The Parkinson's Disease Educational Course for Industry Professionals
Honolulu, Hawaii, USA | October 4, 2025

International Parkinson and Movement Disorder Society

Non-motor Parkinson's-spotlight on subtypes

Karolina Popławska-Domaszewicz, MD, PhD

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Department of Neurology
Poznan University of Medical Sciences
Parkinson Foundation Centre of Excellence
Kings College Hospital London

Disclosures

Advisory boards	**Stada, AbbVie (Poland)**
Grants (investigator initiated)	GKC, Altoida
Honoraria	**AbbVie, AbbVie (Poland), Bial, Britannia, GKC, Stada**

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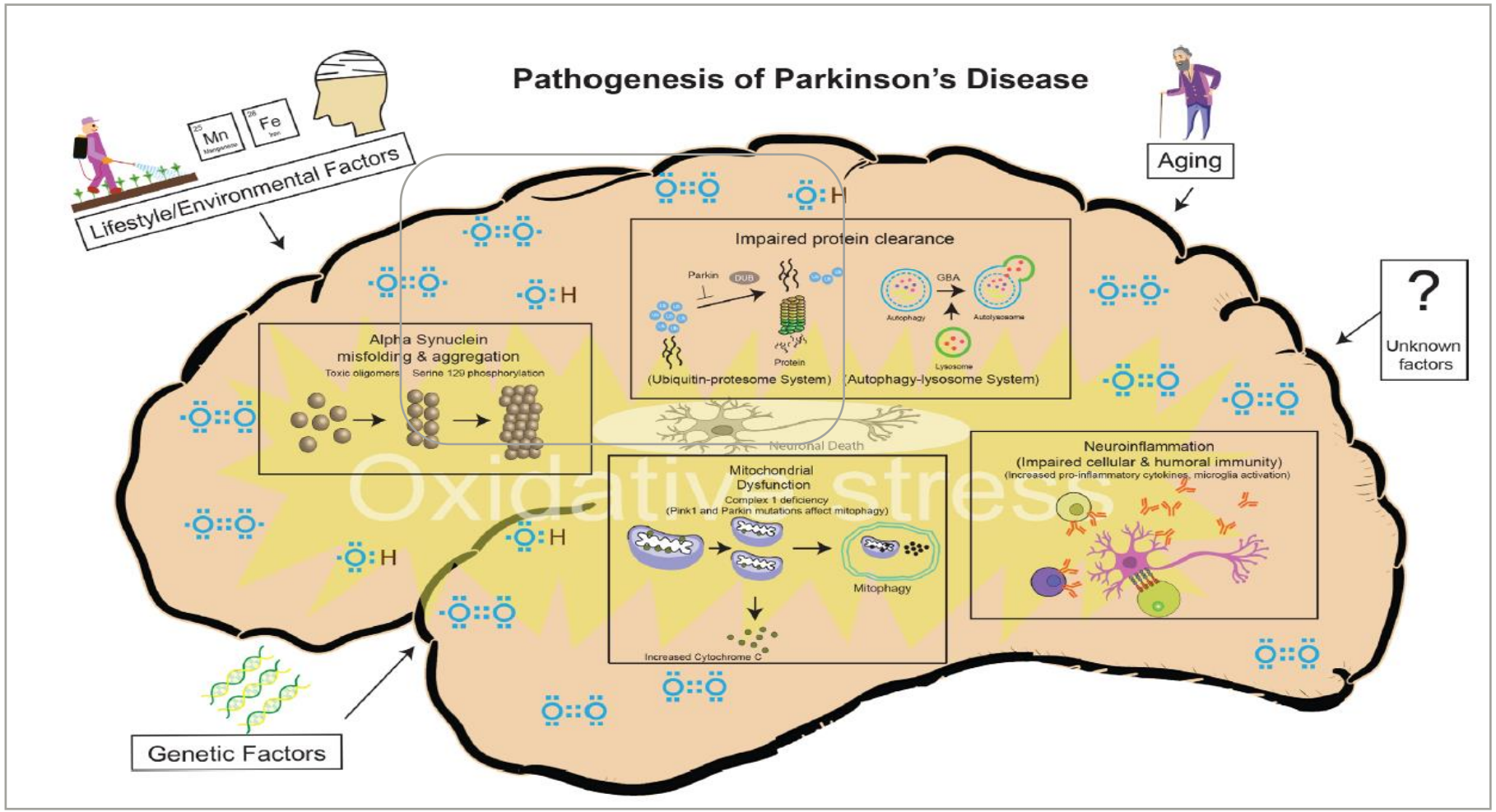
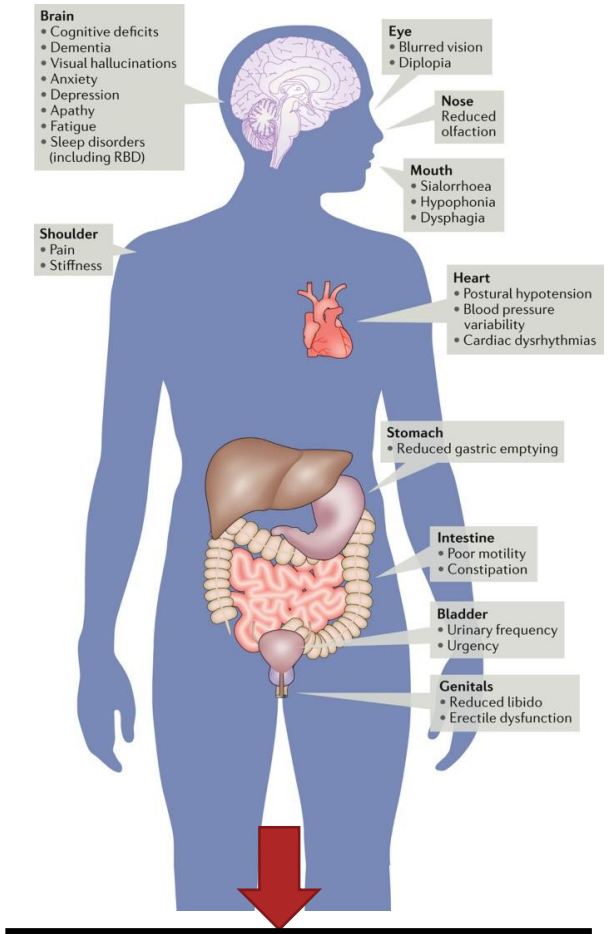


Jankovic J, Tan EK. *J Neurol Neurosurg Psychiatry* 2020;91:795–808. doi:10.1136/jnnp-2019-322338

