

**Non-Motor Symptoms of
Parkinson's Disease:
Quality of Life Beyond Tremor Control**

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George Washington University / Medical Faculty Associates**

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No Financial Disclosures

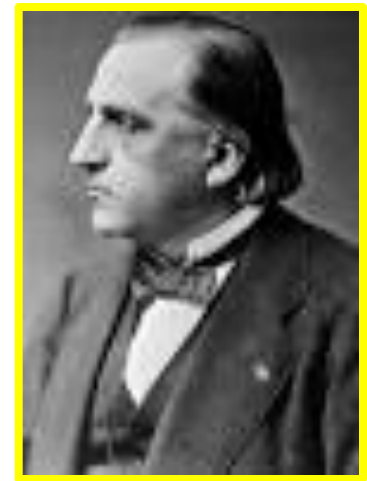
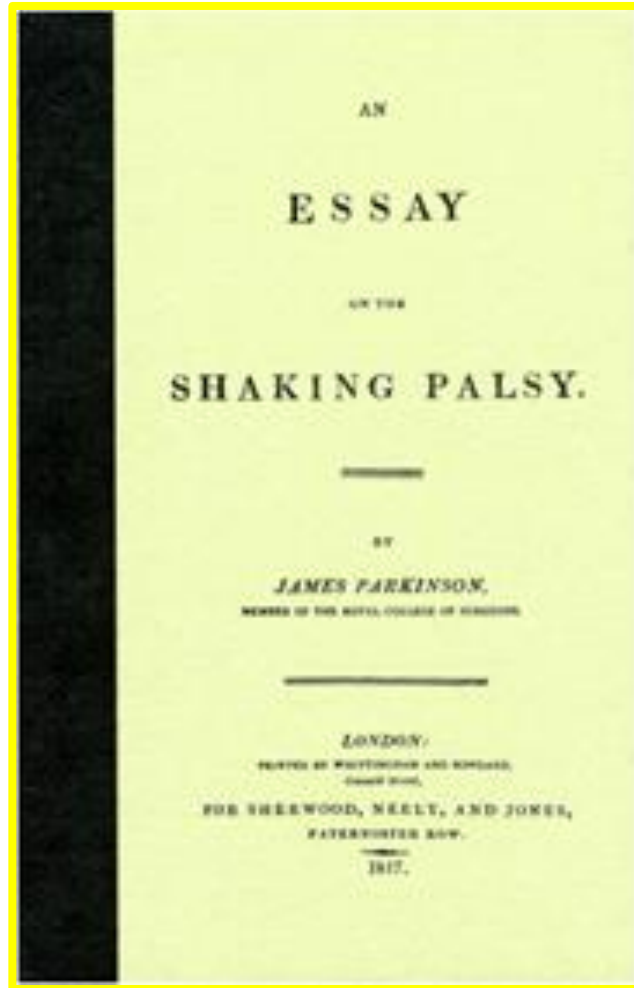
Learning Objectives

- **To describe common non-motor symptoms (NMS) in Parkinson's disease**
- **To discuss some non-pharmacologic and pharmacologic approaches to managing NMS**
- **To recognize the importance of discussing NMS with your neurologist and primary care provider**
- **To recognize the value of promoting communication between your doctors**

Outline

- **Non-Motor Symptoms (NMS)**
- **NMS Timeline**
- **NMS and Dopamine**
- **Focus: 3 Common NMS Disturbances**
- **Take-Home Messages**

Parkinson's Disease



<http://www.allaboutparkinsons.com/james-parkinson.html>

<http://www.sciencemuseum.org.uk/hommedia.ashx?id=91831&size=Small>

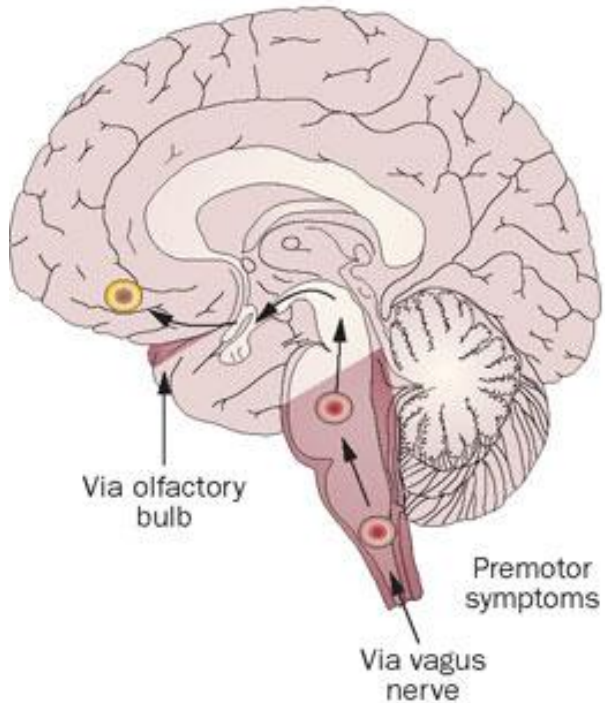
Parkinson's Disease: Cardinal Features

- Bradykinesia -- slowness executing movement
“paucity” of movement
- Muscular Rigidity -- increased tone
velocity-independent
cogwheel = rigidity + tremor
- Postural Instability -- primary
not visual, proprioceptive,
vestibular, cerebellar
- Rest Tremor -- “pill-rolling,” asymmetric

