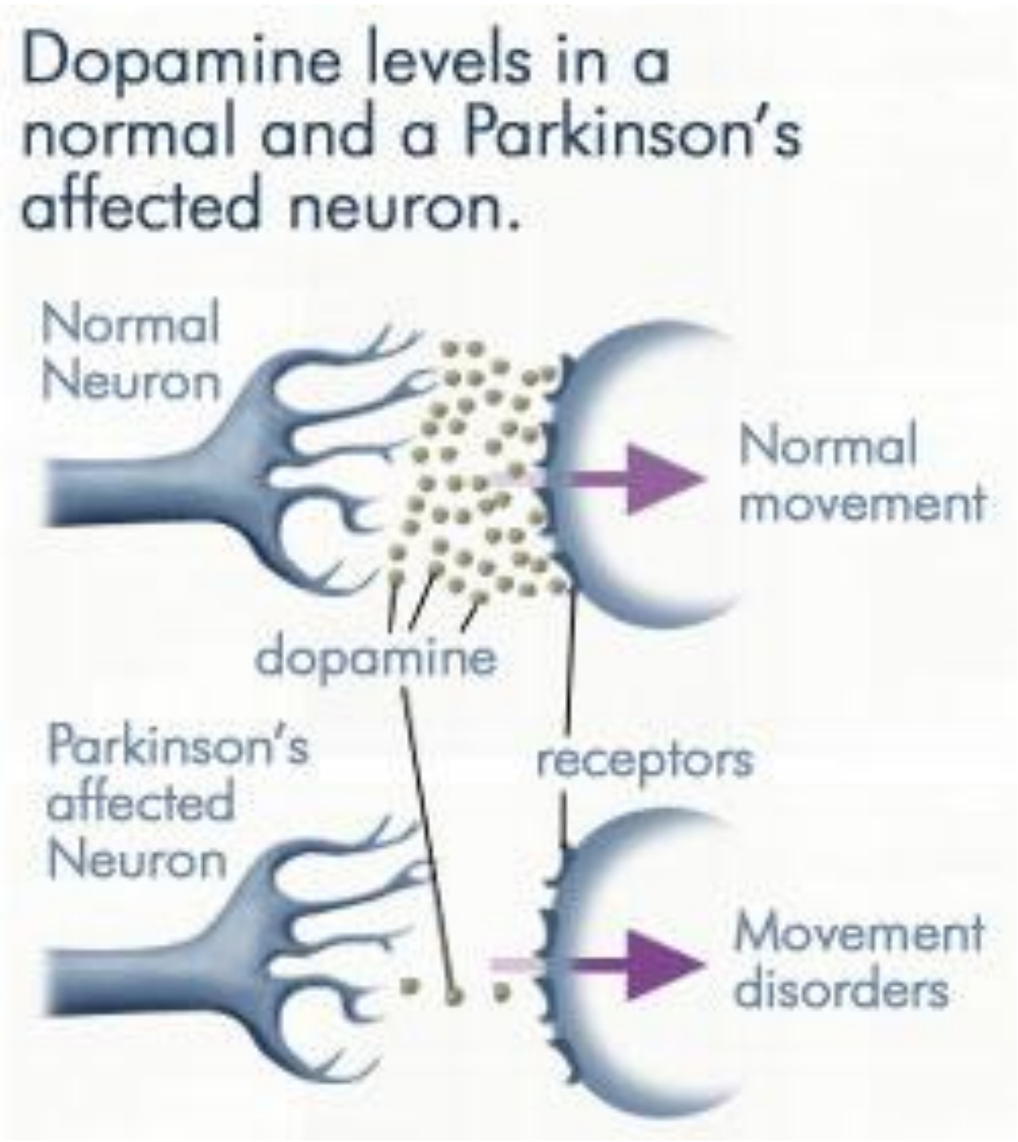
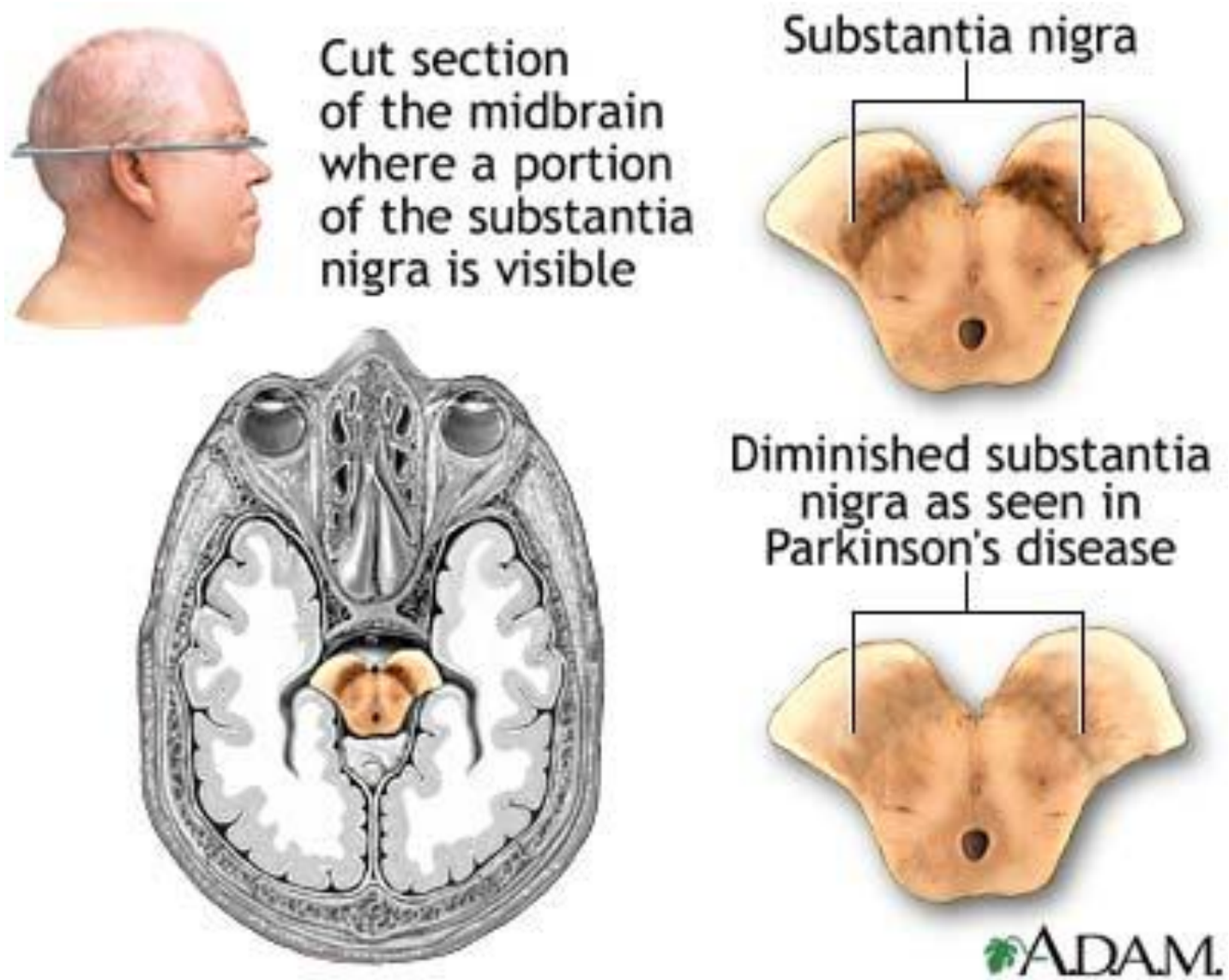
Major neuro-pathological feature in PD:

progressive degeneration of dopamine producing neurons in the substantia nigra pars compacta (SNc) and ventral tegmental area (VTA)



Cause


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
A.D.A.M.