Heterogeneity



Non Motor Subtype

Schapira, Chaudhuri, Jenner 2017

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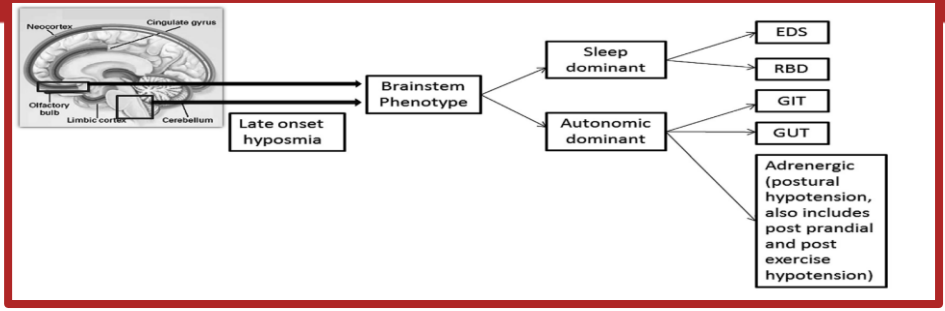
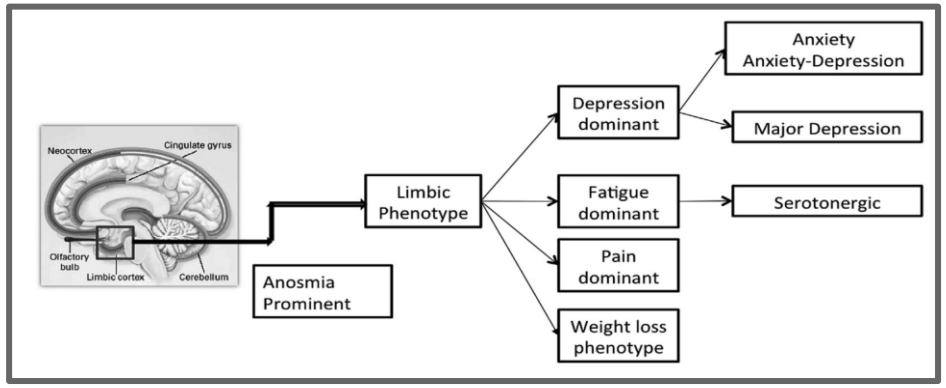
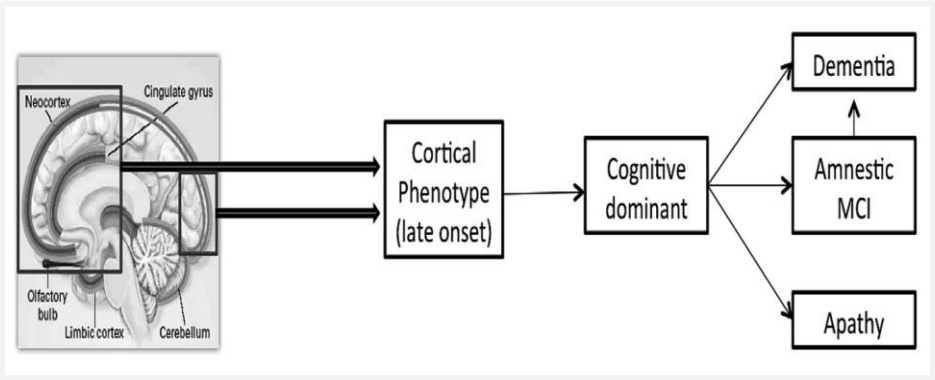






Review > Parkinsonism Relat Disord. 2016 Jan:22 Suppl 1:S41-6.
doi: 10.1016/j.parkreldis.2015.09.027. Epub 2015 Sep 11.

Non motor subtypes and Parkinson's disease

Anna Sauerbier [1], Peter Jenner [2], Antoniya Todorova [1], K Ray Chaudhuri [3]

Park sleep

Park autonomic

Park depression/anxiety

Park fatigue

Park pain

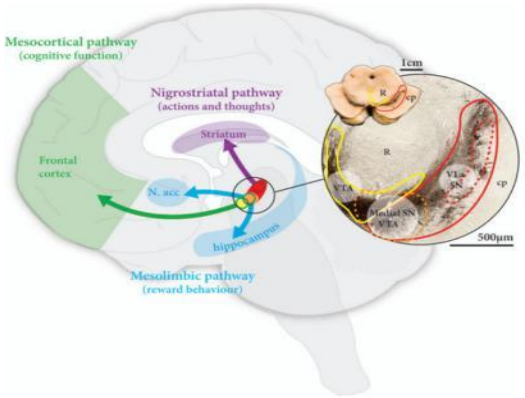
Park cognitive

Park apathy

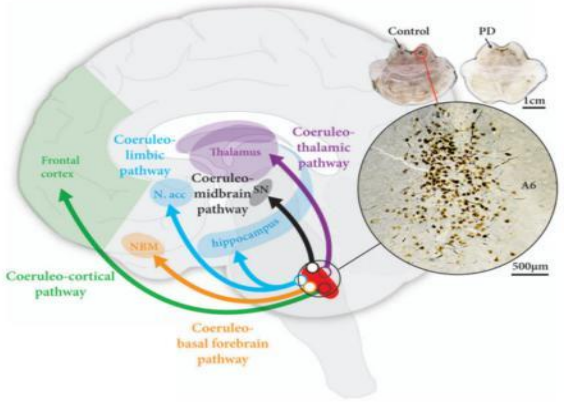
7 subtypes of PD

Contributors to the different phenotypes in Parkinson's disease

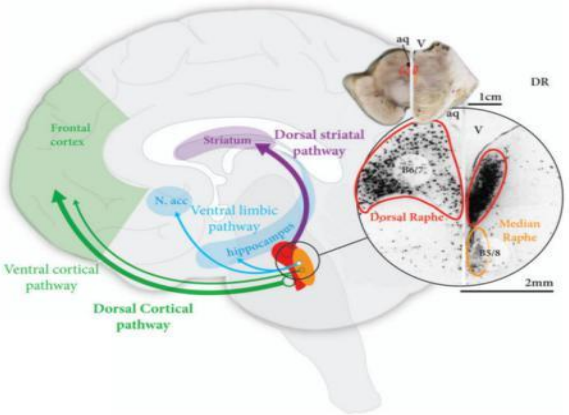
At least four distinct neurotransmitter systems are affected by α-synuclein pathology and contribute to the many symptoms in Parkinson's disease



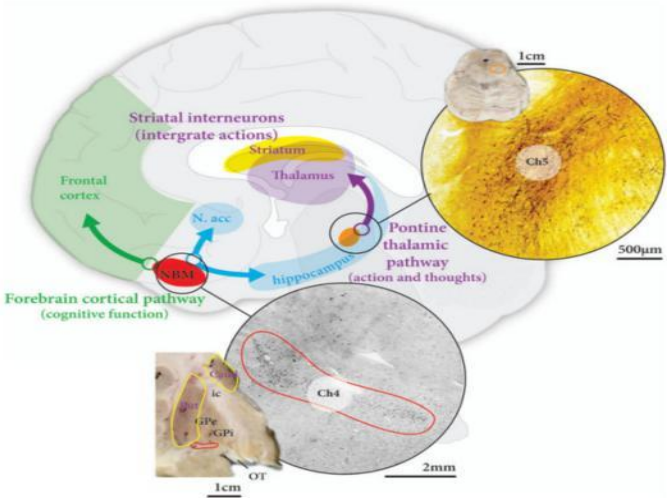
Dopamine pathway



Noradrenaline pathway



Serotonin pathway



Cholinergic pathway

Halliday GM, *et al. Mov Disord* 2014; **29**:634–650; Titova N, *et al. J Neuro! Transm* 2017; **124**:907–914.

