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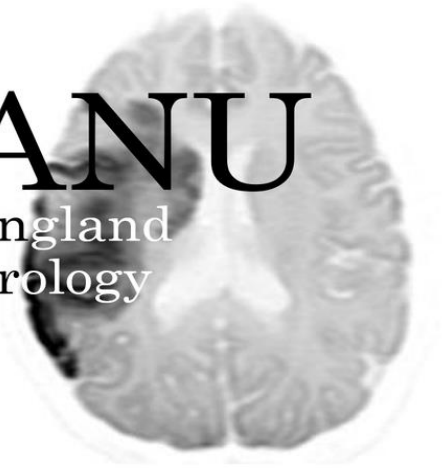
Update



Parkinson's disease

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MANCHESTER 1824
The University of Manchester

Manchester Centre for Clinical Neurosciences

Salford Royal NHS
NHS Foundation Trust

Disclosures

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- Grant funding
  - Parkinson's UK
  - Multiple System Atrophy Trust
- Speaker honoraria
  - Bial
  - Britannia Pharmaceuticals
  - Abbvie
- Travel to international meeting
  - Abbvie
  - Bial Pharma

- Trustee and Chair of Scientific Advisory Panel, Multiple System Atrophy Trust
- Deputy chair, ABN Movement Disorders Advisory Group
- Diagnostics Advisory Group, NICE
- International Parkinson and Movement Disorder Society, Evidence-based medicine committee member

Objectives

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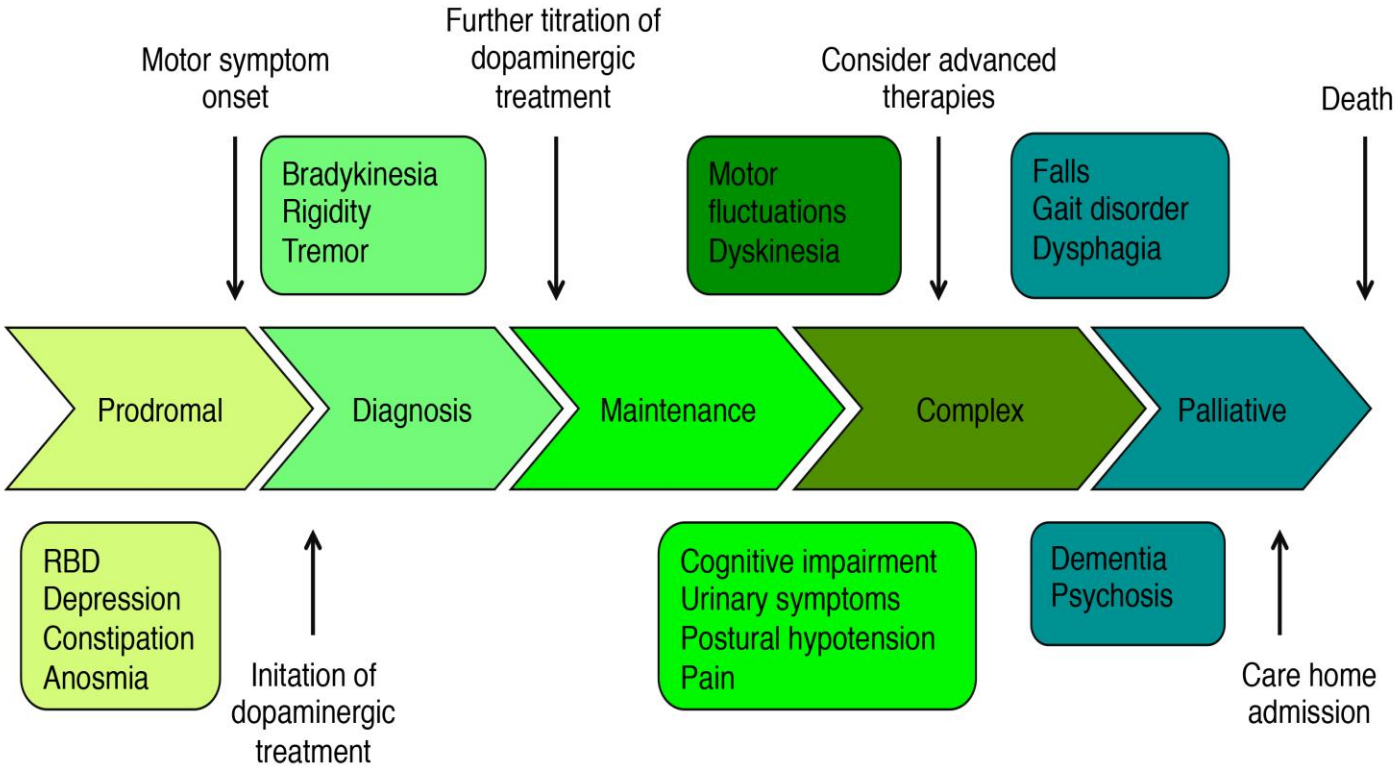
- Five important points in the diagnosis and management of Parkinson's and related conditions