Cardinal Pathology: Lewy Bodies

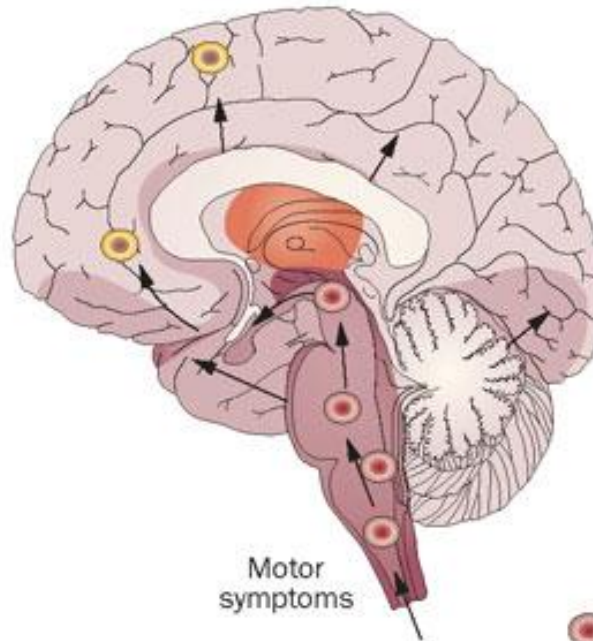
Braak stages 1 and 2

Autonomic and olfactory disturbances



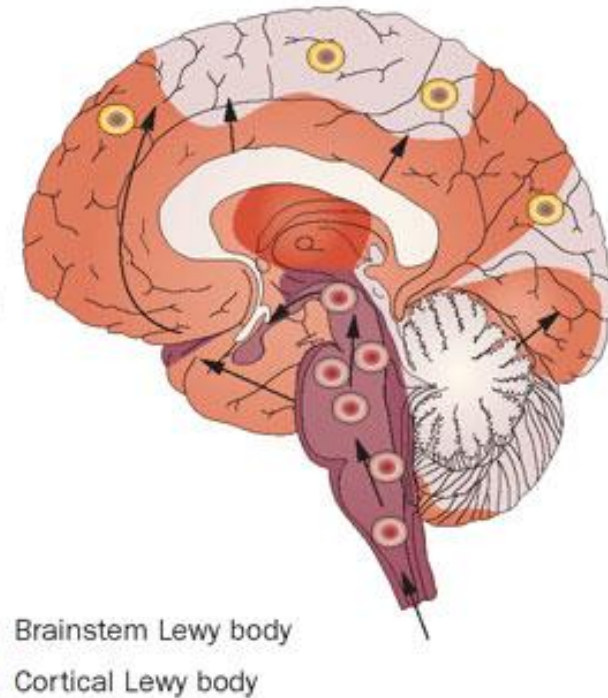
Braak stages 3 and 4

Sleep and motor disturbances

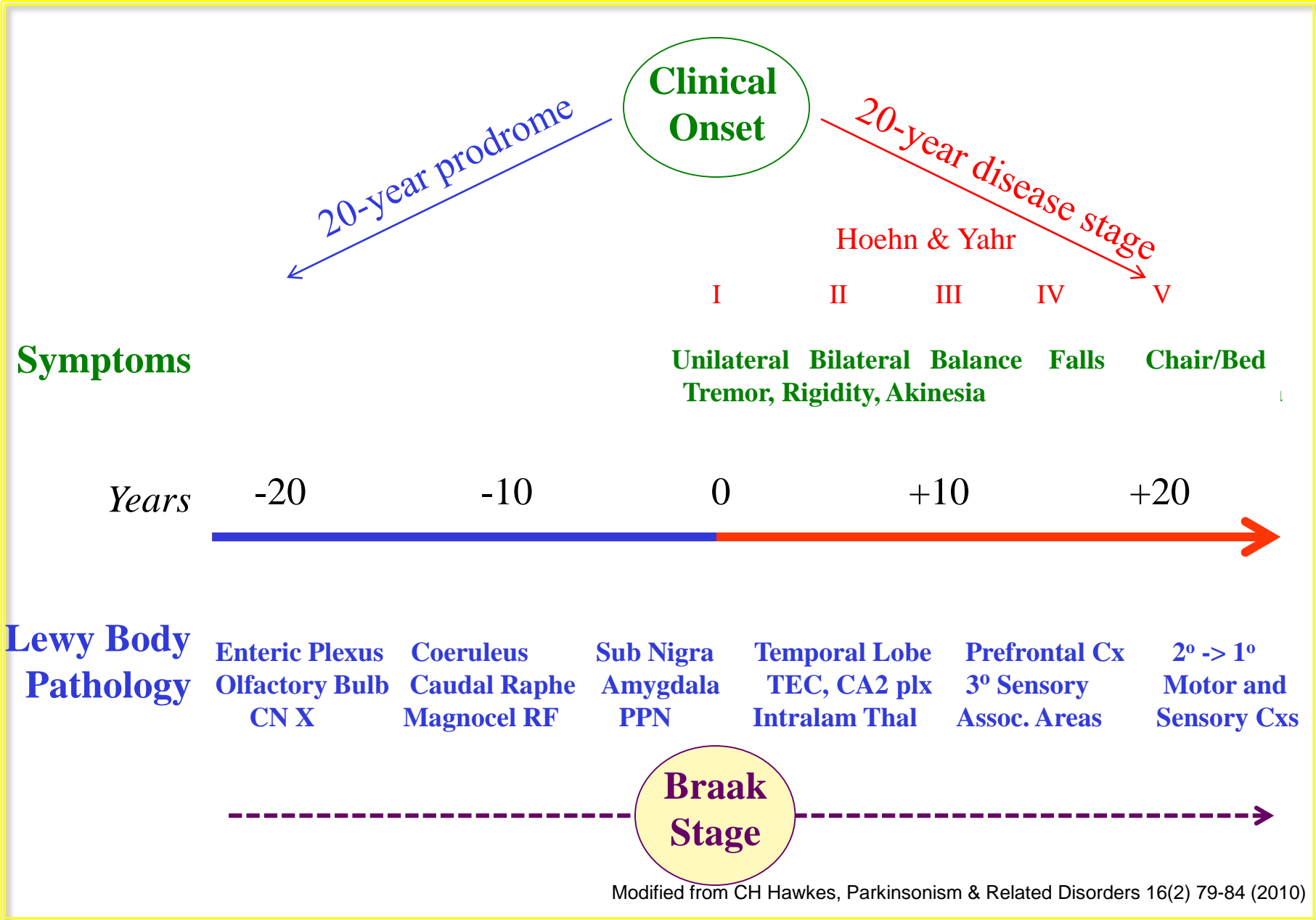


Braak stages 5 and 6

Emotional and cognitive disturbances