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Parkinsonism and Related Disorders 130 (2025) 107208

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

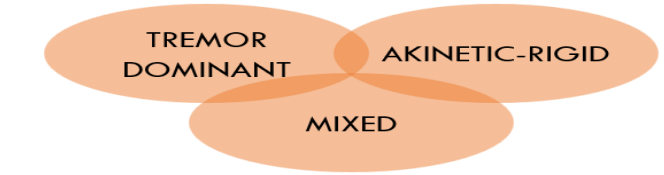
Review article

Parkinson's disease subtypes: Approaches and clinical implications

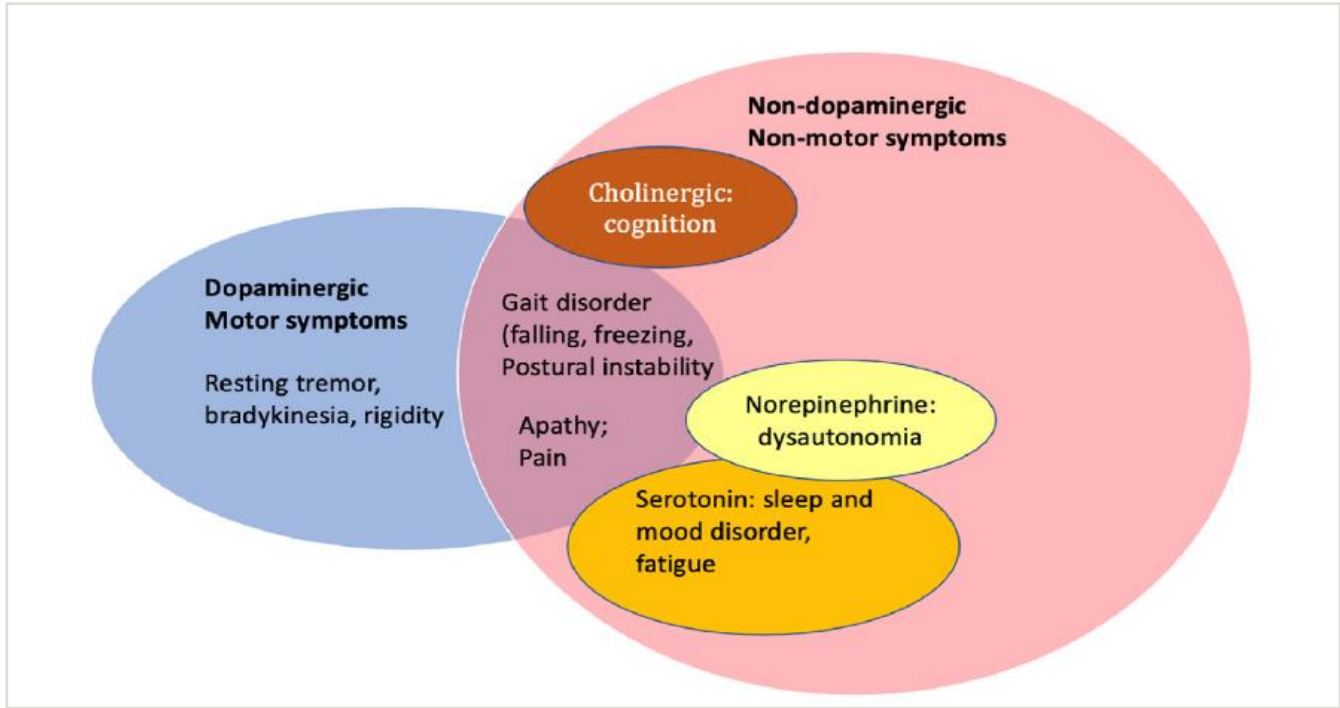
Xiao Deng [a,b], Anish Mehta [c], Bin Xiao [a,b], K. Ray Chaudhuri [d,e], Eng-King Tan [a,b,1], Louis CS. Tan [a,b,1,*]

Motor Subtypes

Jankovic et al. 1990



Schiess et al. 2000
Kang et al. 2005



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Parkinson's disease subtypes: Approaches and clinical implications

Xiao Deng [a,b], Anish Mehta [c], Bin Xiao [a,b], K. Ray Chaudhuri [d,e], Eng-King Tan [a,b,1], Louis CS. Tan [a,b,1,*]

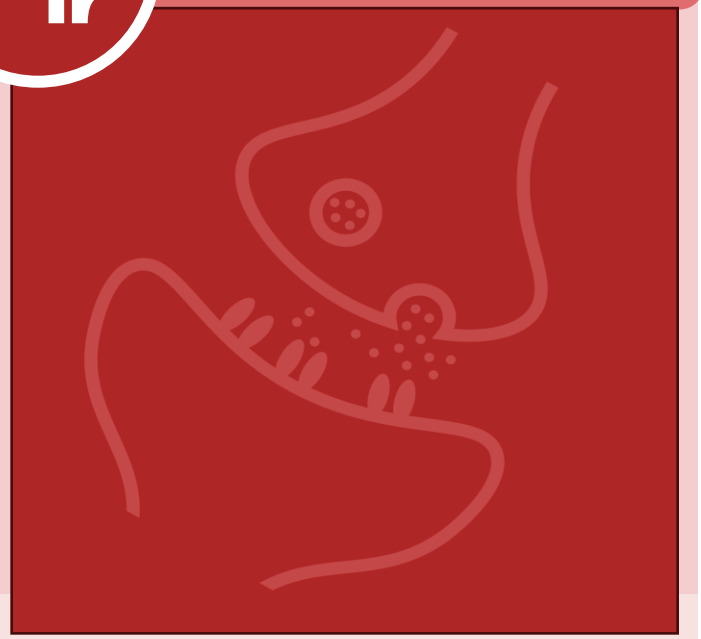
Table 1
Characterization of motor subtypes.

Motor subtype	Potential pathophysiology	Concurrent symptoms	Clinical prognosis	Blood biomarkers	CSF markers	Imaging markers
TD	Mainly dopaminergic denervation	Hyposmia	Better	Serum UA increased	N.A.	cerebellar grey matter atrophy
PIGD	Non-dopaminergic dysfunction: (cholinergic …)	NMS: depression, apathy, sexual dysfunction, MCI	Worse, greater risk of dementia and falls	Plasma NfL increased; LRRK2, GBA	Non-dopaminergic deficits	1)Frontal lobe grey matter atrophy 2)White matter damage

Abbreviations: TD: tremor dominant; PIGD: postural instability and gait difficulty.
MCI: Mild cognitive impairment; UA: uric acid; NfL: Neurofilament light chain; CSF: cerebrospinal fluid.