- Examples from routine clinical practice

Stages of Parkinson's



Kobylecki C. *Clin Med* 2020;20:393-398.

Case 1

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- 74 year old man with PD
- On madopar 125 mg qds, entacapone 200 mg qds, pramipexole 1.5 mg
- Normally some cognitive problems, hallucinations
- Admitted with pneumonia, increased confusion
- Impaired swallow, unable to take oral medications
- What would you do here?

Decisions…

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Hold medication until swallow improved?

NG tube insertion?

Convert medication to rotigotine patch?

- It is *vital* that antiparkinsonian medications are given on time
- Evidence of increased morbidity and possible mortality if not given correctly
- Abrupt withdrawal of meds can lead to neuroleptic malignant-like syndrome

Parkinsonism-hyperpyrexia

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- Cessation or reduction of dopaminergic medications
- Presentation
  - Increased rigidity, autonomic fluctuations, sweating
  - Reduced conscious level, coma, renal failure
  - Raised CK, WCC
- Management
  - Restart antiparkinsonian medications
  - Critical care input

Typical neuroleptics or dopamine blocking anti-emetics can cause NMS = Do not prescribe in PD!

Serotonin syndrome
Recent changes to serotoninergic meds
Altered mental status
Fever, myoclonus, brisk reflexes

- Usual medications/ timings?
- Recent additions e.g. neuroleptics?
- Changes in formulation?

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Patient with Parkinson's disease or other parkinsonian syndrome?

Nil by mouth
Having swallowing problems
At risk of not absorbing medication (e.g. bowel obstruction)
Vomiting
Reduced conscious level

NO → Ensure usual medication prescribed
Ensure timings accurate

YES → Assess potential causes
e.g. infection, drug changes, missed medication

Can an NG tube be safely inserted and used?

NO → Start rotigotine patch
Refer to PDNS
No delirium/dementia= Convert dose*
Delirium/dementia present= Recommend to start at 2-4 mg/24h

YES → Insert NG tube and use for usual medication
Refer to PDNS

Normal medications available?

YES → Use own medications until supplied by pharmacy

NO → Emergency cupboard/ on call pharmacist

Conversion to rotigotine:
www.pdmedcalc.co.uk

Key points

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- Swallow problems common in in-patients with PD
- NG tube is preferred
- Caution with rotigotine particularly in dementia/delirium
- Aim is to get back to normal medications ASAP

Case 2

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- 60 year old female
- Idiopathic PD diagnosed 10y ago
  - Taking Sinemet 200/50 mg qds, rotigotine 6 mg/24h
- 3-4 month history visual hallucinations
- Complex delusions
  - people in house performing illegal acts, e.g. prostitution
  - Being monitored via webcams
  - Turning water supply off as concerned being poisoned

Parkinson's disease psychosis

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Frequency

- Visual hallucinations in up to 30%
- Delusions in 5-10%

Risk factors

- PD severity, duration
- Older age
- Cognitive impairment
- Depression

Outcomes

- Risk for:
- Care home placement
- Increased mortality

Management

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- Exclude underlying cause
- Coping strategies[1]
- Good sleep hygiene
- Avoid “typical” neuroleptics

- Medication reduction
- Consider (with specialist input)
  - Cholinesterase inhibitors
  - Quetiapine, clozapine

Box 5 | Coping strategies for patients with hallucinations[a]

Visual techniques
- Looking in another direction
- Looking at another object
- Focusing on the object in question more precisely
- Approaching or trying to touch the hallucinations

