Parkinson’s disease is more than motor dysfunction

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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
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 parkinsonism
- Secondary parkinsonism
United Kingdom PD Society Brain Bank Criteria

- Parkinsonism
- Exclusions (red flags) absent
- Supportive features present
- Parkinson disease

Step 1: Diagnosis of parkinsonism

Bradykinesia

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
• 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

BRAAK STAGE 1 & 2 PD
Autonomic/olfactory disturbances

BRAAK STAGE 3 & 4 PD
Sleep/Motor disturbances

BRAAK STAGE 5 & 6 PD
Emotional/cognitive disturbances

Olfactory bulb
Premotor
Motor symptoms
Brainstem Lewy body
Cortical Lewy body
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)
• 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

<table>
<thead>
<tr>
<th>Neuropsychiatric Symptoms</th>
<th>Treatments</th>
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</thead>
<tbody>
<tr>
<td>Depression and depressive symptoms</td>
<td>Dopamine agonist (Pramipexole*); TCA (amitriptyline, nortriptyline, desipramine); SSRI (Venlafaxine*, fluoxetine, paroxetine, etc.)</td>
</tr>
<tr>
<td>Anxiety and anxiety symptoms</td>
<td>CBT, SSRIs, SNRIs</td>
</tr>
<tr>
<td>Apathy</td>
<td>Pirebedil; Rivastigmine</td>
</tr>
<tr>
<td>Psychosis</td>
<td>Clozapine*, pimavanserin, quetiapine</td>
</tr>
<tr>
<td>Impulse control and related disorders</td>
<td>Cognitive behavioural therapy</td>
</tr>
<tr>
<td>Dementia</td>
<td>Rivastigmine*, Donepezil, Galantamine,</td>
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<tr>
<td>Mild cognitive impairment</td>
<td>Insufficient evidence</td>
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## Autonomic dysfunction

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>Constipation</td>
<td>Macrogol; probiotics and prebiotic fibre;</td>
</tr>
<tr>
<td>Drooling</td>
<td>Glycopyrrolate; botulinum toxin A, B</td>
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<tr>
<td>Orthostatic hypotension</td>
<td>Fludrocortisone, midodrine</td>
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<tr>
<td>Urinary dysfunction (e.g. overactive bladder)</td>
<td>Solifenacin, Oxybutinin, Tolterodine; scheduled bathroom trips;</td>
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<tr>
<td>Erectile dysfunction</td>
<td>Sildenafil</td>
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<tr>
<td>Anorexia, nausea vomiting (LD/DA-induced)</td>
<td>Domperidone</td>
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</tbody>
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## Disorders of sleep and wakefulness

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>Insomnia and sleep fragmentation</td>
<td>Melatonin (3-5mg); Eszopiclone; Sleep hygiene; CBT</td>
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<tr>
<td>Rapid eye movement sleep behavioural disorder</td>
<td>Clonazepam, Melatonin</td>
</tr>
<tr>
<td>Excessive daytime sleepiness</td>
<td>Modafinil, Caffeine, CPAP (OSA)</td>
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# Pain and other disturbances

<table>
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<tr>
<th>Disturbance</th>
<th>Treatment</th>
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</thead>
<tbody>
<tr>
<td>Pain</td>
<td><strong>Oxycodone-naloxone prolonged release</strong></td>
</tr>
<tr>
<td>Fatigue</td>
<td><strong>Methylphenidate; Rasagiline; Modafinil</strong></td>
</tr>
<tr>
<td>Olfactory dysfunction (hyposmia, anosmia)</td>
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<tr>
<td>Ophthalmologic dysfunction</td>
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Summary

Diagnose PD based on the diagnostic criteria

Communicate the diagnosis and provide information and support

- Manage motor symptoms
- Manage non-motor symptoms
- Optimize medications along disease course
- Refer for/invite multidisciplinary care