Cause

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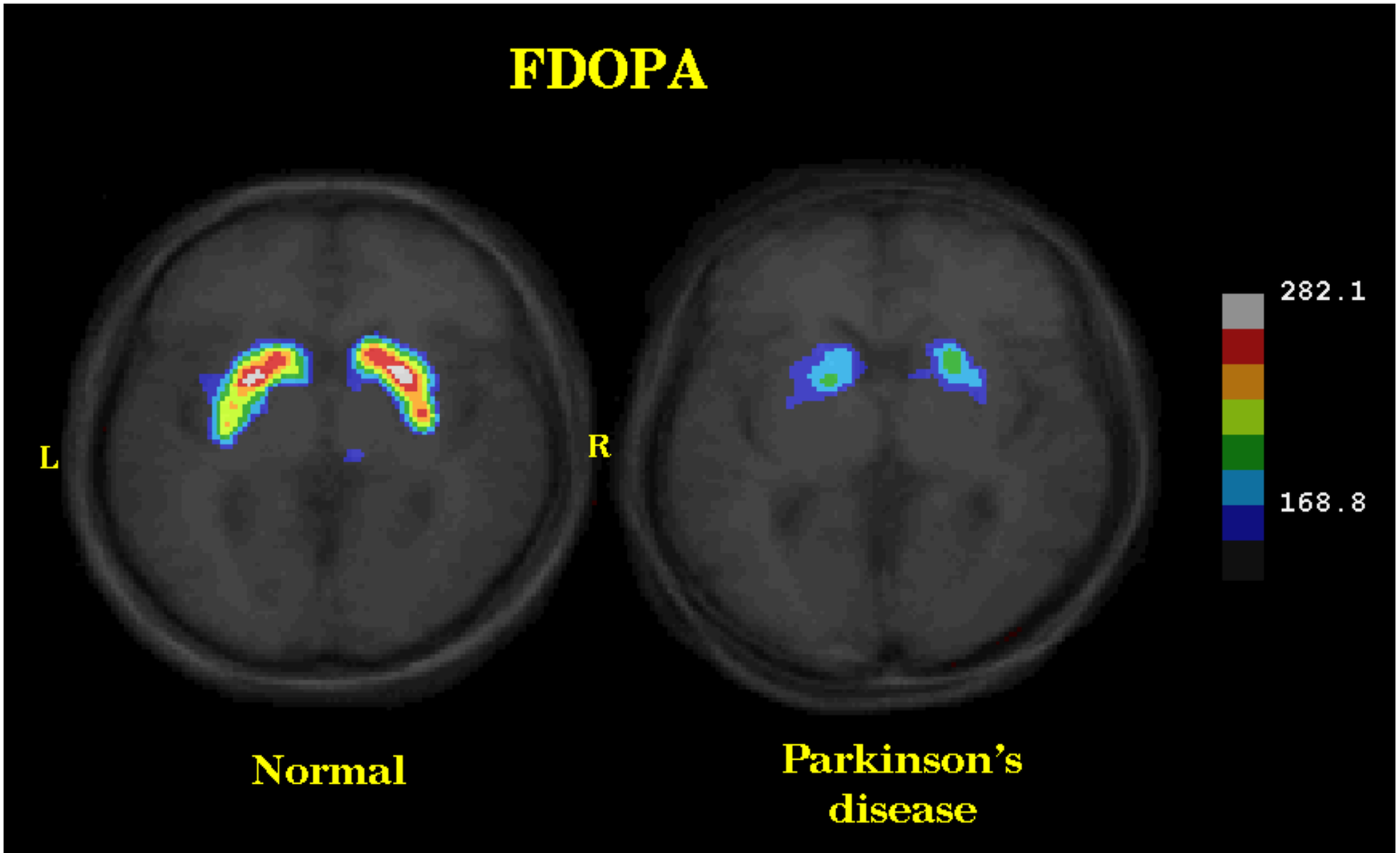
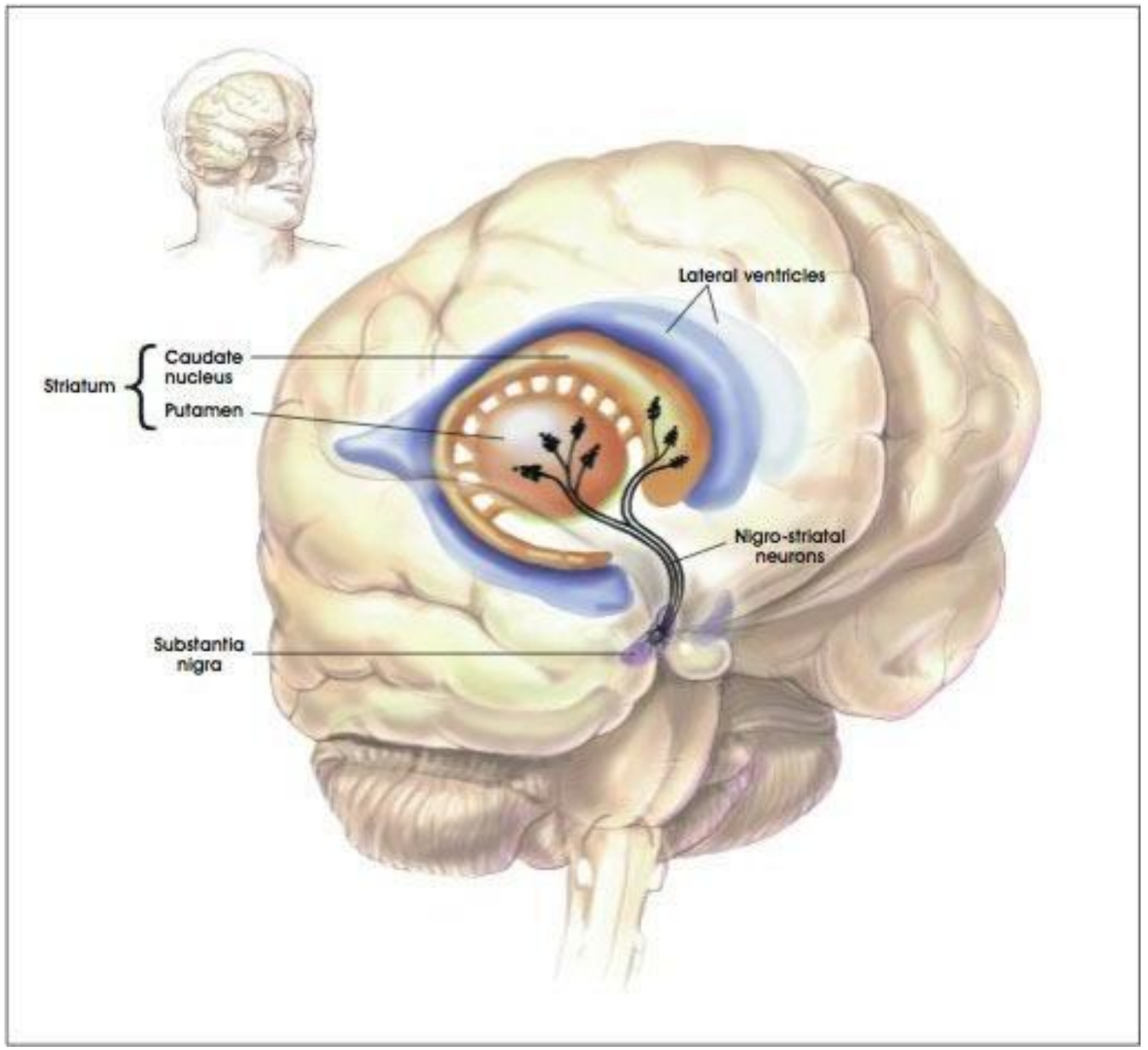