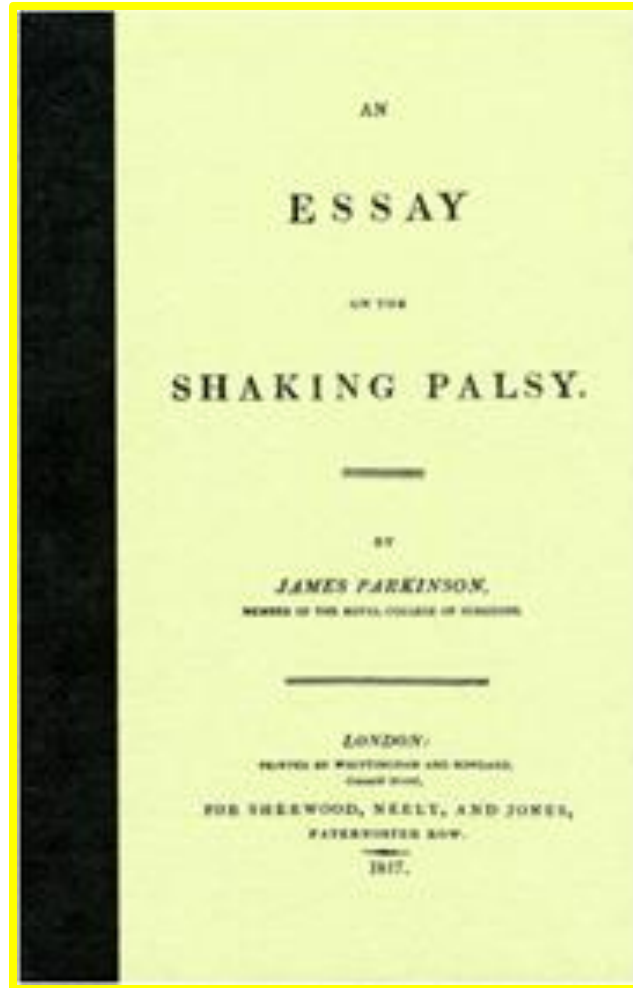
Model Timeline of Parkinson's Disease



Modified from CH Hawkes, Parkinsonism & Related Disorders 16(2) 79-84 (2010)

Non-Motor Symptoms

Parkinson's Disease

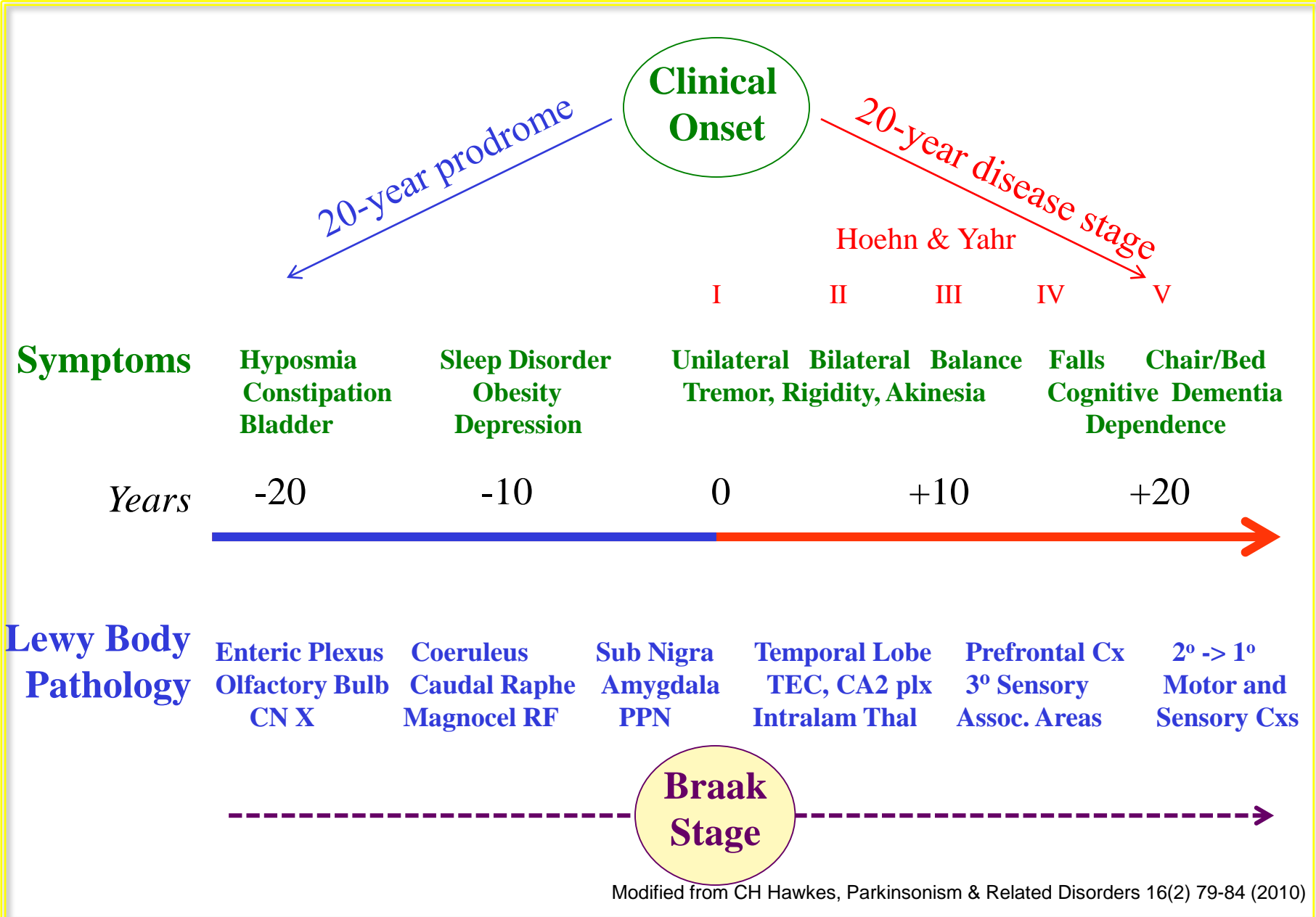


Sleep Disturbance
Constipation
Speech Disturbance
Swallow Disturbance
Drooling
Urinary Incontinence
Sleepiness
Mild Confusion