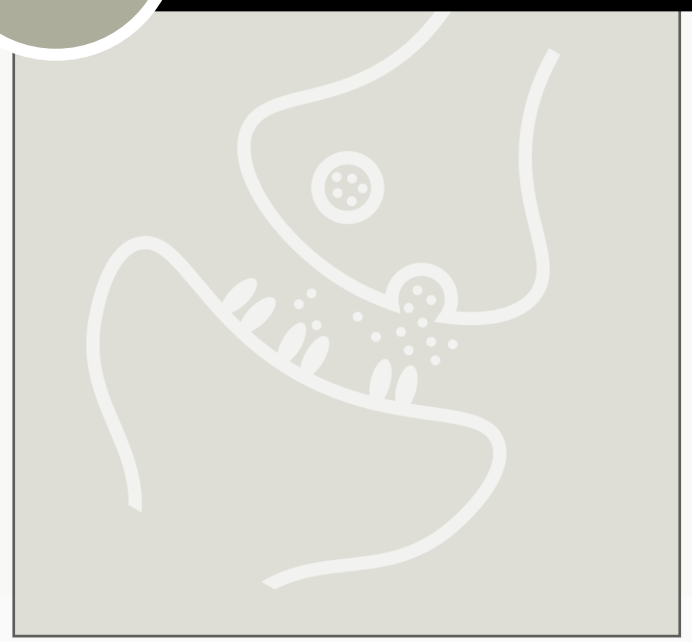
Why and how subtype ?
Real Life Non-motor subtypes: the evidence base

Cholinergenic[1,2]



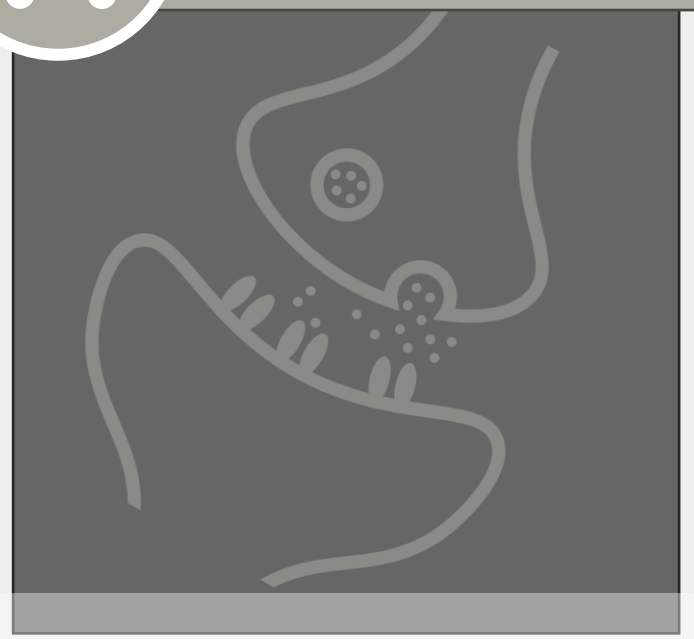
- Severe cholinergic deficits are associated with dementia in Parkinson's

Park Sleep[3]



- The Park Sleep subtype is characterised by EDS, along with insomnia as a secondary phenomenon

Noradrenergic



- Noradrenergic dysfunction can result in a cluster of symptoms such as rapid eye movement sleep disorder,[4] pain,[5] anxiety[6] and dysautonomia[7]

EDS, excessive daytime somnolence.

1. Aarsland D, et al. *Nat Rev Dis Primers* 2021;7:47; 2. Bohnen NI, et al. *Lancet Neurol* 2022;21:381–92; 3. Tall P, et al. *Exp Opin Pharmacother* 2023;24:1725–36; 4. Popkirov S. *Sleep*. 2017;40:zsx132; 5. Taylor BK and Westlund KN. *J Neurosci Res*. 2017;95:1336–46; 6. Yamamoto K, et al. *Psychiatry Clin Neurosci*. 2014;68:1–20; 7. Sharabi Y, et al. *Neuron*. 2022;110:1432.E1.

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Movement Disorders
CLINICAL PRACTICE

The Cholinergic Brain in Parkinson's Disease

Jacopo Pasquini, MD,[1,2] David J. Brooks, MD, DSc,[3,4] and Nicola Pavese, MD, PhD[2,4,*]

Review > Lancet Neurol. 2022 Apr;21(4):381-392. doi: 10.1016/S1474-4422(21)00377-X. Epub 2022 Feb 4.

Cholinergic system changes in Parkinson's disease: emerging therapeutic approaches

Nicolaas I Bohnen [1], Alison J Yarnall [2], Rimona S Weil [3], Elena Moro [4], Mark S Moehle [5], Per Borghammer [6], Marc-André Bedard [7], Roger L Albin [8]

Curr Neurol Neurosci Rep (2013) 13:377
DOI 10.1007/s11910-013-0377-9

NEUROIMAGING (DJ BROOKS)

Cholinergic Dysfunction in Parkinson's Disease

Martijn L. T. M. Müller · Nicolaas I. Bohnen

> Brain. 2024 Mar 4:awae069. doi: 10.1093/brain/awae069. Online ahead of print.

Cholinergic changes in Lewy body disease: implications for presentation, progression and subtypes

Niels Okkels [1 2], Michel J Grothe [3 4 5], John-Paul Taylor [6], Steen Gregers Hasselbalch [7], Tatyana D Fedorova [2], Karoline Knudsen [2], Sygrid van der Zee [8], Teus van Laar [8], Nicolaas Bohnen [9 10 11 12 13], Per Borghammer [2 14], Jacob Horsager [2]

Towards a clinical identification of a Cholinergic Subtype of Parkinson's disease

EAN 2024

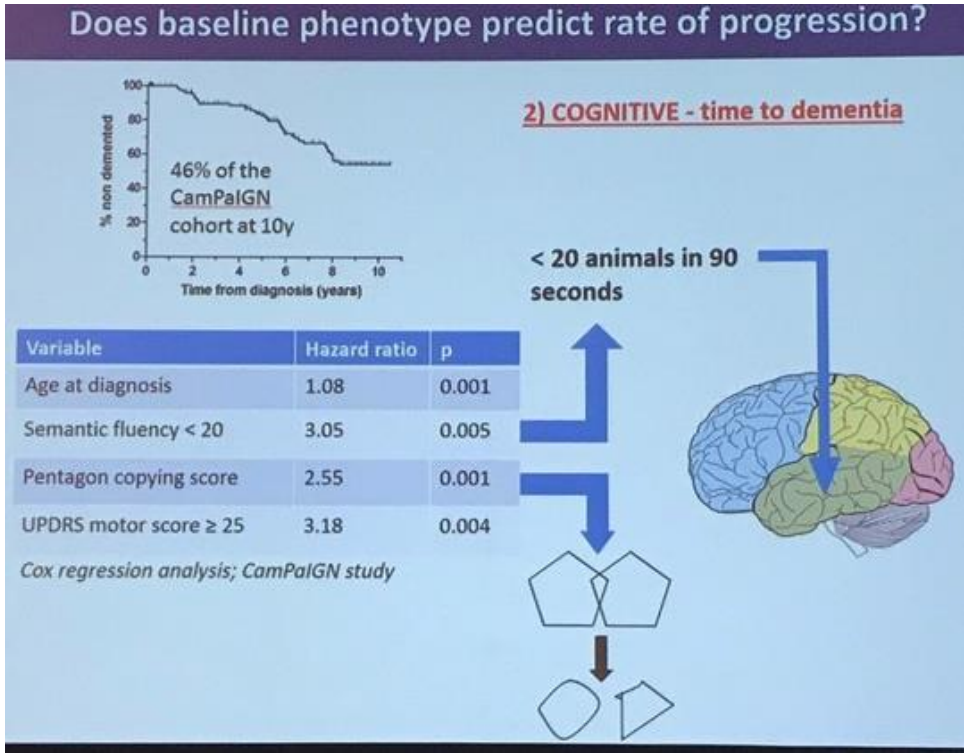
Lucia Batzu[1,2], Aleksandra M Podlewska[1,2], Mubasher A Qamar[1,2], Alexandra Rizos[1,2], Dag Aarsland[3,4], Per Svenningsson[1,5], K Ray Chaudhuri[1,2]