Cause


Lateral ventricles
Striatum
Caudate nucleus
Putamen
Nigro-striatal neurons
Substantia nigra

Cause

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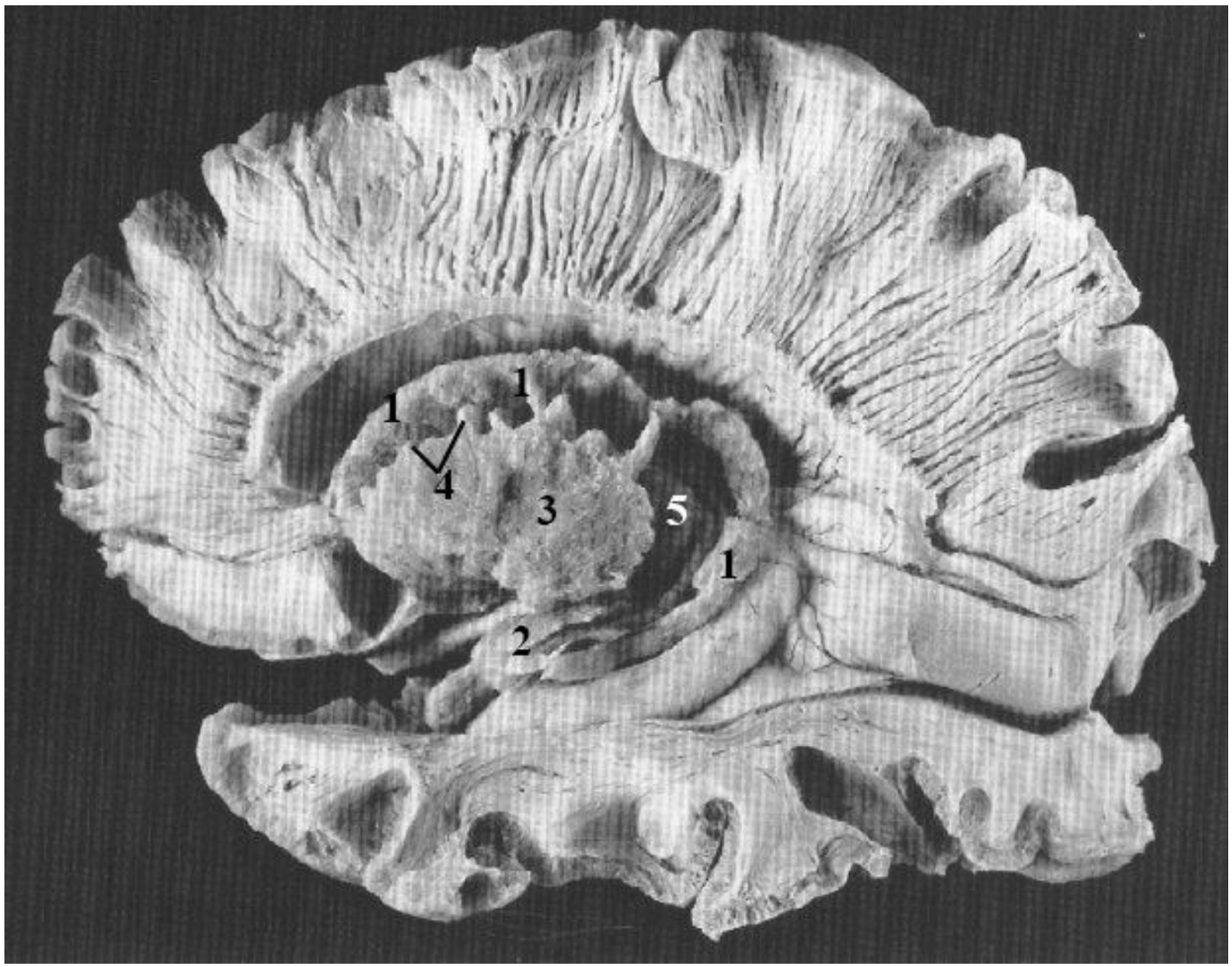
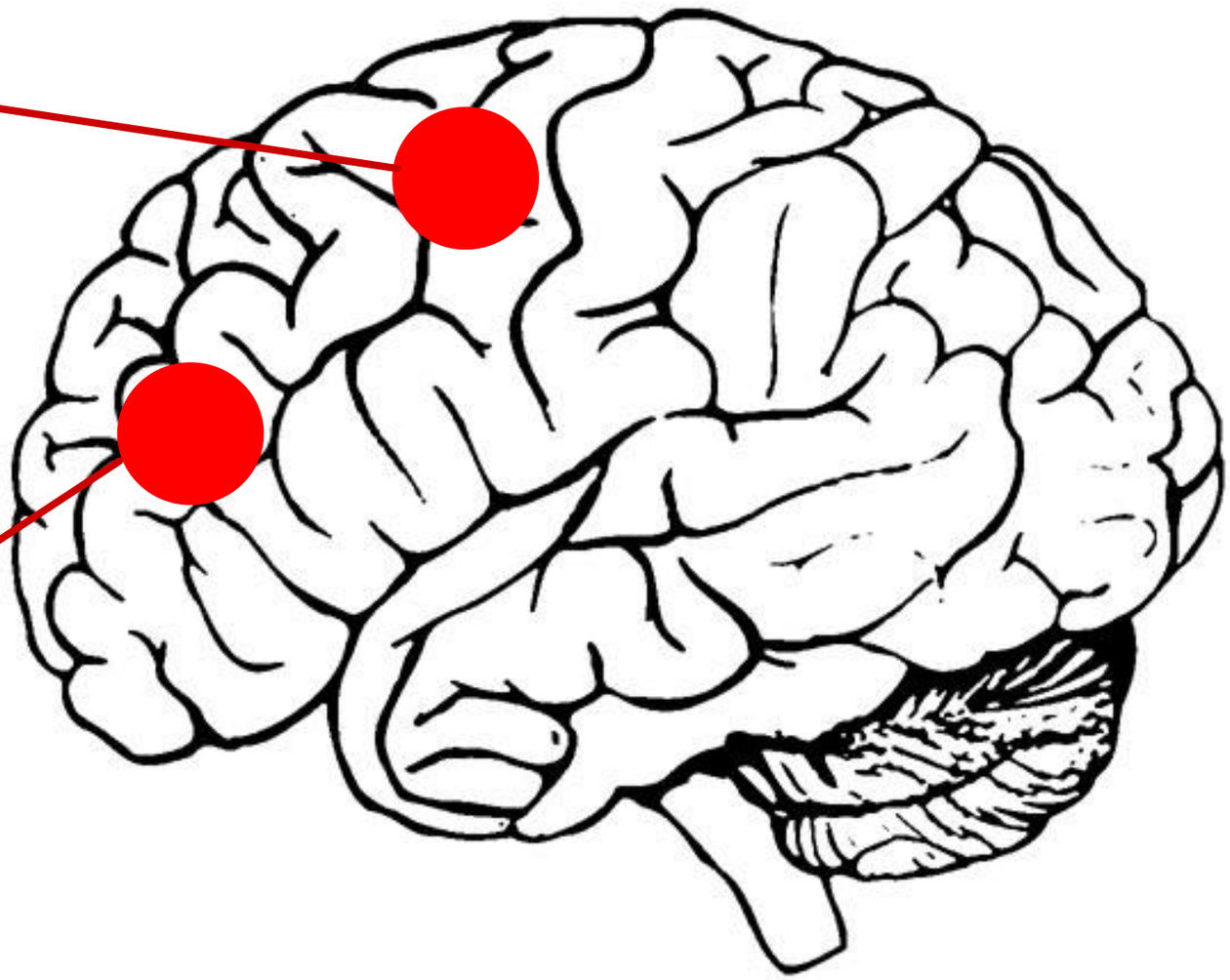
The basal ganglia