Cognitive techniques
- Patient convincing himself/herself mentally of the nonreality of the phenomenon
- Waiting for the natural disappearance of the hallucinations
- Turning on the light during the night

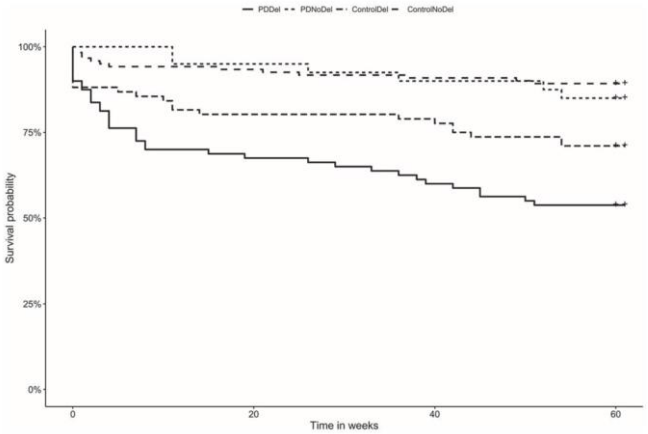
Interactive techniques
- Speaking to the spouse or caregiver in order to check the nonreality of the phenomenon, to get comfort or without a specific goal

[a]These strategies are derived from a study by Diederich and colleagues.[130]

1. Diderich NJ *et al. Nat Rev Neurol* 2009;5:331-42.

Delirium in Parkinson's

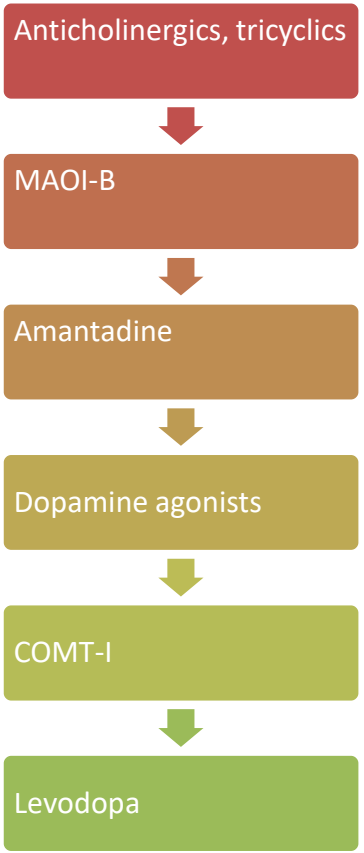
- Inpatient prevalence up to 60%
  - Vs 30% in other older adults
- Increased mortality and risk of dementia
  - 48% institutionalized at 12 months
- Important to screen hospital inpatients



Gerakios F *et al. Age Ageing* 2024;53:afae046

Delirium in Parkinson's

- Assess and treat intercurrent illness, screen for causes
- Explain and reassure (patient, carer)
- Reduce sensory deprivation or overstimulation
- Stepwise reduction in medications
- Medical management (cholinesterase inhibitors, atypical antipsychotics) only with specialist input



Case 3

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- 55 year old male, PD diagnosed 8y ago
- Low mood
- Increased problems with gambling, scratchcards
  - Spent £10,000 in past month
  - Problems with paying bills and relationships
- Medication
  - Madopar 100/25 mg x 5
  - Opicapone 50 mg night
  - Pramipexole MR 4.5 mg salt daily