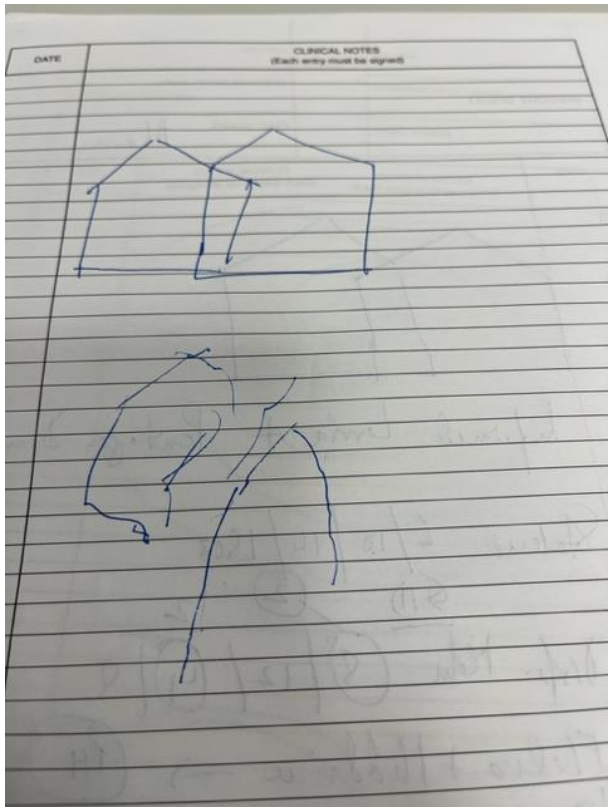
Cholinergenic subtype

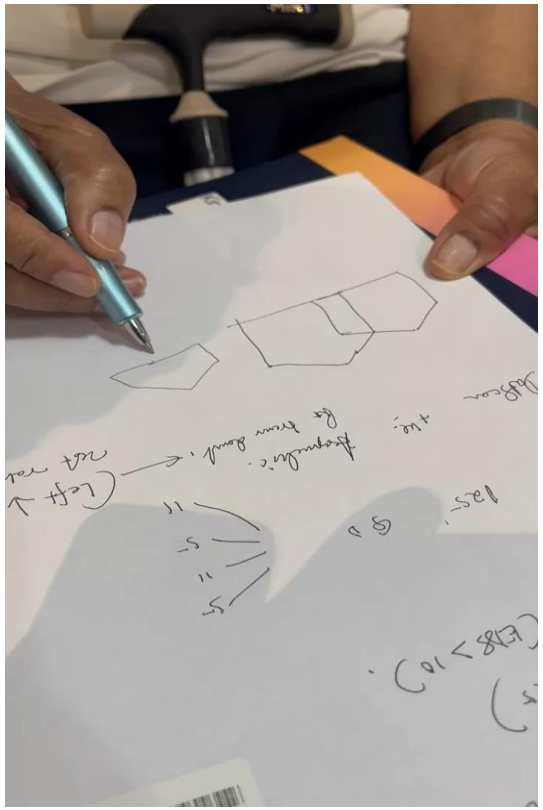
> J Neurol Neurosurg Psychiatry. 2013 Nov;84(11):1258-64. doi: 10.1136/jnnp-2013-305277. Epub 2013 Jun 18.

The CamPaIGN study of Parkinson's disease: 10-year outlook in an incident population-based cohort

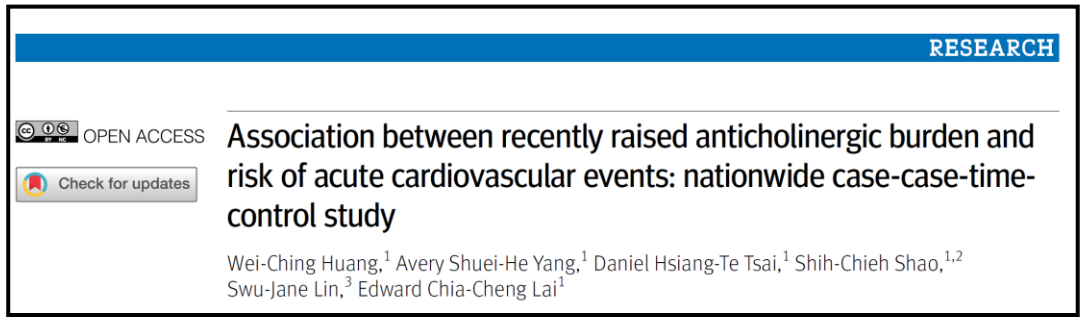
Caroline H Williams-Gray [1], Sarah L Mason, Jonathan R Evans, Thomas Foltynie, Carol Brayne, Trevor W Robbins, Roger A Barker







BMJ



RESEARCH

OPEN ACCESS

Check for updates

Association between recently raised anticholinergic burden and risk of acute cardiovascular events: nationwide case-case-time-control study

Wei-Ching Huang,[1] Avery Shuei-He Yang,[1] Daniel Hsiang-Te Tsai,[1] Shih-Chieh Shao,[1,2] Swu-Jane Lin,[3] Edward Chia-Cheng Lai[1]

Main findings:

Nationwide population-based study;
248,579 current cases

Among older adults with acute cardiovascular events, an increased total anticholinergic burden in the 30-day hazard windows vs reference windows was observed

Conclusion:

