Parkinson's disease is more than motor dysfunction

Njideka Okubadejo, Nigeria – IPMDS

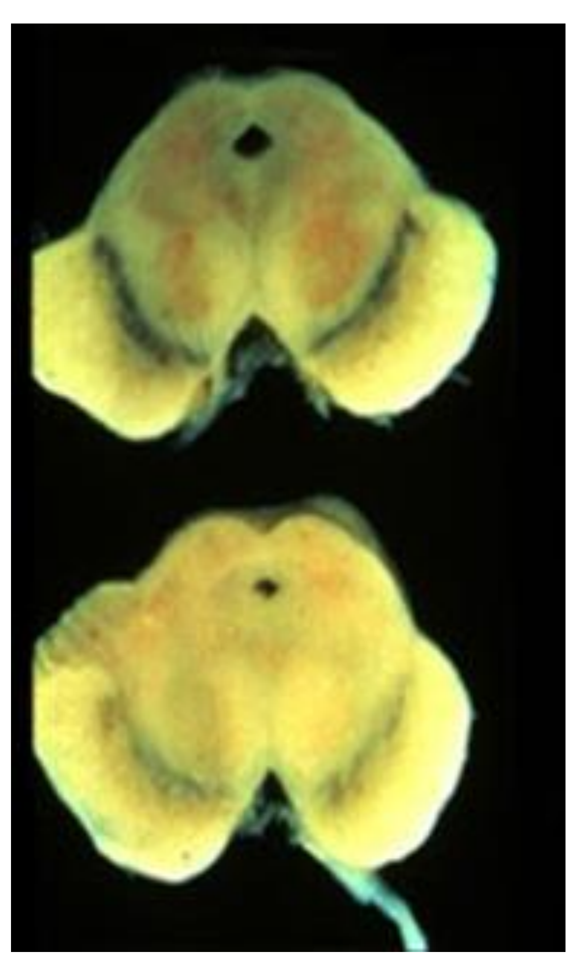
Objectives

- Describe the spectrum of motor and non-motor features of PD
- Highlight the approach to recognition and treatment

Outline

- Diagnosis of Parkinson's disease
- Non-motor features of PD
- Approach to management of NMS in PD

Parkinson’s disease



Stooped posture
Masked Face
Back rigidity
Forward tilt of trunk
Flexed elbows and wrists
Reduced arm swing
Hand tremor
Tremors in the legs
Slightly flexed hip and knees
Shuffling, short stepped gait

Autonomic dysfunction
Sensory and other complaints
Non-motor symptoms
Neuro-psychiatric problems
Sleep disorders

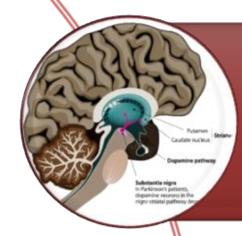
Global, regional, and national burden of Parkinson's disease, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016

*GBD 2016 Parkinson's Disease Collaborators**

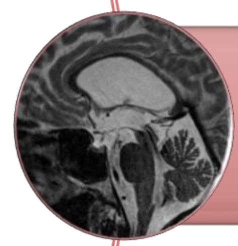
Lancet Neurol 2018; 17: 939–53

- Fastest growing neurological disorder globally
- Increased age-standardized prevalence, DALY, and death rates in most regions
- Leading source of disability globally

Classification of parkinsonism



Parkinson disease



Other degenerative parkinsonisms

Secondary parkinsonism

United Kingdom PD Society Brain Bank Criteria

Hughes AJ, Daniel SE, Kilford L, Lees AJ. JNNP 1992;55:181-184

Step 1: Diagnosis of parkinsonism

Bradykinesia
+ ≥1

Muscular rigidity	4-6 Hz rest tremor	Postural instability: **NOT DUE TO** primary visual, vestibular, cerebellar, or proprioceptive dysfunction

Step 2: Exclusions (i)

- repeated strokes with stepwise progression
- repeated head injury
- history of definite encephalitis
- oculogyric crises
- neuroleptic (or dopamine depleting drug) use at onset
- >1 affected relative**
- sustained remission
- strictly unilateral features >3 years

Step 2: Exclusions (ii)