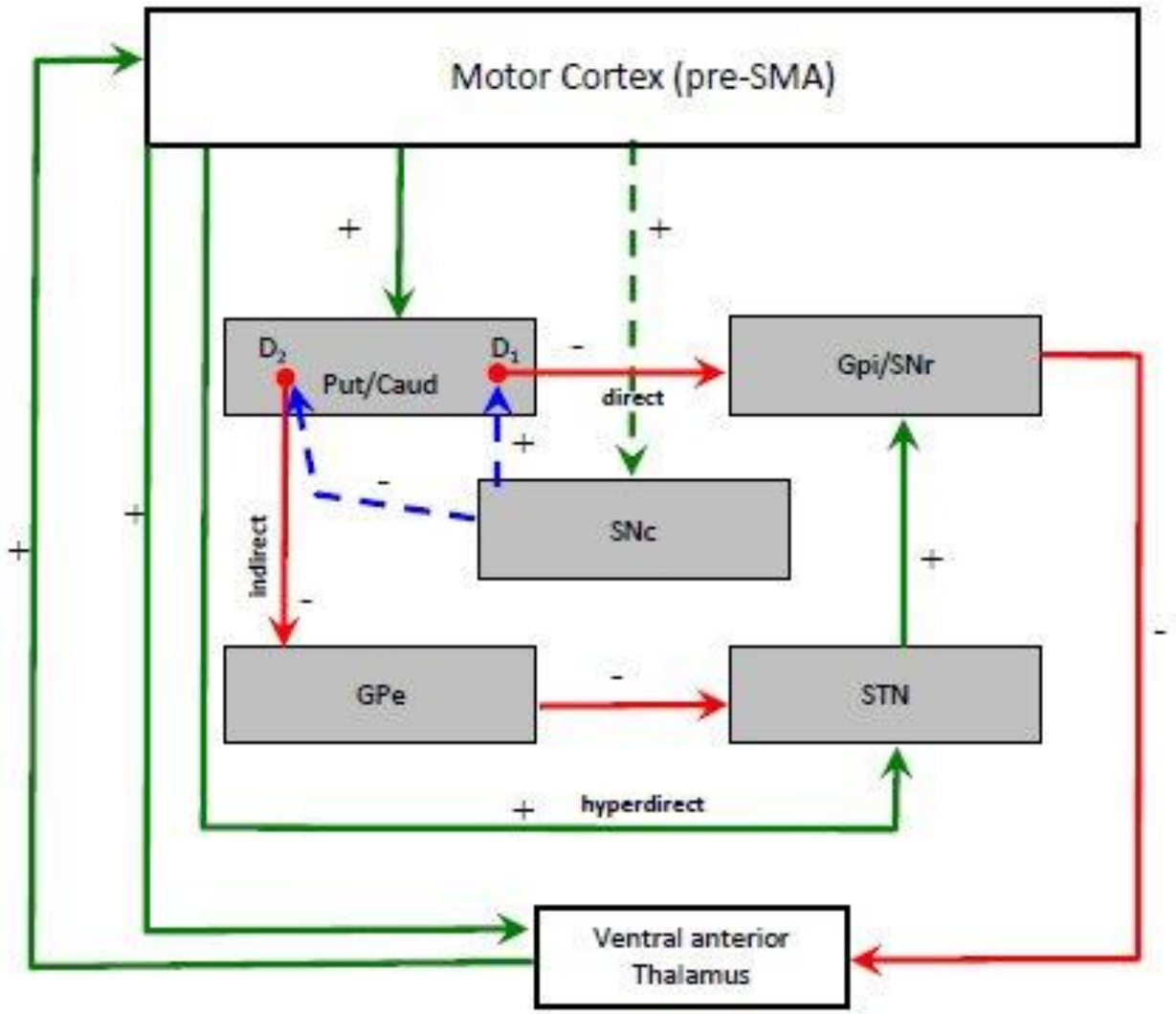
Cause

Motor en premotor cortex

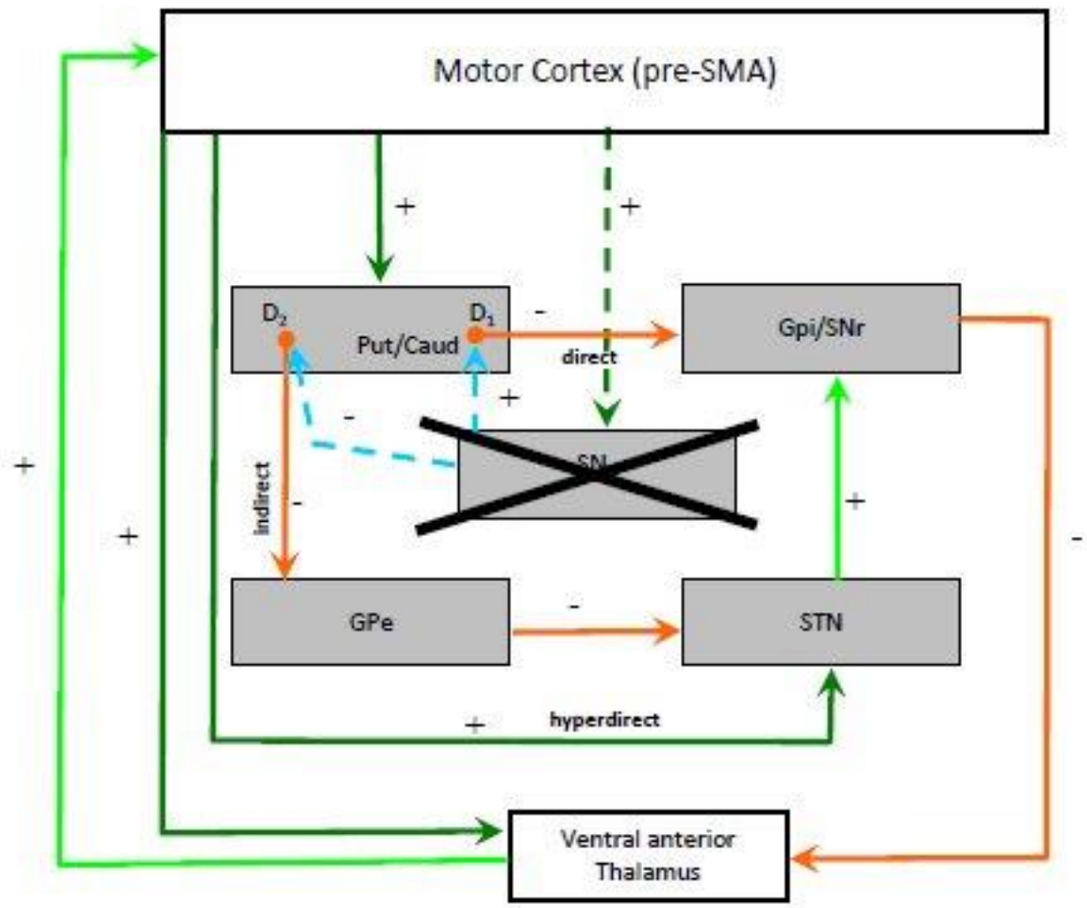


Dorsolateral Prefrontal cortex

Cortico-striato-cortical circuits



PD pathology



SUMMARY NEUROPATHOLOGY

>The cells of the Subtantia 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