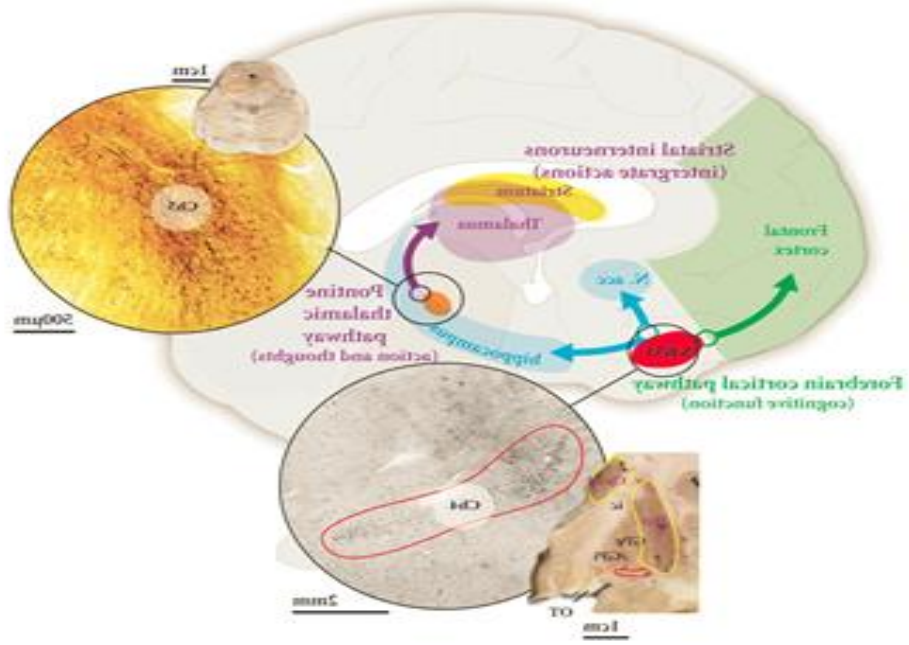
An association between recently raised anticholinergic burden and acute cardiovascular events in older adults was found

Medications with anticholinergic effect

Very strong	Strong	Moderate
3 points per drug	2 points per drug	(1 point per drug)
Amitriptyline	Amantadine	Carbidopa-Levodopa
Atropine	Baclofen	Entacapone
Benzatropine	Cetirizine	Haloperidol
Carisoprodol	Cimetidine	Methocarbamol
Cyproheptadine	Clozapine	Metoclopramide
Chlorpheniramine	Cyclobenzaprine	Mirtazapine
Chlorpromazine	Desipramine	Paroxetine
Dicycloverine (also known as Dicyclomine)	Loperamide	Pramipexole
Diphenhydramine	Nortriptyline	Quetiapine
Fluphenazine	Olanzapine	Ranitidine
Hyoscyamine (also known as Hyoscine)	Prochlorperazine	Risperidone
Imipramine	Pseudoephedrine	Selegiline
Meclizine	Tolterodine	Trazodone
Oxybutynin		Ziprasidone
Perphenazine		
Promethazine		
Thioridazine		
Thiothixene		
Tizanidine		
Trifluoperazine		

Very strong risk: final points total ≥3.

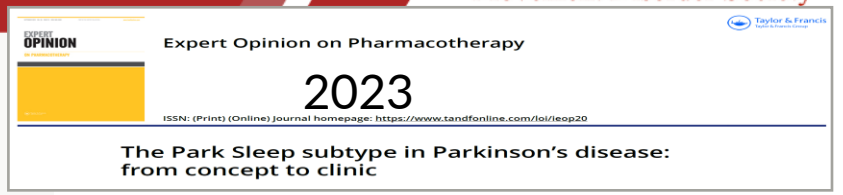
Cholinergic



- Counselling regarding cognitive decline
- Forward planning
- Consider DRT + AchE ↓ drugs + Gait training
- Cognitive training/CBT
- Avoid anticholinergics
- Probiotics (large bowel active)

Marras, Chaudhuri et al Neurotherapeutics. 2020

Risk of injuries and RTA and drownning



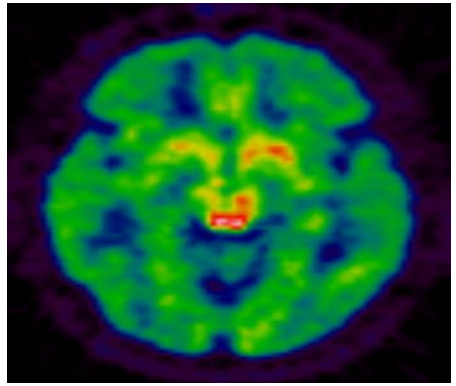
Neurology®

Falling asleep at the wheel: Motor vehicle mishaps in persons taking pramipexole and ropinirole

Frucht, *et al. Neurology* 1999

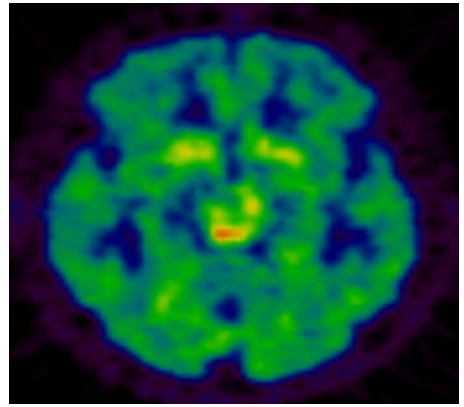
Park Sleep[3]

? Biomarker



- **The Park Sleep subtype is characterised by EDS, along with insomnia as a secondary phenomenon**

DAS B PET



EDS, excessive daytime somnolence.

1. Aarsland D, et al. *Nat Rev Dis Primers* 2021;7:47; 2. Bohnen NI, et al. *Lancet Neurol* 2022;21:381–92; 3. Tall P, et al. *Exp Opin Pharmacother* 2023;24:1725–36; 4. Popkirov S. *Sleep.* 2017;40:zsx132; 5. Taylor BK and Westlund KN. *J Neurosci Res.* 2017;95:1336–46; 6. Yamamoto K, et al. *Psychiatry Clin Neurosci.* 2014;68:1–20; 7. Sharabi Y, et al. *Neuron.* 2022;110:1432.E1.
2. Pavese et al. NeuriImage, vol 59, Issue 2, 2012

Preference D_3 versus D_2 receptor subtypes within the D2 family*

*Ratio of binding affinities (K_i-values):
The higher the number, the higher the D_3 preference vs. D_2

(Adopted from Piercey MF et al. Eur J Pharmacol 1996; 312: 35-44)

Sleep Medicine 16 (2015) 540–544

Contents lists available at ScienceDirect

Sleep Medicine

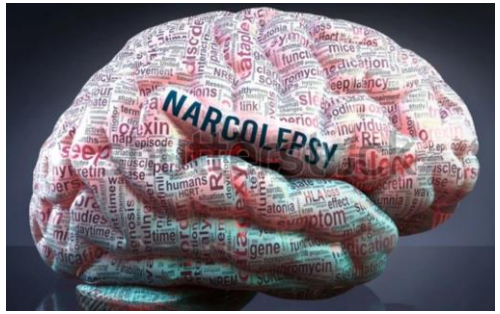
journal homepage: www.elsevier.com/locate/sleep