<http://www.allaboutparkinsons.com/james-parkinson.html>

<http://www.sciencemuseum.org.uk/hommedia.ashx?id=91831&size=Small>

Model Timeline of Parkinson's Disease



Modified from CH Hawkes, Parkinsonism & Related Disorders 16(2) 79-84 (2010)

NMS: System and Onset

Sensory Symptoms

Pain

Olfactory disturbance

Restless legs syndrome

Visual blurring

Gastrointestinal Symptoms

Constipation

Dysphagia

Drooling

Nausea, Vomiting

Sleep Disorders

Insomnia

REM sleep behavior disorder

Sleep disordered breathing

Periodic leg movements

Non-REM parasomnias (wandering)

Excessive daytime somnolence

Autonomic Dysfunction

Orthostatic hypotension

Bladder dysfunction (urgency, frequency, nocturia)

Sexual dysfunction (may be drug-induced)

Sweating abnormalities (hyperhidrosis)

Neuropsychiatric Symptoms

Depression

Anxiety

Apathy

Hallucinations, delusions, illusions

Delirium (may be drug induced)

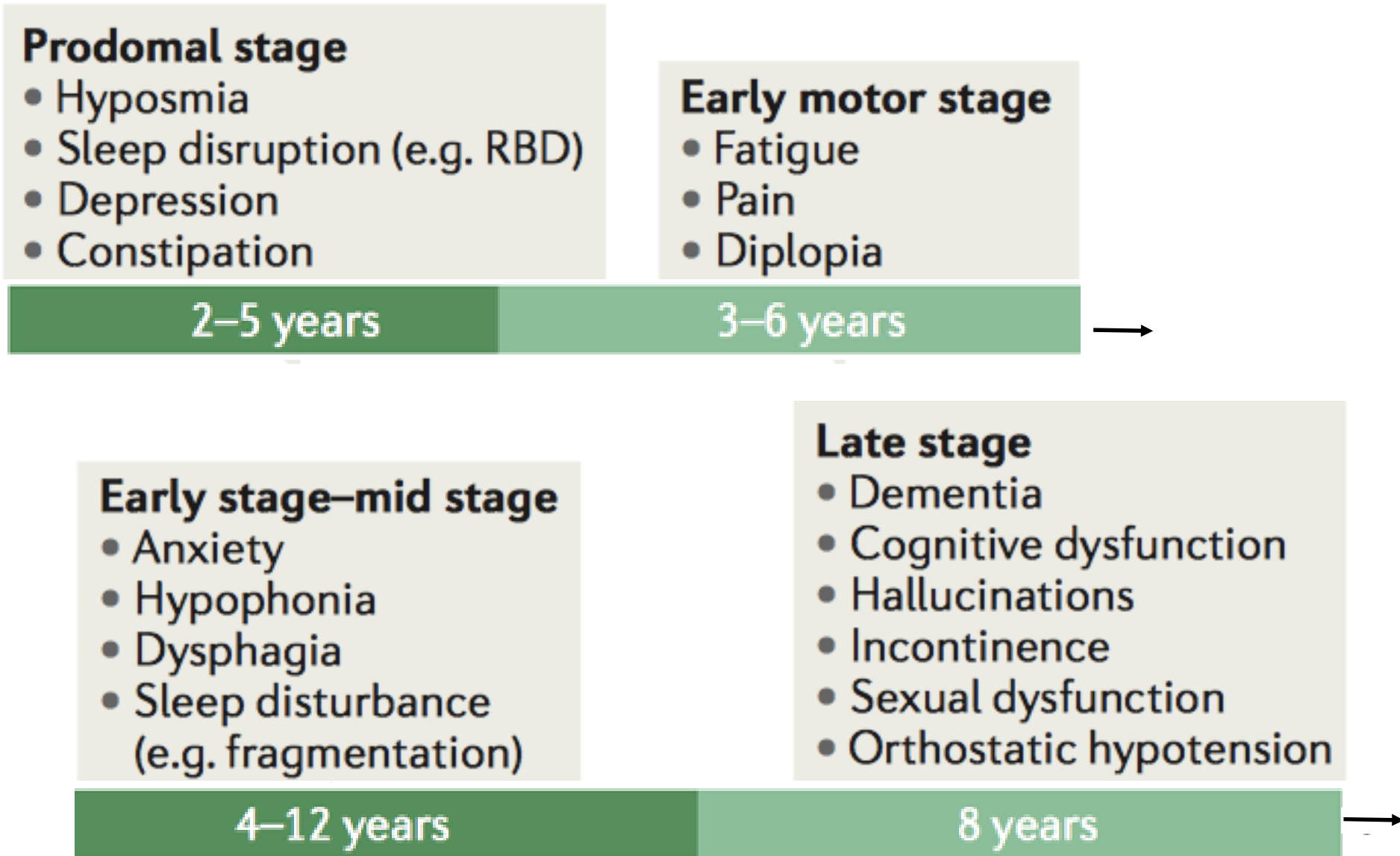
Cognitive Impairment / Dementia

BLUE = premotor stage of PD.

NMS: Inter-Individual Variability

“Multisystem involvement develops to varying levels of severity and in a variable sequence in different patients.”