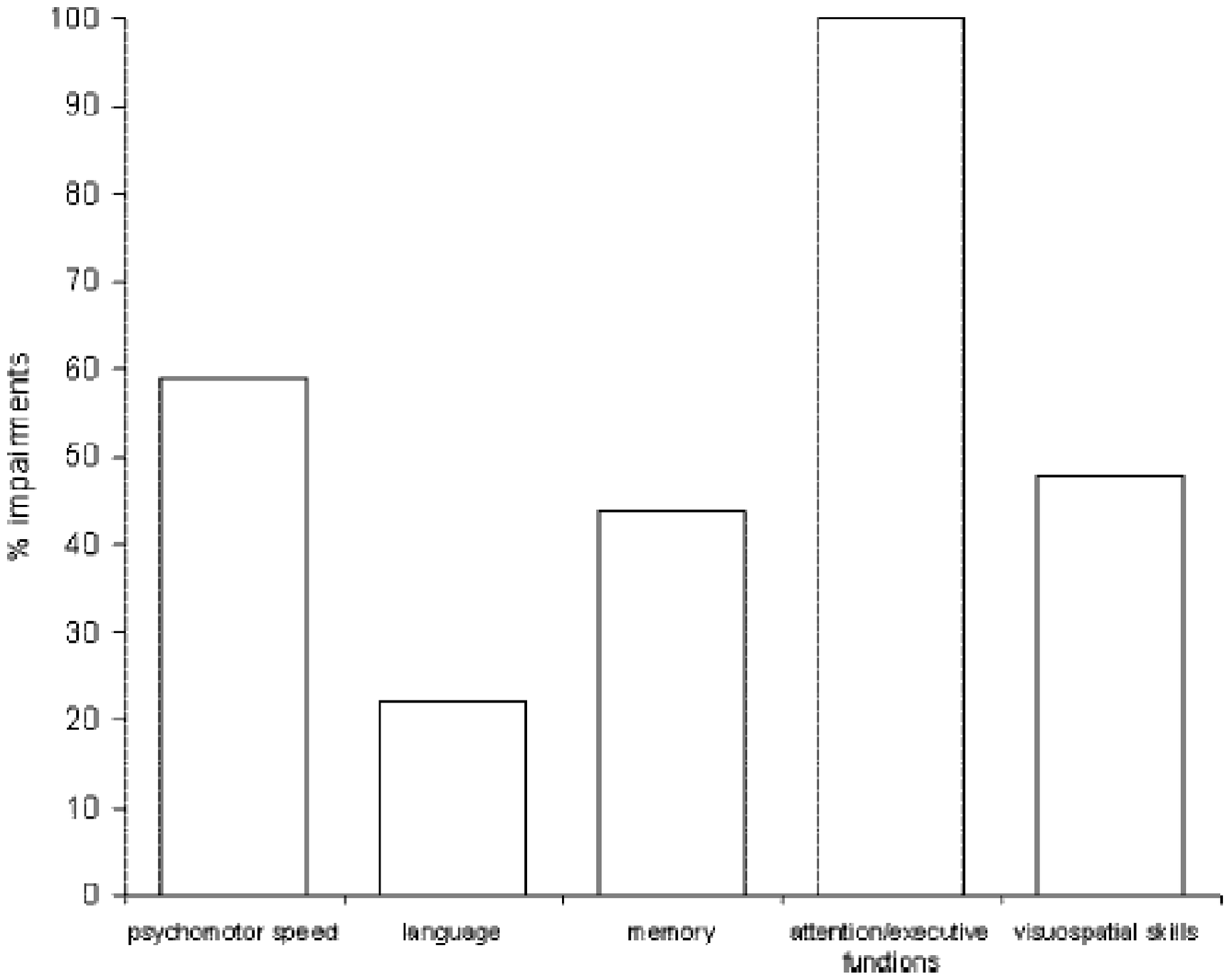
>Movie clip: The_Unknown_Mr_Parkinson

Non-motor symptoms

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

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

Cognition



Muslimovic et al., 2005

Cognition

>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

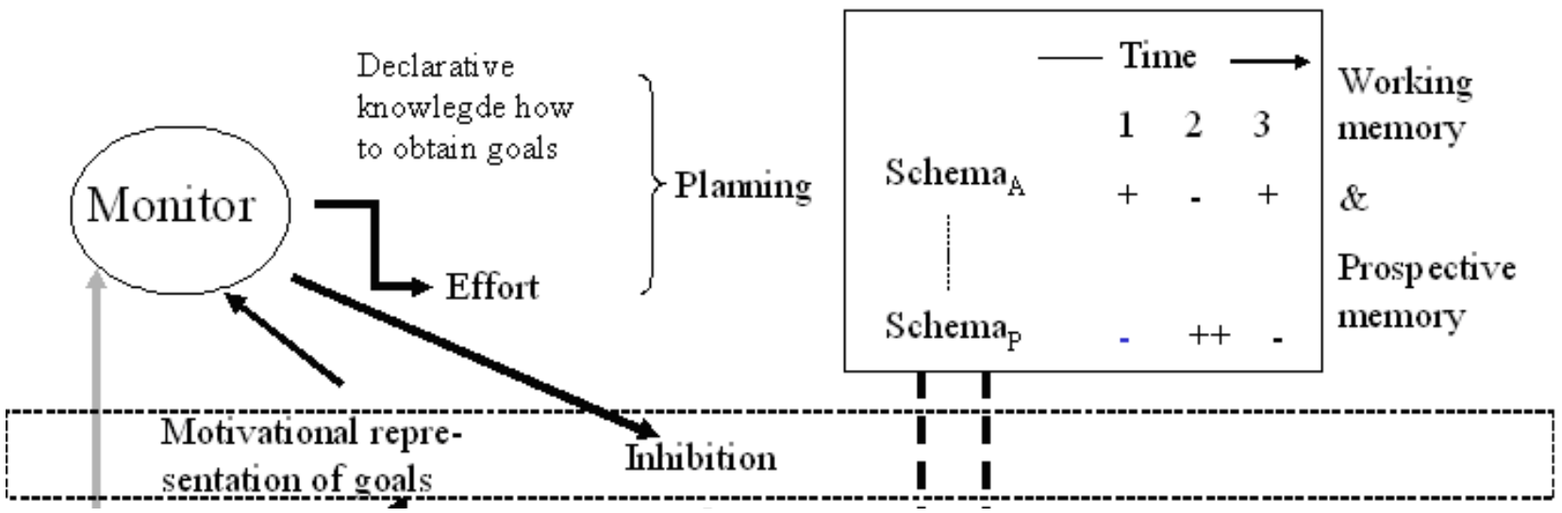
>New situations / tasks

Cognition

>Blanket term

- Cognitive flexibility
- Inhibition
- Working memory
- Prospective memory
- Planning
- Motivation / Effort
- Monitoring