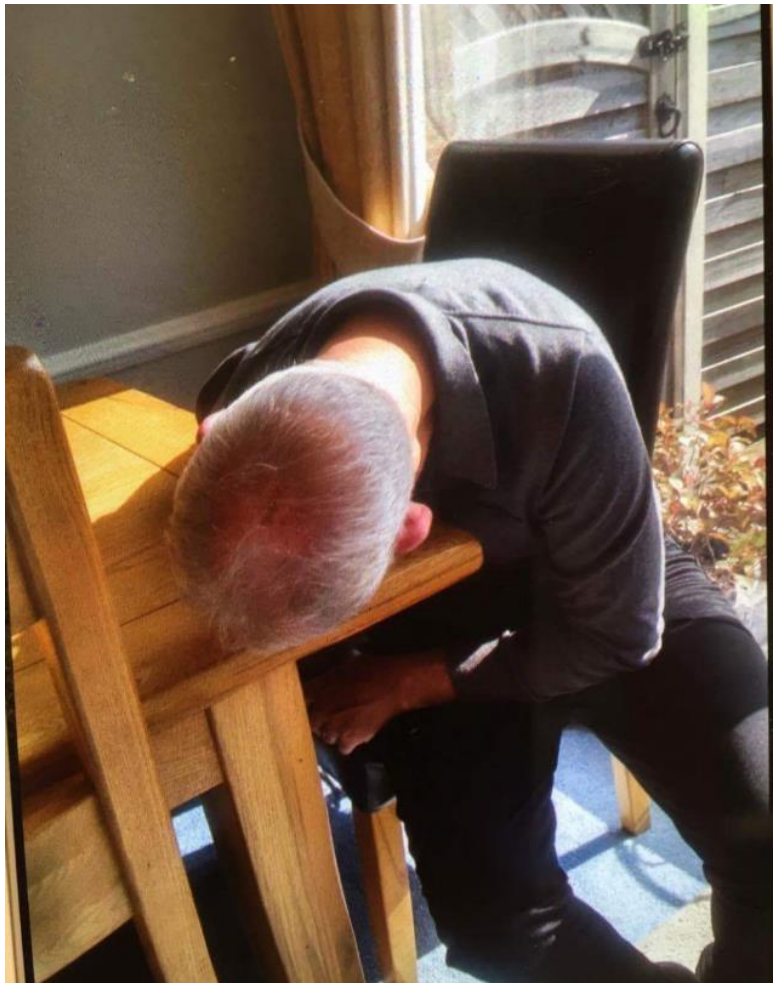
Original Article

Parkinson's disease and narcolepsy-like symptoms

Ari Ylikoski [a,b,*], Kirsti Martikainen [c], Tomi Sarkanen [a,d], Markku Partinen [a,e]

[a] Vitalmed Research Center, Helsinki Sleep Clinic, Helsinki, Finland





Journal of Neural Transmission
https://doi.org/10.1007/s00702-025-02995-z

NEUROLOGY AND PRECLINICAL NEUROLOGICAL STUDIES - ORIGINAL ARTICLE

"Dozing off" in the car and excessive daytime sleepiness (EDS) in Parkinson's disease: a survey of 125 patients

Carolina Sportelli[1,2] · Karolina Poplawska-Domaszewicz[3] · Corinne Borley[1,2] · Vinod Metta[1,2,4] · Valentina Leta[1,2,5] · Kit Wu[1,2] · Anna Sauerbier[1,2,6] · Carlo Santoro[7] · Salvatore Landolfo[7] · Daniele Urso[1,2,7] · Rosabel Chen[1,2,8] · Yogini Chokeepermal-Naidu[9] · Cristian Falup-Pecurariu[10] · K. Ray Chaudhuri[1,2,8,11]

Received: 20 May 2025 / Accepted: 22 July 2025

- **42.8%** high likelihood of dozing off while stationary in a car → high risk while driving, operating machinery, or swimming

- DA intake associated with high risk
- Please do an Epworth scale assessment
- Score over 10 and specially 12 associated with
- High risk of dozing while driving
- Please rule out sleep aponea

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nature reviews neurology

https://doi.org/10.1038/s41582-023-00802-5

Nat Rev Neurol 202

Review article

Check for updates

The noradrenergic subtype of Parkinson disease: from animal models to clinical practice

K. Ray Chaudhuri[1,2,7], Valentina Leta[1,2,7], Kirsty Bannister[3], David J. Brooks[4,5] & Per Svenningsson[1,6]

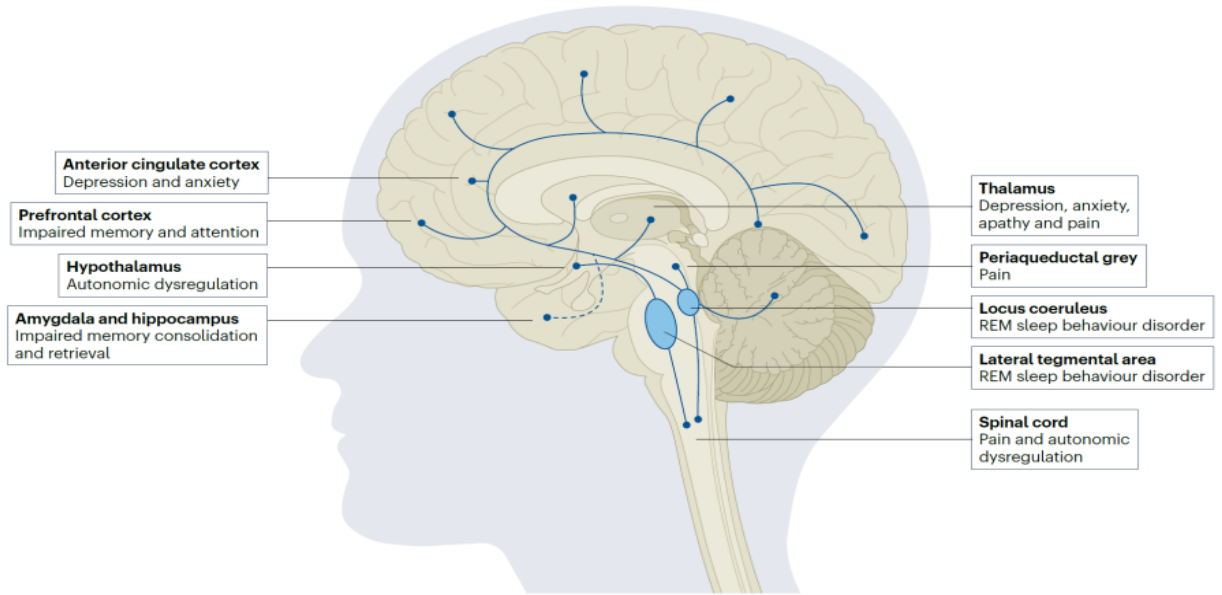
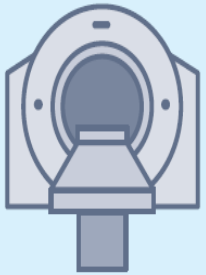


Fig. 2 | Noradrenergic projections in the CNS. The locus coeruleus is the principal generator of noradrenaline in the CNS. Noradrenergic projections from the locus coeruleus and lateral tegmental area to different regions of the brain and spinal cord are shown, along with clinical manifestations that are potentially associated with central noradrenergic dysfunction[30,126]. REM, rapid eye movement.