NMS Stages



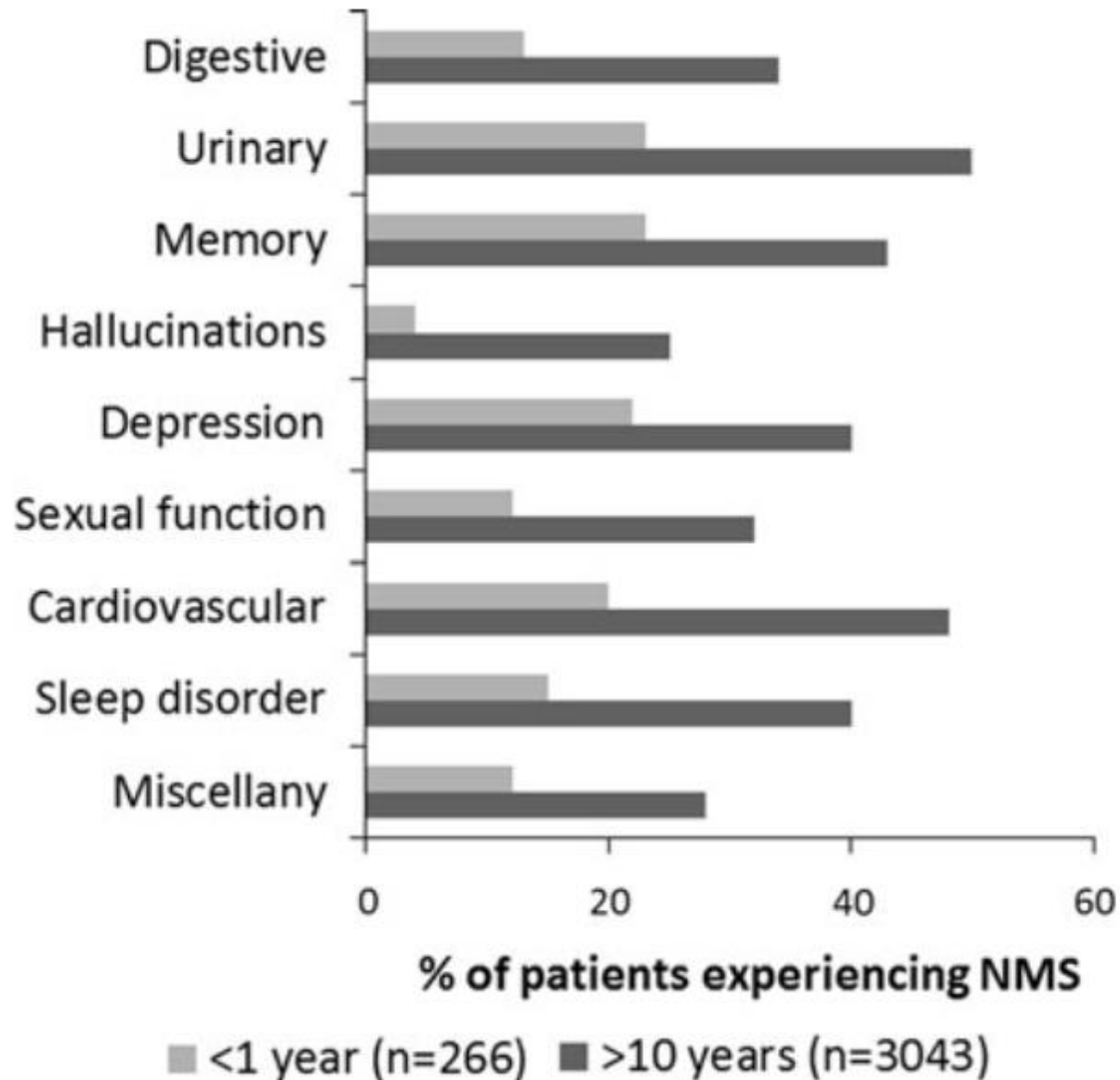
Non-motor features of Parkinson disease A.H.V. Schapira, K.R.Chaudhuri, P. Jenner. *NATURE REVIEWS | NEUROSCIENCE* 18:435-50 (2017)

2006 NMS Questionnaire (NMS-Quest)

Have you experienced any of the following in the last month?