Impulse control disorders

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Frequency

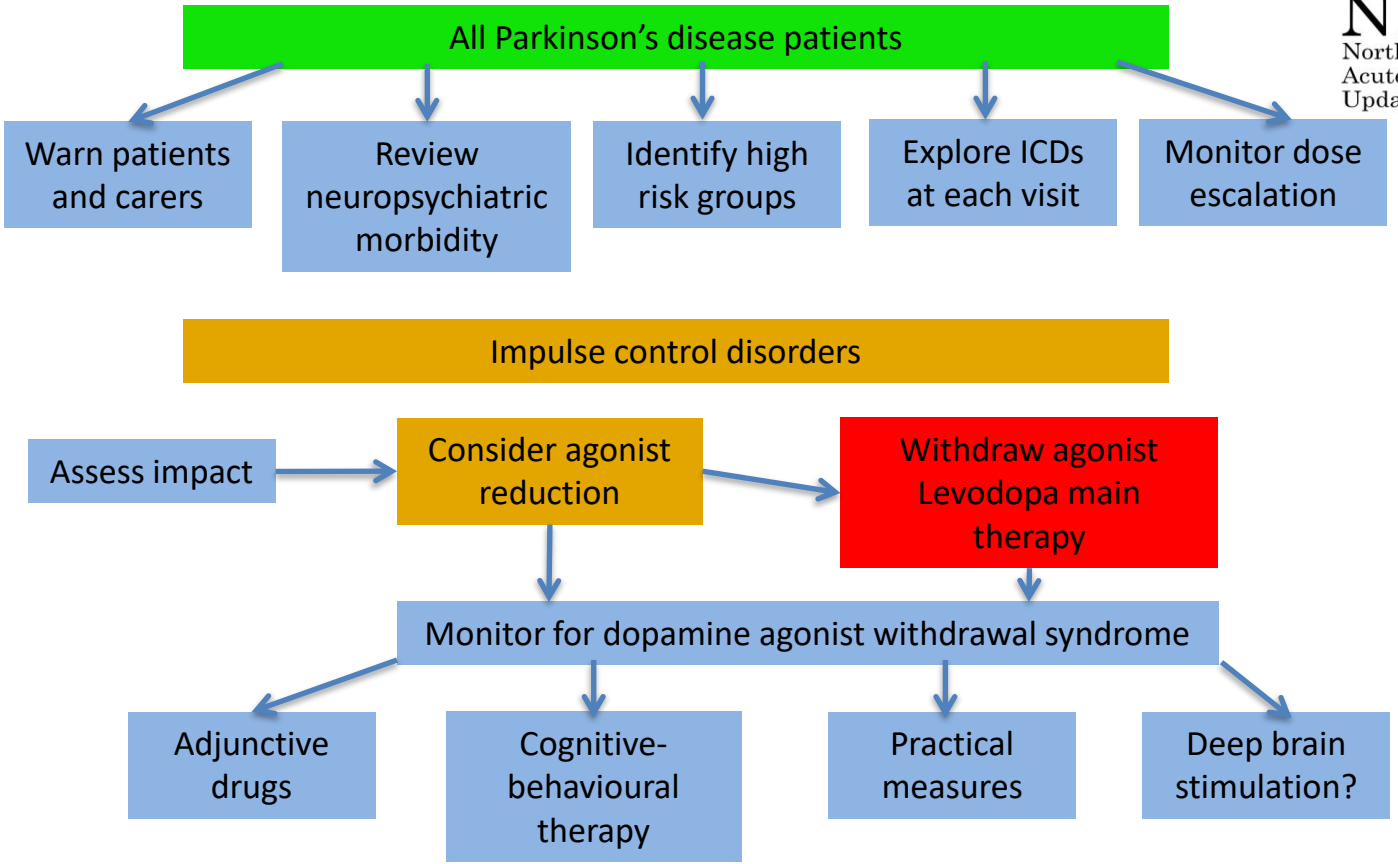
- 14% patients with PD
- Up to 40% over time with dopamine agonists

Features

- Gambling
- Hypersexuality
- Compulsive shopping
- Binge eating
- Hobbyism
- Compulsive medication use

Risk factors - 5 ‘A’s

- Dopamine **A**gonists>> levodopa
- **A**ndrogen (Male sex)
- Younger **A**ge
- **A**nxiety
- **A**ddiction (personal or family history)



Modified from MacPhee G *et al. Br J Hosp Med* 2013;74

Dopamine agonist withdrawal syndrome

Movement disorders

RESEARCH PAPER

Clinical features of dopamine agonist withdrawal syndrome in a movement disorders clinic

Margarita Pondal, Connie Marras, Janis Miyasaki, Elena Moro, Melissa J Armstrong, Antonio P Strafella, Binit B Shah, Susan Fox, L K Prashanth, Nicolas Phielipp, Anthony E Lang

ORIGINAL CONTRIBUTION

Dopamine Agonist Withdrawal Syndrome in Parkinson Disease

Christina A. Rabinak, BSE; Melissa J. Nirenberg, MD, PhD

Arch Neurol. 2010;67(1):58-63

- After dopamine agonist withdrawal/reduction
- Refractory to other meds apart from DA
- Symptoms include
  - Anxiety, panic attacks, depression, agitation
  - irritability, dysphoria
  - insomnia, fatigue, pain, cravings, autonomic features