Executive functions: model Koerts, Leenders & Brouwer (2009)



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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; Natsopoulos 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)

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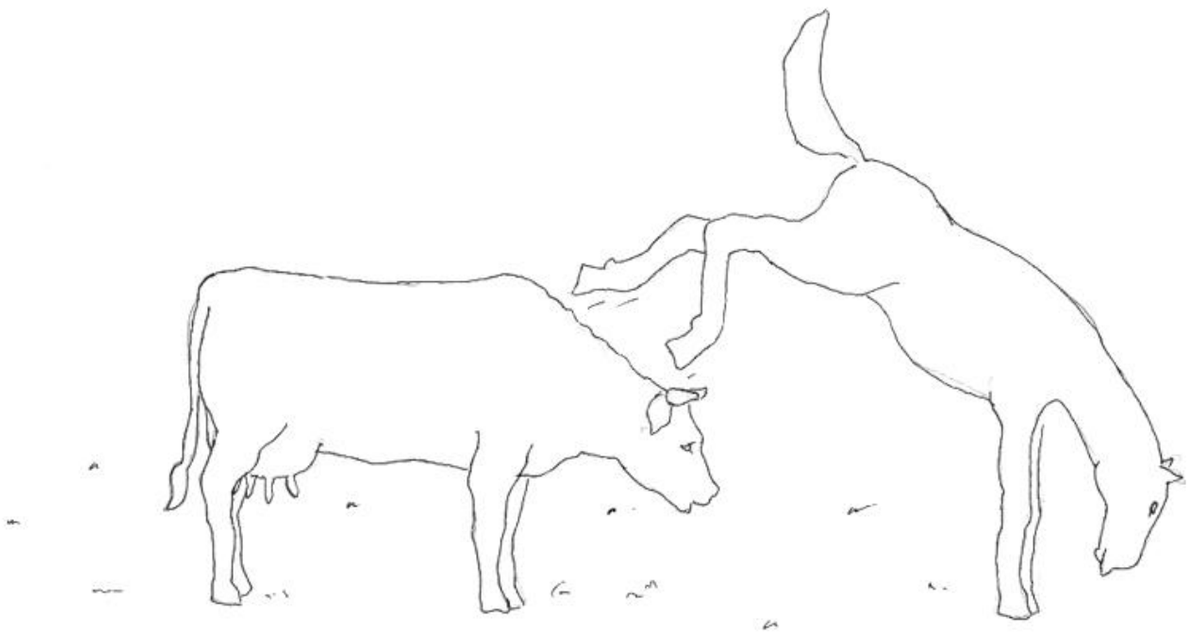
Sentence Comprehension

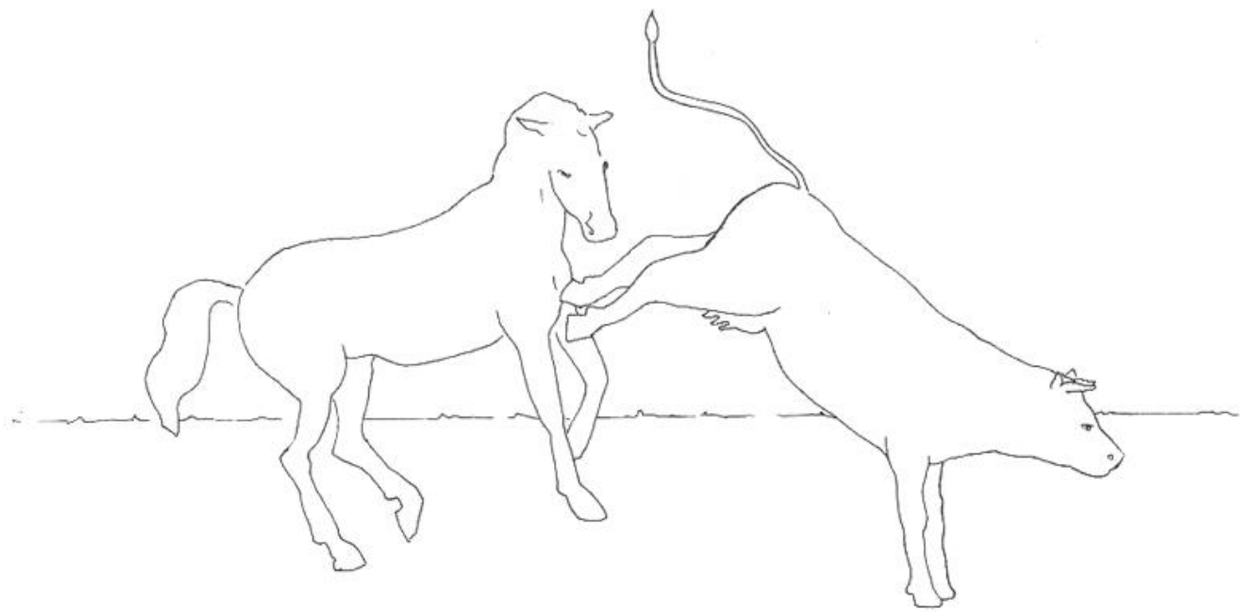
- Deficit in comprehension of complex syntactic structures: non-canonical constructions such as passives, sentences with center embedded clauses
- Off-line tasks: sentence picture matching or grammaticality judgement tasks
- On-line tasks: priming studies, eyetracking studies, word detection tasks

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?

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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

r esent

. e j ongen l eest een boek.

he boy r eads a book.

ast

. e j ongen l as gi st er en een boek.

he boy r ead yest er day a book.

erived = matrix

e jongen Leest een boek.

he boy reads a book.

ase = matrix + embedded

it is de jongen die een boek Leest .

his is the boy who a book reads.

Statistical analysis:

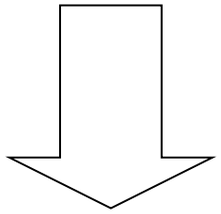
>Mokken-model (Mokken, 1971) : 45 item scale

>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.