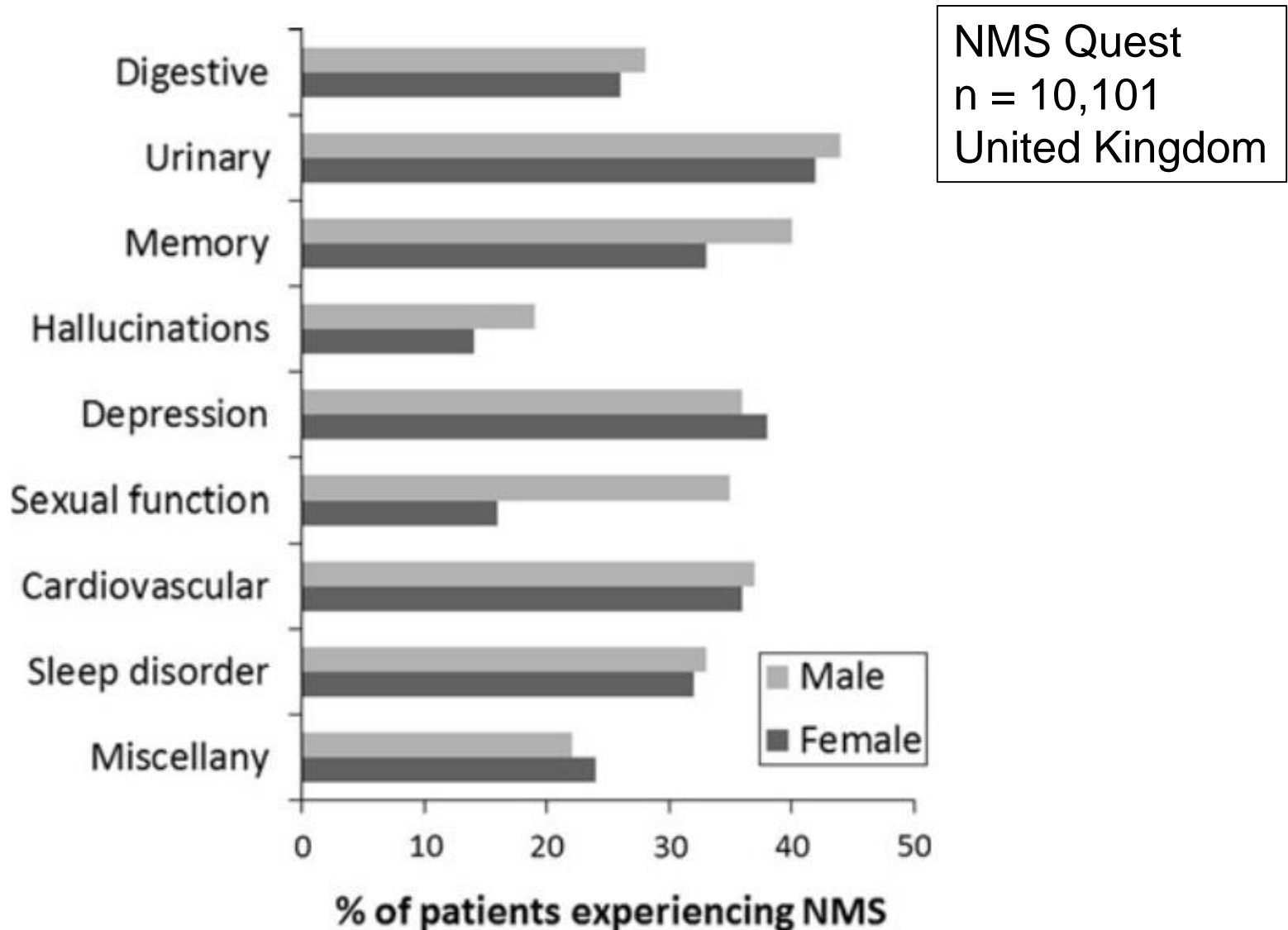
- | | Yes | No | | Yes | No |
|---------------------------------------------------------------------------------------------------------|--------------------------|--------------------------|------------------------------------------------------------------------------------------------------------|--------------------------|--------------------------|
| 1. Dribbling of saliva during the daytime | <input type="checkbox"/> | <input type="checkbox"/> | 16. Feeling sad, 'low' or 'blue' | <input type="checkbox"/> | <input type="checkbox"/> |
| 2. Loss or change in your ability to taste or smell | <input type="checkbox"/> | <input type="checkbox"/> | 17. Feeling anxious, frightened or panicky | <input type="checkbox"/> | <input type="checkbox"/> |
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| 4. Vomiting or feelings of sickness (nausea) | <input type="checkbox"/> | <input type="checkbox"/> | 19. Finding it difficult to have sex when you try | <input type="checkbox"/> | <input type="checkbox"/> |
| 5. Constipation (less than 3 bowel movements a week) or having to strain to pass a stool (faeces) | <input type="checkbox"/> | <input type="checkbox"/> | 20. Feeling light headed, dizzy or weak standing from sitting or lying | <input type="checkbox"/> | <input type="checkbox"/> |
| 6. Bowel (fecal) incontinence | <input type="checkbox"/> | <input type="checkbox"/> | 21. Falling | <input type="checkbox"/> | <input type="checkbox"/> |
| 7. Feeling that your bowel emptying is incomplete after having been to the toilet | <input type="checkbox"/> | <input type="checkbox"/> | 22. Finding it difficult to stay awake during activities such as working, driving or eating | <input type="checkbox"/> | <input type="checkbox"/> |
| 8. A sense of urgency to pass urine makes you rush to the toilet | <input type="checkbox"/> | <input type="checkbox"/> | 23. Difficulty getting to sleep at night or staying asleep at night | <input type="checkbox"/> | <input type="checkbox"/> |
| 9. Getting up regularly at night to pass urine | <input type="checkbox"/> | <input type="checkbox"/> | 24. Intense, vivid dreams or frightening dreams | <input type="checkbox"/> | <input type="checkbox"/> |
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| 11. Unexplained change in weight (not due to change in diet) | <input type="checkbox"/> | <input type="checkbox"/> | 26. Unpleasant sensations in your legs at night or while resting, and a feeling that you need to move | <input type="checkbox"/> | <input type="checkbox"/> |