- supranuclear gaze palsy
- cerebellar signs
- early severe autonomic involvement
- early severe dementia
- Babinski sign (unexplained)
- cerebral tumor or communication hydrocephalus on imaging
- negative response to large doses of levodopa in absence of malabsorption
- neurotoxin exposure (e.g. MPTP)

Step 3: Supportive criteria

Requires ≥3 for diagnosis of definite PD

- Unilateral onset
- Rest tremor present
- Progressive disorder
- Persistent asymmetry affecting side of onset most
- Excellent response (70-100%) to levodopa
- Severe levodopa-induced chorea
- Levodopa response for 5 years or more
- Clinical course of ten years or more

REVIEW

MDS Clinical Diagnostic Criteria for Parkinson's Disease

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Mov Disord. 2015 Oct;30(12):1591-601.

- **Define parkinsonism**
  - motor parkinsonism i.e. bradykinesia + rest tremor and/or rigidity

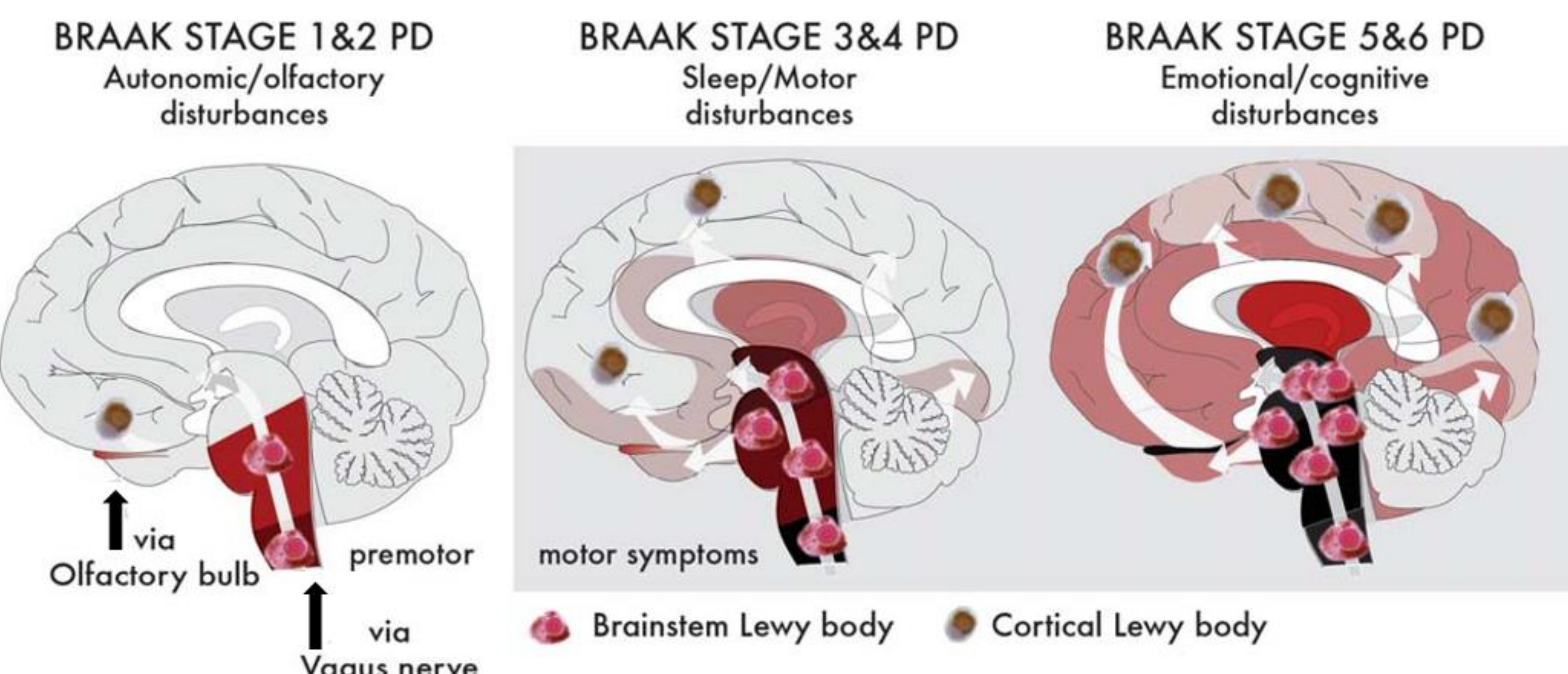
- **Determine if parkinsonism is attributable to PD**
  - absolute exclusion criteria (rule out PD)
  - red flags (must be counterbalanced by additional supportive criteria)
  - supportive criteria (positive features that increase confidence of diagnosis)