Target	Number of analyzable items	Cut-off score in %	Errors in %
Present tense	31	1.61	13.59
• Base position	16	3.13	18.75
• Derived position	15	3.33	8.10
• Regular	15	3.33	12.38
• Irregular	16	3.13	14.73

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

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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)

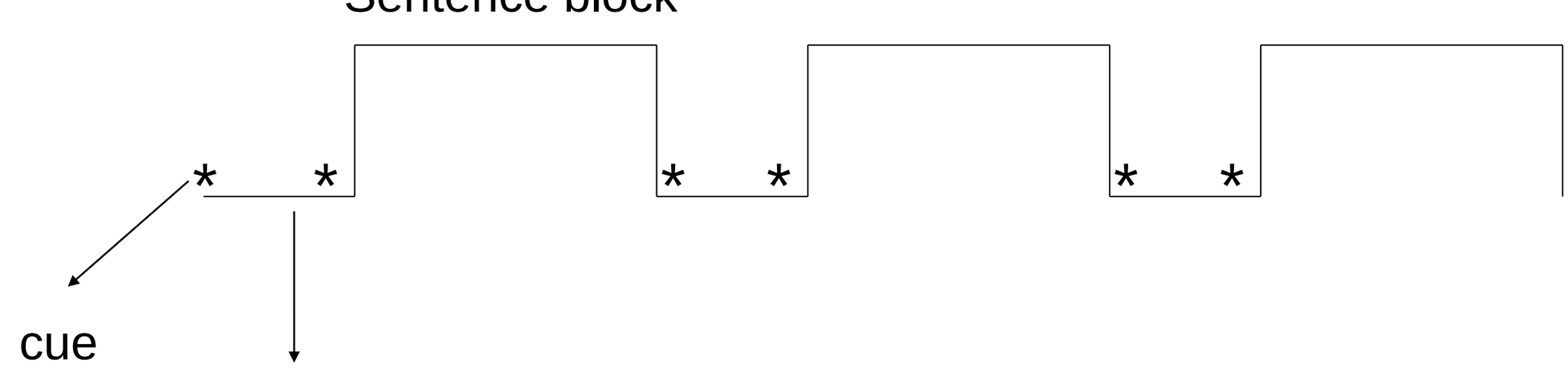
>Visual control condition: consonant strings

e.g.: Vm gthsv/ kcrtf/ pg btcpkh/ bcpfhsvhn

Materials

Gram.	Canonicity	
	Active	Passive
N	*De juwelier/ heeft/ de poelier/ <u>getipt.</u>* The jeweler has the poulterer tipped off.	*De pater/ wordt door/ de militair/ <u>getipt.</u>* The father is by the soldier tipped off.
I	*De juwelier/ heeft/ de poelier/ <u>tipt.</u>* The jeweler has the poulterer tips off.	*De pater/ wordt door/ de militair/ <u>tipt.</u>* The father is by the soldier tips off.
VA	*De juwelier/ heeft/ de poelier/ <u>geproest.</u>* The jeweler has the poulterer snorted.	*De pater/ wordt door/ de militair/ <u>geproest.</u>* The father is by the soldier snorted.
C	Vm gthsv/ kcrtf/ pg btcpkh/ bcpfhsvhn.	Vm mglbsfv/ vsntf hmcg/ pg vbntjsg/ kjgpfvbgsd.

- Mixed blocked/event related design
- 4 runs (11 min per run): 6 visual control blocks, 5 sentence blocks