2013 NMS by Year of Diagnosis



NMS Quest
n = 10,101
United Kingdom

2013 NMS by Gender

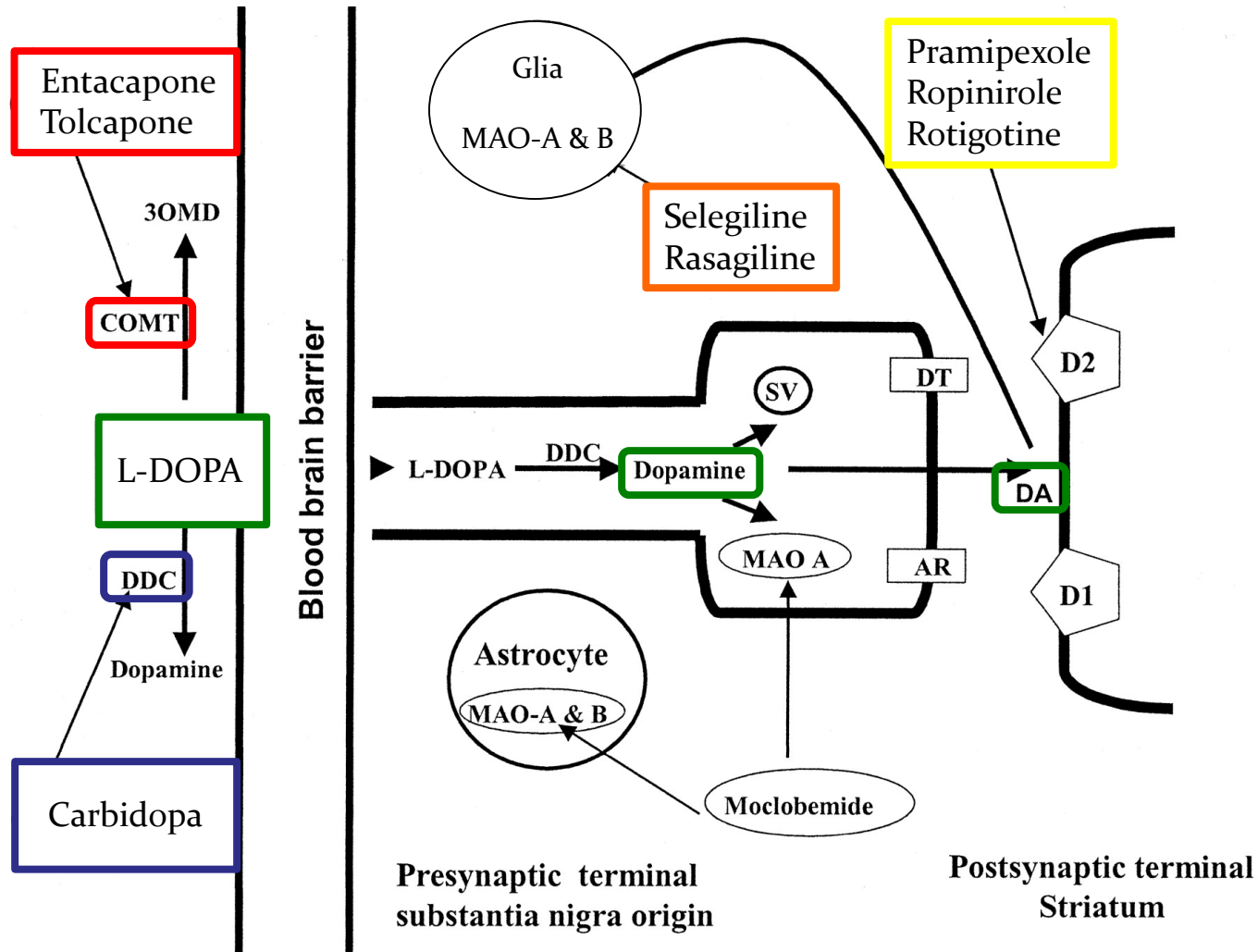


NMS and Dopamine

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Parkinson's Disease: Medication Pathways



NMS and Dopamine

Sensory Symptoms

Pain

Olfactory disturbance

Restless legs syndrome

Visual blurring

Gastrointestinal Symptoms

Constipation

Dysphagia

Drooling

Nausea, Vomiting

Sleep Disorders

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Neuropsychiatric Symptoms

Depression

Anxiety

Apathy

Hallucinations, delusions, illusions

Delirium (may be drug induced)

Cognitive Impairment / Dementia

GREEN = dopaminergic improvement

RED = dopaminergic worsening

Selected Dopaminergic Side Effects

Orthostatic Hypotension (Lightheaded → Falls → Injury)

Cognitive/Behavioral

Hallucinations, Delusions

Impulse Control Disorders

Dopamine Dysregulation Syndrome

Fatigue

Nausea

Narcolepsy-type “sleep attack”

Ankle Swelling

Dyskinesia

START LOW and GO SLOW...and RE-ASSESS.

Three Common NMS Disturbances

2006 NMS Scale

TABLE 3. Percentage of patients reporting each non-motor symptom as measured by the NMSS

Items	Patients*	
	N	%
1. Light-headedness	167	40.6
2. Fainting	38	9.2
3. Daytime sleepiness	195	47.4
4. Fatigue	271	65.9
5. Difficulty falling asleep	207	50.4
6. Restless legs	131	31.9
7. Lost interest in surroundings	141	34.3
8. Lack motivation	179	43.6
9. Feel nervous	208	50.6
10. Seem sad	204	49.6
11. Flat mood	132	32.1
12. Difficulty experiencing pleasure	121	29.4
13. Hallucinations	72	17.5
14. Delusions	40	9.7
15. Double vision	72	17.5

TABLE 3. Percentage of patients reporting each non-motor symptom as measured by the NMSS

Items	Patients*	
	N	%
16. Concentration	222	54.0
17. Forget things or events	209	50.9
18. Forget to do things	172	41.8
19. Saliva	178	56.7
20. Swallowing	121	29.4
21. Constipation	202	49.1
22. Urgency	224	54.5
23. Frequency	224	54.5
24. Nocturia	281	68.4
25. Altered interest in sex	135	32.8
26. Problems having sex	115	28.0
27. Pain	162	39.4
28. Taste or smell	171	41.6
29. Weight change	122	29.7
30. Excessive sweating	125	30.4

n = 411

International, Multi-Center Study

Fatigue / Excessive Daytime Sleepiness (EDS)

- Degeneration of Sleep-Wake Cycle Regulators
- Medication Side Effects: Dopamine Agonists, Levodopa, Anti-cholinergics, Amantadine
- *Other:* Nocturia, Sleep Apnea, Mood Disorders
Medical Conditions, Other Medications

Managing Fatigue / EDS

- **Lifestyle**

1. Stimulating environment
2. Intense light during the day
3. Exercise (daily, routine)

- **Pharmacological**

1. Review Medications
2. Caffeine (100-200 mg twice daily)
3. Modafinil (100-400 mg daily)
4. Others

Drooling

- Cause = bradykinesia: impaired mouth movements and swallowing
- Complications:
 - Social Embarrassment
 - Choking
 - Aspiration Pneumonia*

Managing Drooling

- **Non-pharmacological:** Gum, Hard Candy
- **Pharmacological**

1. Anticholinergics

Potential side-effects: mouth dryness, blurry vision, constipation, urinary retention, and worsened hallucinations and memory problems

