Objectives

- Importance of age in diagnosis
- Diagnostic challenges
- Brain Bank criteria
- Differential diagnoses
- Challenge testing
- Imaging: structural & functional
What is Parkinson’s disease?

**Neuropsychiatric**
- Dementia
- Depression
- Anxiety
- Apathy
- Hallucinations
- Delusions
- Psychosis

**Sleep disturbance**
- REM sleep behaviour disorder
- Restless legs
- Excessive daytime somnolence
- Insomnia
- Vivid dreams

**Autonomic**
- Urinary urgency / frequency
- Nocturia
- Sweating
- Orthostatic hypotension
- Erectile dysfunction

**Sensory**
- Pain
- Paraesthesia
- Hyposmia
- Visual symptoms

**Gastrointestinal**
- Sialorrhoea
- Dysphagia
- Gastroparesis
- Constipation

**Much more than a motor disorder**

Age & Parkinson’s disease
Parkinson’s disease

- Age is the single greatest risk factor for PD
- 1-2% of over 65s
- 3-5% of over 85s

Alves et al, J Neurol 2008; 255: p18-32

Diagnostic challenges
Diagnostic challenges?

- Clinical diagnosis
- No diagnostic test
- Some signs & symptoms may be attributed to normal ageing
- Overlap of symptoms with other conditions
- Evolving signs and symptoms
- Misinterpretation of imaging

Diagnosing PD can be challenging

- 50% PD diagnosed in the community is not PD
- Suspected new cases should be referred (untreated) to an experienced clinician
- Diagnostic criteria should be used
- But a 5-10% diagnostic inaccuracy rate persists
What do the guidelines say?

**1.2 Diagnosing Parkinson’s disease**

**1.2.1 Definition and differential diagnosis**

PD should be suspected in people presenting with tremor, stiffness, slowness, balance problems and/or gait disorders.

**1.2.2 Expert versus non-expert diagnosis**

People with suspected PD should be referred quickly and untreated to a *specialist* with expertise in the differential diagnosis of this condition.

**1.2.3 Clinical versus post-mortem diagnosis**

PD should be diagnosed clinically and based on the UK Parkinson’s Disease Society Brain Bank Criteria.

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**Diagnosis**

The diagnosis of Parkinson’s disease depends on the presence of a specific set of symptoms and signs (bradykinesia plus one of the following: rigidity, rest tremor or postural instability), the absence of atypical features, a slowly progressive course, and a response to drug therapy.

**Clinical diagnosis compared with pathological confirmation**

- Clinicians should be aware of the poor specificity of a clinical diagnosis of Parkinson’s disease in the early stages of the disease, and consider this uncertainty when giving information to the patient and when planning management.
- Patients should be offered long-term, regular follow-up to review the diagnosis of Parkinson’s disease. This should include a review of the ongoing benefits in those started on dopamine replacement therapy.
- Formal research criteria should not be used in isolation for diagnosing Parkinson’s disease in a clinical setting but clinicians should take them into account when making a clinical diagnosis.
How do we make the diagnosis?

Tests
Examination
History

A new referral

Parkinsonism
Degenerative
Synucleinopathies
- PD
- MSA
- DLB

Non-degenerative
- Drug induced
- Metabolic
- Infective
- Structural

Tremor
- Essential tremor
- Dystonic
- Thyrotoxicosis
- Neuropathic
- Drug induced
- Task specific

Tauopathies
- PSP
- CBD
- Vascular
A new referral

**Parkinsonism**
- Degenerative
  - Synucleinopathies
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**Tremor**
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Brain Bank Criteria
# Diagnostic criteria for idiopathic Parkinson’s disease

- **UK Parkinson’s Disease Society Brain Bank Criteria**
  1. Diagnosis of a parkinsonian syndrome
  2. Exclusion criteria
  3. Supportive features

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<table>
<thead>
<tr>
<th>Step 1</th>
<th>Diagnosis of a parkinsonian syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bradykinesia plus at least one of the following</td>
<td></td>
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</tbody>
</table>
| • Rigidity  
• Rest tremor (4-6Hz)  
• Postural instability |

<table>
<thead>
<tr>
<th>Step 2</th>
<th>Exclusion criteria for PD</th>
</tr>
</thead>
</table>
| • Repeated strokes  
• Repeated head injury  
• Encephalitis  
• Oculogyric crises  
• Neuroleptic treatment  
• >1 affected relative  
• Sustained remission  
• Unilateral only after 3 years  
• Supranuclear gaze palsy  
• Cerebellar signs  
• Early severe autonomic involvement  
• Early severe dementia  
• Babinski’s sign  
• Cerebral tumour or hydrocephalus on CT  
• Negative response to large Ldopa doses  
| MPTP exposure |

<table>
<thead>
<tr>
<th>Step 3</th>
<th>Supportive prospective positive criteria (3 or more required for definite diagnosis)</th>
</tr>
</thead>
</table>
| • Unilateral onset  
• Rest tremor  
• Progressive disorder  
• Persistent asymmetry – first side worst  
• Excellent Ldopa response  
• Severe Ldopa chorea  
| Ldopa response >5 years  
• Clinical course >10 years |

My personal approach to diagnosis

History & examination (occasional tests)

- Identify Parkinsonism
- Exclude Red flags
- Supportive Non-motor features

Keep reviewing symptoms & signs
Re-evaluate your diagnosis!