Noradrenergic subtype of PD

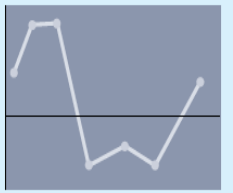
Clinical biomarkers

- RBD
- Dysautonomia (orthostatic hypotension and urinary dysfunction)
- Anxiety
- Pain
- Akinetic rigid syndrome
- Freezing of gait



Neuroimaging biomarkers

- Neuromelanin MRI
- ^{11}C-MeNER PET
- Cardiac MIBG scintigraphy



Psychophysical biomarkers

- Quantitative sensory testing

Neuro–degenerative Diseases

Neurodegenerative Dis 2010;7:341–347
DOI: 10.1159/000314573

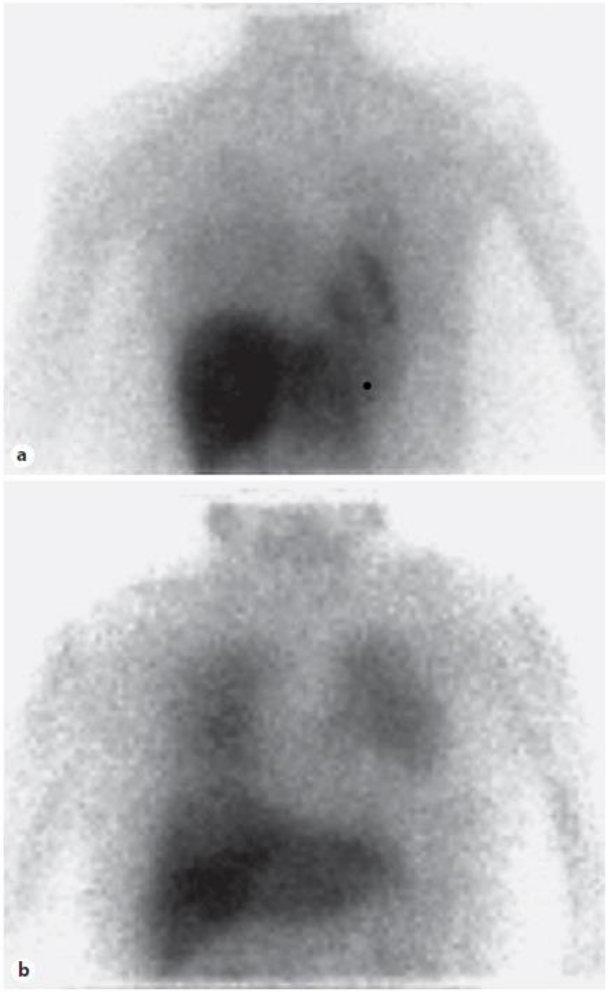
Published online: July 12

Importance of ^{123}I-Metaiodobenzylguanidine Scintigraphy/Single Photon Emission Computed Tomography for Diagnosis and Differential Diagnostics of Parkinson Syndromes

Wolfgang H. Jost[a] Kelly Del Tredici[c] Christian Landvogt[b] Stefan Braune[d]

Departments of [a]Neurology and [b]Nuclear Medicine, Deutsche Klinik für Diagnostik, Wiesbaden, [c]Clinical Neuroanatomy Section, Center for Clinical Research, Department of Neurology, University of Ulm, Ulm, and [d]Neuro Centrum, Prien, Germany

- Dysautonomia
- Central pain
- Anxiety and depression
- RBD



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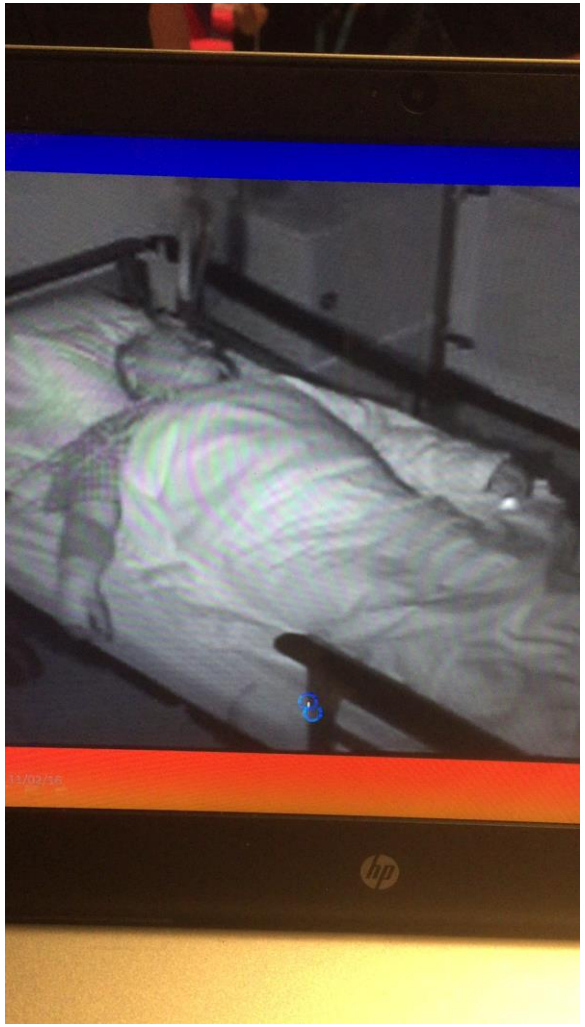

Parkinsonism and Related Disorders xxx (xxxx) xxx

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Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Recognition and characterising non-motor profile in early onset Parkinson's disease (EOPD)

Karolina Poplawska-Domaszewicz [a,b,**], Mubasher A. Qamar [b,c], Cristian Falup Pecurariu [b,d,e], K Ray Chaudhuri [b,c,*]

High NMS burden
High risk of ICD
Higher genetic cases

EOPD genetic basis	Specific genetic mutation	Clinical association
AD pattern	SNCA	Cognitive decline
AR pattern	ATP13A2 (Kufor–Rakeb Syndrome)	Rapid cognitive decline, dementia, and optic atrophy
AR pattern	PRKN	Specific pattern of ICD: compulsive shopping, binge eating, punding, increased hobbyism, and sleep benefit
AR pattern	PINK1	Specific pattern of ICD: hypersexuality, compulsive shopping, and binge eating
AD pattern (GRIN2B)	GRIN2B, DRD1 and DRD2	Strong links with ICD. Racial variations noted
AD pattern (LRRK2) AR pattern (GBA1)	LRRK2 GBA1 (pathogenic mutations)	Increased rates of ICD
AR pattern	GBA1 (pathogenic mutations)	Cognitive decline, RBD, and dysautonomia
AR pattern	PLA2G6 (PLAN)	Rapid cognitive decline and optic atrophy
AR pattern (DJ-1) AR pattern (PINK1)	DJ-1 PINK1	Association with pain in PD. PINK1 lower back pain described in EOPD
NA	DRD2 rs2283265 polymorphism	Association with pain in EOPD