Uncommon at low doses

2. Botulinum Toxin Injections

Parotid and/or submandibular glands

3. Dopaminergics

Nocturia / Bladder Dysfunction

- Detrusor Hyperreflexia / Overactive → Nocturia, Urinary Urge, Frequency, and Incontinence
- Bladder dysfunction is due to degeneration of autonomic bladder neurons, motor areas, higher control areas, and substantia nigra
- Consider Urodynamic Studies

Managing Nocturia / Bladder Dysfunction

- **Pharmacological**

1. **Dopaminergics: Levodopa**

2. B3 Adrenergic Agonist: Mirabegron (Myrbetriq)

3. Anti-cholinergics

Oxybutynin (Ditropan), Darifenacin (Enablex), Solifenacin (Vesicare), Tolterodine (Detrol), Trospium Chloride (Sanctura)

Side Effects: constipation, memory, hallucinations

3. Detrusor Chemodenervation: Botulinum Toxin A

4. Desmopressin nasal spray

Some Useful Online Resources

<http://www.parkinson.ca/resources/educational-publications/>

Ronald Postuma, Christos Galatas

A **Guide** to the *Non-Motor Symptoms* of **Parkinson's Disease**



A patient-friendly booklet for:

This booklet is to help you understand Parkinson's Disease and prepare for the treatments ahead. Please review it with your family. Bring it with you to your clinic appointments.



Centre universitaire de santé McGill
McGill University Health Centre

**NMS Quest
(search pdf)**

PD NMS QUESTIONNAIRE

Name: Date: Age:

Centre ID: Male Female

NON-MOVEMENT PROBLEMS IN PARKINSON'S

The movement symptoms of Parkinson's are well known. However, other problems can sometimes occur as part of the condition or its treatment. It is important that the doctor knows about these, particularly if they are troublesome for you.

A range of problems is listed below. Please tick the box 'Yes' if you have experienced it during the past month. The doctor or nurse may ask you some questions to help decide. If you have not experienced the problem in the past month tick the 'No' box. You should answer 'No' even if you have had the problem in the past but not in the past month.

Have you experienced any of the following in the last month?

- | | Yes | No | | Yes | No |
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| 1. Dribbling of saliva during the daytime | <input type="checkbox"/> | <input type="checkbox"/> | 16. Feeling sad, 'low' or 'blue' | <input type="checkbox"/> | <input type="checkbox"/> |
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| 11. Unexplained change in weight (not due to change in diet) | <input type="checkbox"/> | <input type="checkbox"/> | 26. Unpleasant sensations in your legs at night or while resting, and a feeling that you need to move ... | <input type="checkbox"/> | <input type="checkbox"/> |
| 12. Problems remembering things that have happened recently or forgetting to do things | <input type="checkbox"/> | <input type="checkbox"/> | 27. Swelling of your legs | <input type="checkbox"/> | <input type="checkbox"/> |
| 13. Loss of interest in what is happening around you or doing things | <input type="checkbox"/> | <input type="checkbox"/> | 28. Excessive sweating | <input type="checkbox"/> | <input type="checkbox"/> |
| 14. Seeing or hearing things that you know or are told are not there | <input type="checkbox"/> | <input type="checkbox"/> | 29. Double vision | <input type="checkbox"/> | <input type="checkbox"/> |
| 15. Difficulty concentrating or staying focussed | <input type="checkbox"/> | <input type="checkbox"/> | 30. Believing things are happening to you that other people say are not true | <input type="checkbox"/> | <input type="checkbox"/> |

All the information you supply through this form will be treated with confidence and will only be used for the purpose for which it has been collected. Information supplied will be used for monitoring purposes. Your personal data will be processed and held in accordance with the Data Protection Act 1998.

Developed and validated by the International PD Non Motor Group
For information contact: susanna.tluk@uh.lnhs.uk or alison.forbes@uh.lnhs.uk

Take-Home Messages

- Non-motor symptoms (NMS) are common.
- NMS-Quest can be a useful tool for you and your doctors.
- Discuss NMS with your neurologist and, when appropriate, other members of your medical team.
- Optimal NMS management may involve pharmacologic and non-pharmacologic approaches.
- The more precisely you report WHEN and WHAT symptoms are most bothersome, the more thoughtfully you and your doctor can develop optimal treatment strategies.

Take your medications on schedule and keep a log.

Thank you!

Additional References

- R Postuma, SS Romenets, R Rakhej, Physician Guide: Non-motor symptoms of Parkinson's Disease (2012)
http://www.parkinson.ca/site/c.kgLNIWODKpF/b.3536143/k.3545/For_Health_Care_Professionals.html
- KR Chaudhuri, "Under-recognized Nonmotor Symptoms of Parkinson's Disease" (2013) http://www.pdf.org/en/parkinson_briefing_nonmotor

First Comprehensive Evaluation of NMS and QoL

RESEARCH ARTICLE

The Impact of Non-Motor Symptoms on Health-Related Quality of Life of Patients with Parkinson's Disease

Pablo Martinez-Martin, MD, PhD,^{1,2*} Carmen Rodriguez-Blazquez, BS,¹ Monica M. Kurtis, MD,³
and K. Ray Chaudhuri, MD, FRCP, DSC,^{4,5} on Behalf of the NMSS Validation Group

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³Movement Disorders Unit, Department of Neurology, Ruber International Hospital, Madrid, Spain

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⁵Department of Neurology, University Hospital Lewisham, Kings College, London, United Kingdom

***Movement Disorders* 26(3): 399-406 (2011)**

First Comprehensive Evaluation of NMS and QoL

“The results show that non-motor symptoms have, as a whole, a greater impact on health-related quality of life than motor symptoms...”

“...and non-motor symptoms progression contributes importantly to health-related quality of life decline in patients with Parkinson’s disease.”

2016 Clinical Phase Model of PD