- **NMS considered:** red flag = absence of common NMS despite 5 years disease

Non-motor symptoms in PD

- Neuropsychiatric symptoms
- Autonomic dysfunction
- Disorders of sleep and wakefulness
- Pain and other sensory disturbances

Why do people with PD have NMS



Assessing NMS in the clinic

- Be aware and ask directly about specific symptoms
- Use screening questionnaires (global or symptom specific)
- Global screening questionnaires
  - Non-motor symptoms scale (NMSS)
  - Non-motor symptoms questionnaire (NMS-Quest)
  - IPMDS Nonmotor Rating Scale (MDS-NMS)
    - NoMoFA (non-motor fluctuations in levodopa-treated PD)
  - MDS-UPDRS (Part 1: Non-Motor Aspects of EDL (nM-EDL))

General approach to managing NMS

- Identify the NMS and time of occurrence (on or off dopaminergic therapies)
- Consider and carefully assess triggers or contributing factors
- Adapt the antiparkinsonian drug regime as first step
- Consider specific treatment of the NMS (**pharmacological and non-pharmacological combination typically required)**
- Off-label use of medications (with attention to interactions and safety)

MDS COMMISSIONED REVIEW

Update on Treatments for Nonmotor Symptoms of Parkinson's Disease—An Evidence-Based Medicine Review

Klaus Seppi, MD,[1*] K. Ray Chaudhuri, MD,[2] Miguel Coelho, MD,[3] Susan H. Fox, MRCP (UK), PhD,[4] Regina Katzenschlager, MD,[5] Santiago Perez Lloret, MD,[6] Daniel Weintraub, MD,[7,8] Cristina Sampaio, MD, PhD,[9,10]
and the collaborators of the Parkinson's Disease Update on Non-Motor Symptoms Study Group on behalf of the Movement Disorders Society Evidence-Based Medicine Committee

Mov Disord. 2019;34(2):180-198

- Provides an update on evidence-based treatments for NMS in PD
- Highlights the paucity of evidence-based treatments for some NMS
- Describes the application of non-PD specific treatment recommendations

Neuropsychiatric symptoms

Depression and depressive symptoms	*Dopamine agonist (Pramipexole*);TCA (amitriptyline, nortriptyline, desipramine); SSRI (Venlafaxine*, fluoxetine, paroxetine, etc.)*
Anxiety and anxiety symptoms	*CBT, SSRIs, SNRIs*
Apathy	*Pirebedil; Rivastigmine*
Psychosis	*Clozapine*, pimavanserin, quetiapine*
Impulse control and related disorders	*Cognitive behavioural therapy*
Dementia	*Rivastigmine*, Donepezil, Galantamine,*
Mild cognitive impairment	*Insufficient evidence*

Autonomic dysfunction

Constipation	*Macrogol; probiotics and prebiotic fibre;*
Drooling	*Glycopyrrolate; botulinum toxin A, B*
Orthostatic hypotension	*Fludrocortisone, midodrine*
Urinary dysfunction (e.g. overactive bladder)	*Solifenacin, Oxybutinin, Tolterodine; scheduled bathroom trips;*
Erectile dysfunction	*Sildenafil*
Anorexia, nausea vomiting (LD/DA-induced)	*Domperidone*