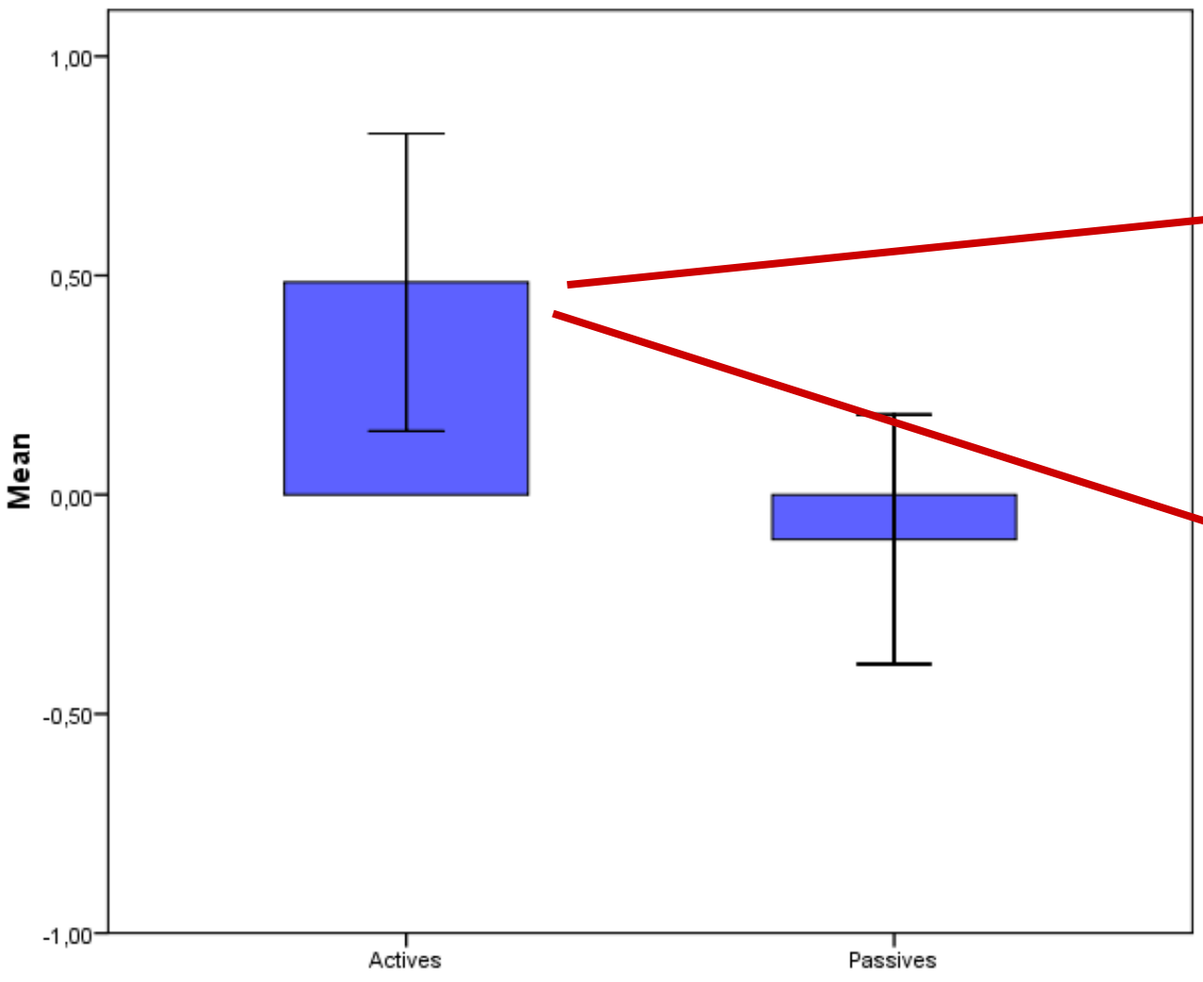
240 target sentences

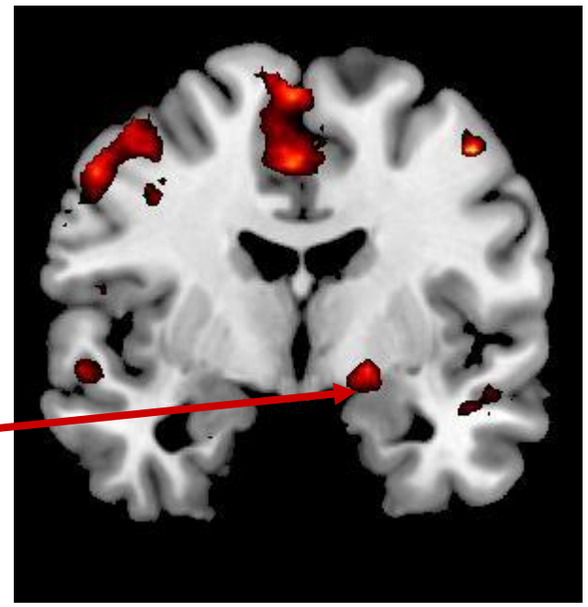
90 fillers

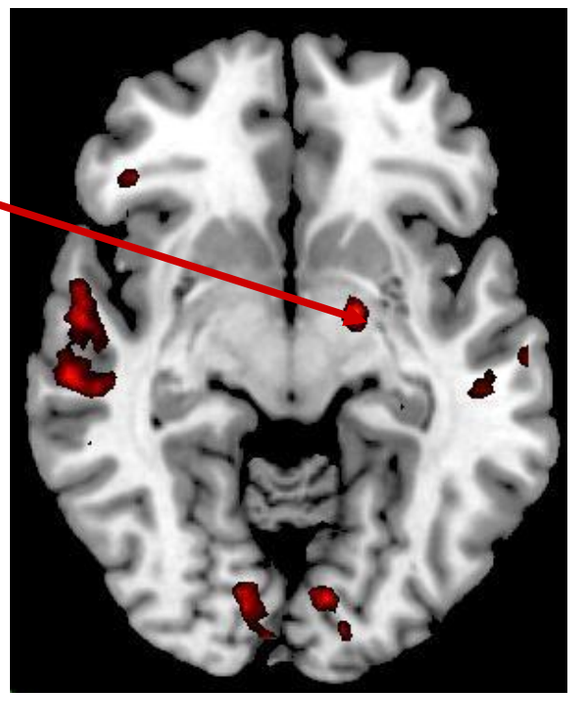
120 consonant strings

- Whole brain analyses
- Region of interest analyses:
  - BA 44
  - BA 45
  - BA 47
  - Nucleus Caudatus
  - Putamen
  - Pallidum

Canonicity (A>P) effect only in HC

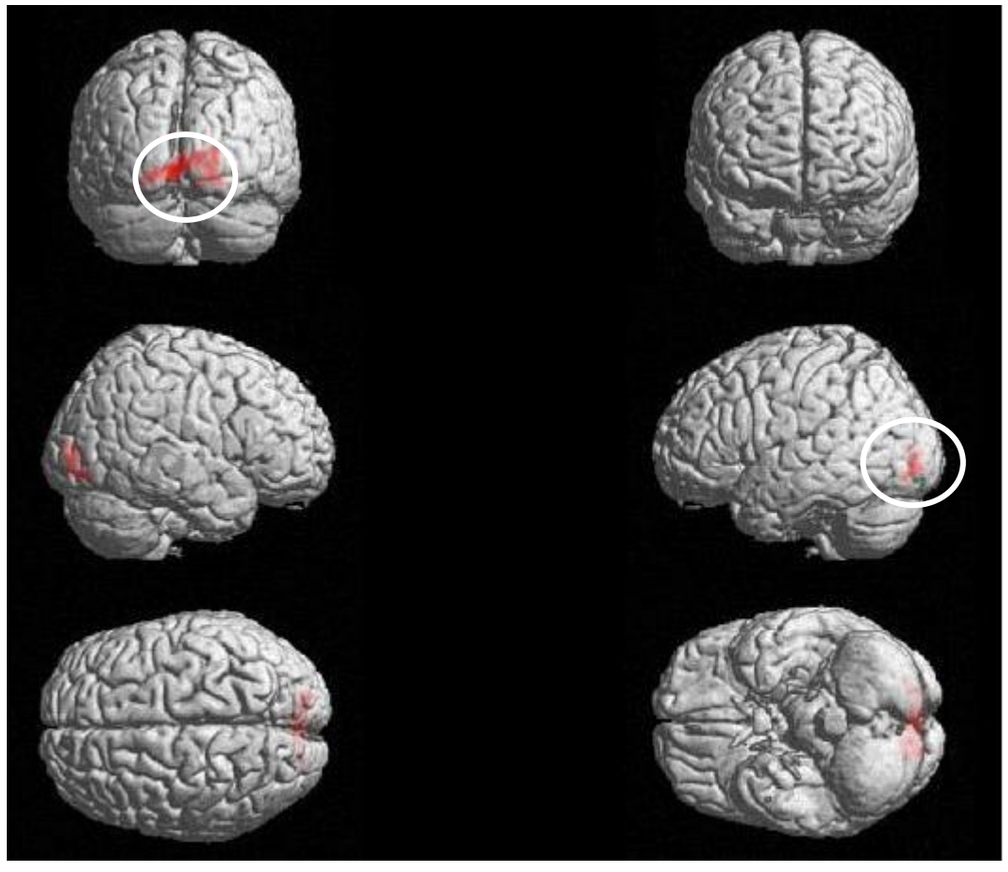




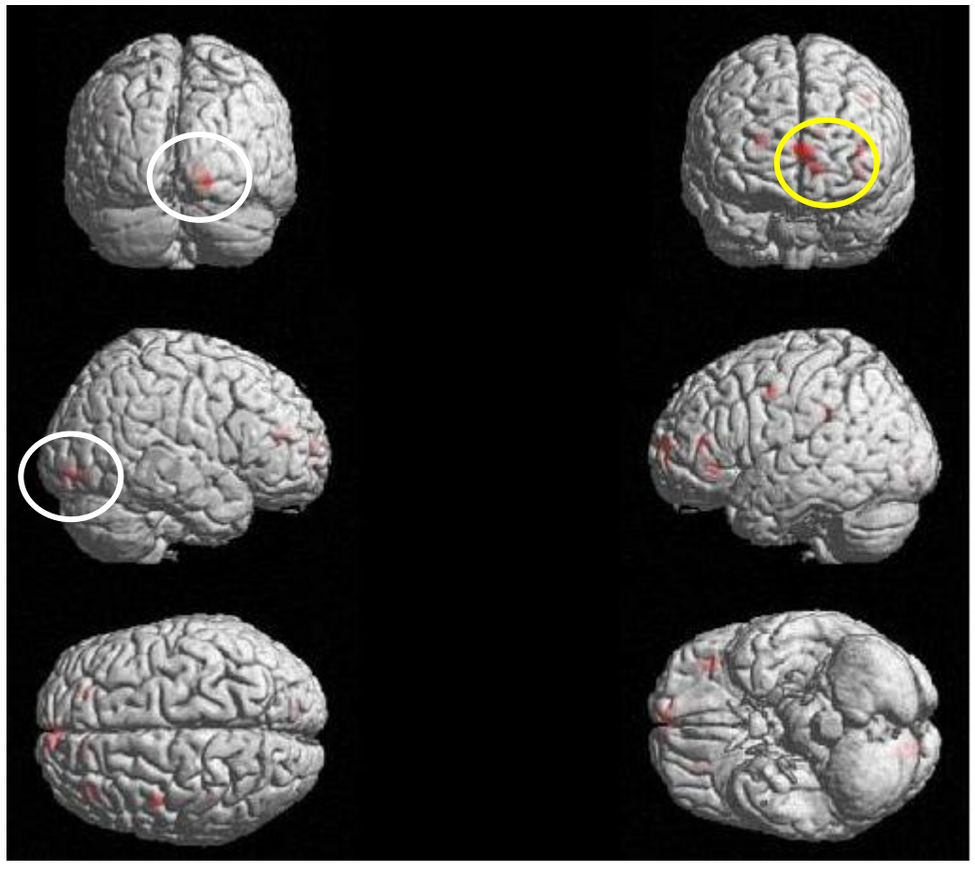


Main effect of canonicity (P>A)

HC



PD



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!