Case 4

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- 72 year old male
- Slowing of movement last 2y
- Backwards falls
- Limited response to levodopa

Progressive supranuclear palsy

- Degenerative tauopathy
- Richardson's syndrome
  - **Early falls**
  - **Supranuclear gaze palsy**
  - Dysarthria, dysphagia
  - Subcortical dementia
- Other subtypes
  - PSP-parkinsonism, gait freezing, frontal, speech/language

Whitwell JL *et al. Mov Disord* 2017;32:955-971.

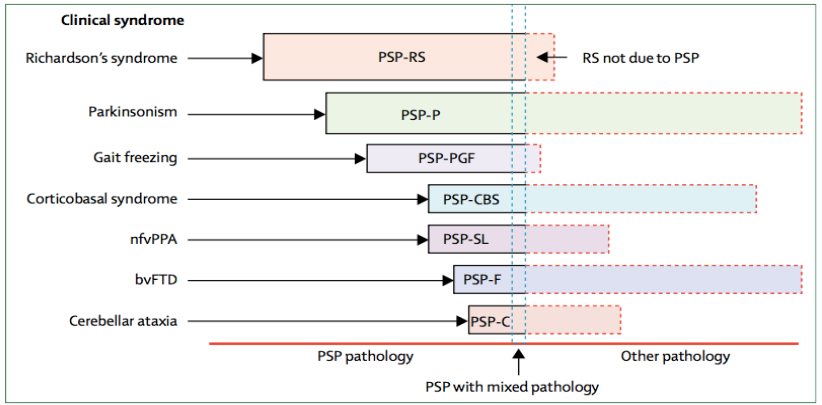

***Figure 2*: Clinical syndromes in progressive supranuclear palsy**

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- 65 year old female
- 4 year history left arm stiffness and slowness
- Urinary incontinence
- Reflexes brisk, plantars extensor

Multiple system atrophy

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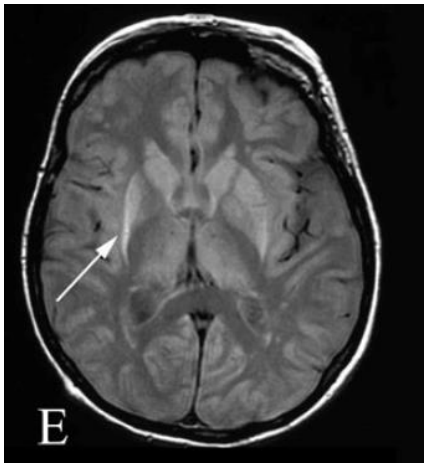
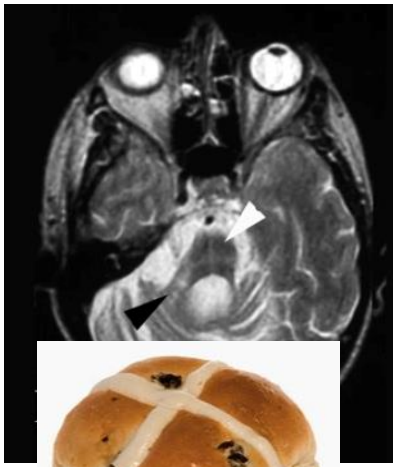
- Autonomic involvement
- Sleep disordered breathing/stridor
- Poor/transient response to levodopa
- Pathology
  - Glial and neuronal α-synuclein inclusions
- Prevalence 4.4/100,000[1]