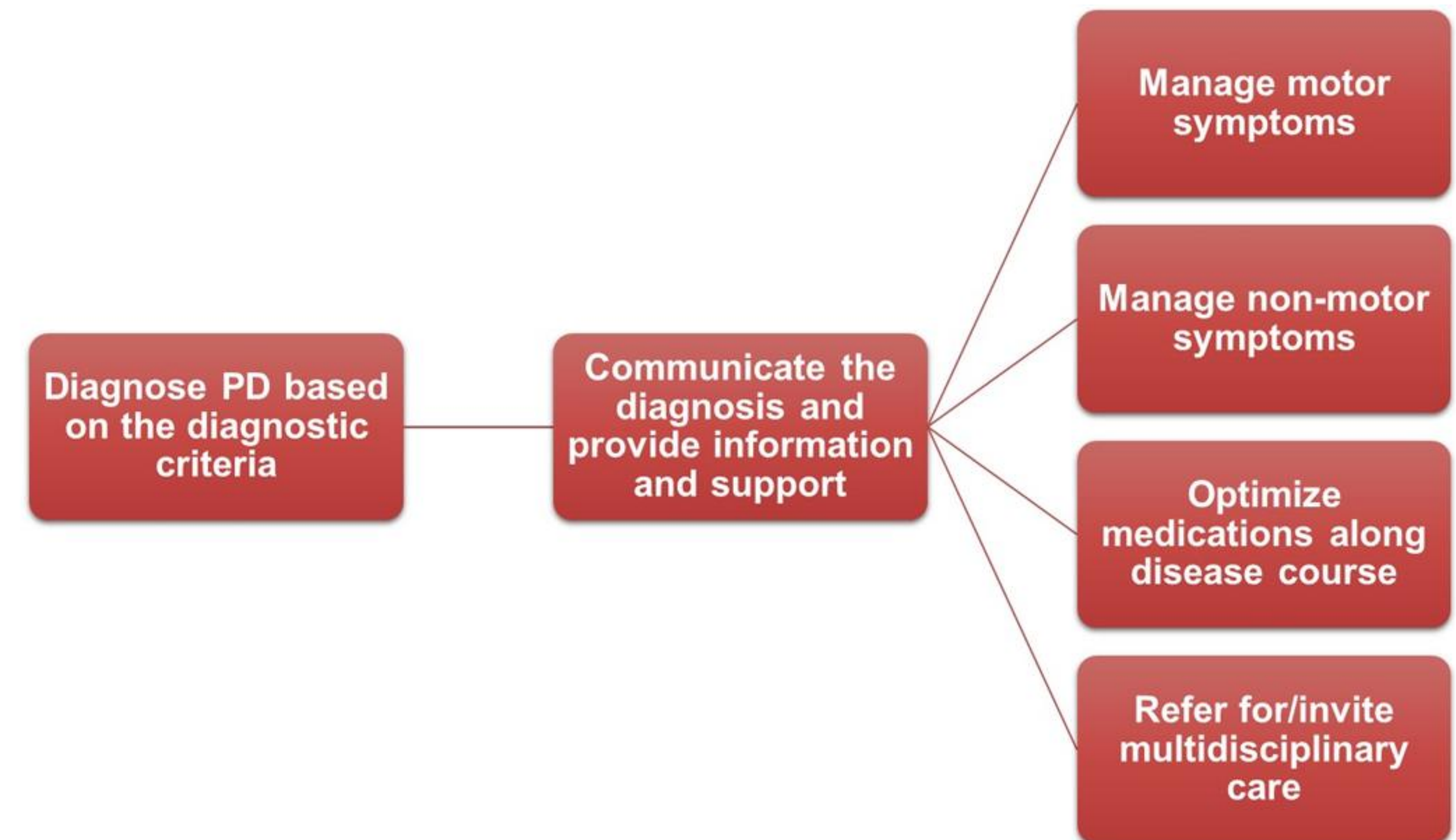
Disorders of sleep and wakefulness

Insomnia and sleep fragmentation	*Melatonin (3-5mg); Eszopiclone; Sleep hygiene; CBT*
Rapid eye movement sleep behavioural disorder	*Clonazepam, Melatonin*
Excessive daytime sleepiness	*Modafinil, Caffeine, CPAP (OSA)*

Pain and other disturbances

Pain	*Oxycodone-naloxone prolonged release*
Fatigue	*Methylphenidate; Rasagiline; Modafinil*
Olfactory dysfunction (hyposmia, anosmia)	
Ophthalmologic dysfunction	

Summary



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