Differential diagnoses
Common differential diagnoses for PD

- Essential tremor (ET)
- Progressive supranuclear palsy (PSP)
- Multiple system atrophy (MSA)
- Vascular / Multi-infarct state

Essential tremor

- 10 times as common as PD
  - ET: 1,500/100,000 (prevalence)
  - PD: 150/100,000
- Onset usually before the age of 60
- Tremor usually present for 2-5 years before referral
- Postural / action tremor
- Head / vocal tremor may occur
- Family history – often but not always
- Improvement with alcohol – not always
- Treatment: Beta-blockers, anti-epileptics, rarely surgery
### PSP

- Symmetrical
- Early postural instability and falls (backwards)
- Retrocollis (neck extensions)
- Supranuclear ophthalmoplegia / gaze palsy
  - Vertical then horizontal
- Frontalis overactivity (startled expression)
- Dementia
- Axial rigidity
- Growling dysarthria & dysphagia
- Poor Ldopa response

### MSA

- Early autonomic features: urinary, erectile dysfunction
- Laryngeal dystonia... stridor... sleep apnoea
- High pitched voice & frequent sighing
- Antecollis (neck flexion)
- Stimulus sensitive myoclonus
- Cognitively intact
- Poor Ldopa response
- Two phenotypes:
  - MSA-P: Parkinsonian
  - MSA-C: Cerebellar
Vascular parkinsonism

- Multiple cerebral infarct state
- Marché à petit pas gait
- Few upper limb signs
- Poor Ldopa response
- Rapid stepwise decline
- Other features of multi-infarct state:
  - Dementia, incontinence, strokes
- Basal ganglia ischaemia on CT / MRI is not diagnostic – common in older patients

Challenge testing
Challenge testing

- Assess response to Levodopa or Apomorphine
- Acute (high dose) exposure
- Chronic (therapeutic dose) exposure
- Has been advocated as a complimentary diagnostic test

The diagnostic accuracy of acute challenge testing is equivalent to that of chronic testing

- Acute testing can cause side effects & is more expensive
- A patient's response to chronic levodopa exposure (where therapeutically indicated) helps to support the diagnosis of PD

Clarke et al, J Neurol Neurosurg Psychiatry 2000; 69: p590-4
What is the role of imaging in suspected PD?

- Not always indicated
- Supportive not necessarily diagnostic
- Needs to be interpreted alongside the clinical evaluation
- The indication for the test must be clear

- The wrong test in the wrong patient can ‘muddy the waters’
Imaging options

Structural
- CT
- MRI

Functional
- SPECT (DAT)
- PET

Structural imaging in Parkinsonism

CT
- Primarily used to exclude other pathology
  - Multiple infarct state
  - Hydrocephalus

MRI
- May help differentiate PSP & MSA from PD
- Better for looking at brainstem & cerebellar atrophy
- DWI may be helpful
MRI in atypical parkinsonism

**MSA**

- Functional imaging
  - Tracers bind to dopamine transporter proteins (DAT) in the nigrostriatal nerve endings
  - Uptake is reduced in degenerative parkinsonian disorders

**PSP**

- Functional imaging
  - Isotopes are made immediately before use
  - $^{18}$F-dopa
  - Less widely available

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SPECT

- Tracers bind to dopamine transporter proteins (DAT) in the nigrostriatal nerve endings
- Uptake is reduced in degenerative parkinsonian disorders

PET

- Isotopes are made immediately before use
- $^{18}$F-dopa
- Less widely available
DAT scanning

Caudate
Putamen

Normal comma  Abnormal full stop

- Does not distinguish between:
  - PD
  - PSP
  - DLB
  - CBD
  - Vascular

Normal in essential tremor and drug-induced parkinsonism

Abnormal in degenerative parkinsonian disorders

Objectives

- Importance of age in diagnosis
- Diagnostic challenges
- Differential diagnoses: tremor & parkinsonism
- Brain Bank criteria
- Challenge testing
- Imaging: structural & functional
Diagnosing PD can be challenging
A clear understanding of the common differential diagnoses is needed
Non-motor symptoms are not part of the diagnostic criteria but may be helpful in supporting it
- Remember PD is more than a motor disorder
- Keep reviewing the clinical features and diagnosis
- Imaging can be helpful if used appropriately
  - pick the right test for the right patient
ANY QUESTIONS?

Thank you