- Parkinsonism 70%
- Cerebellar 30%





1. Schrag A *et al. Lancet* 1999;354:1771-5.

Parkinsonism defined as: Bradykinesia and rest tremor and/or rigidity

Supportive criteria	Exclusion criteria: PD excluded if present	Red flags
	Alternative diagnosis	***Possible alternative diagnosis***
Clear and dramatic response to dopaminergic therapy	Cerebellar signs	Wheelchair use within 5 years of onset
	MSA	*MSA, PSP*
Levodopa-induced dyskinesia	Downward vertical supranuclear gaze palsy or slow downward saccades	Absent progression over 5 years
	PSP	*Non-degenerative eg essential tremor, dystonic tremor, drug-induced*
Limb rest tremor	Behavioural variant FTD or progressive aphasia within 5 years	Early severe dysphonia, dysarthria, dysphagia
	FTD, PSP	*MSA, PSP*
Olfactory loss	Lower limb signs only for >3 years	Inspiratory stridor
	VP, NPH	*MSA*
Abnormal MIBG SPECT	Treatment with dopamine receptor antagonists	Severe autonomic failure within 5 years
	Drug-induced parkinsonism	*MSA*
	Absence of observable response to high dose levodopa (>600 mg/day)	Recurrent falls within 3 years
	MSA, PSP, CBD	*PSP*
	Cortical sensory loss, apraxia, progressive aphasia	Disproportionate antecollis (excessive forward neck flexion) or limb contractures within 10 years
	CBD, AD	*MSA*
	Normal dopaminergic functional imaging (eg dopamine transporter SPECT)	Absence of any non-motor features after 5 years
		Non-degenerative
	Non-degenerative eg essential tremor, dystonic tremor, drug-induced	Otherwise unexplained pyramidal signs
		MSA, VP
		Symmetrical parkinsonism throughout disease course
		Atypical parkinsonism

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Kobylecki C. *Clin Med* 2020;20:393-8.

The importance of correct diagnosis

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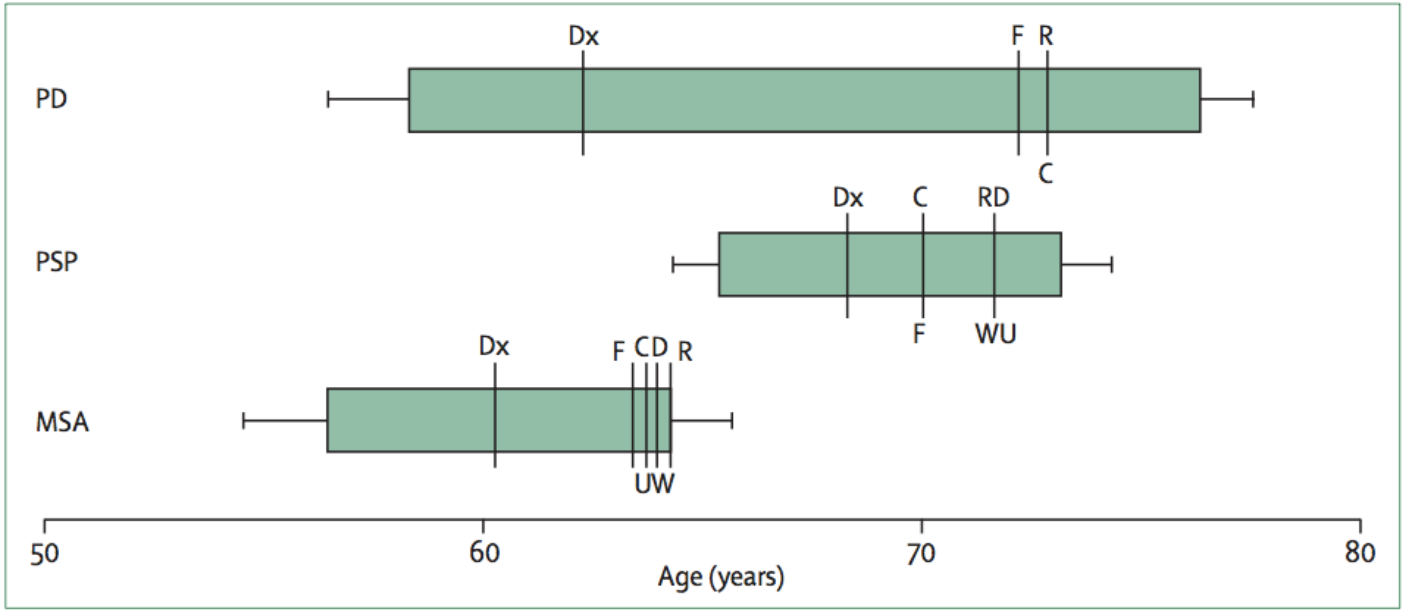

Figure 1: **Milestones of disease advancement and total disease course**
The green rectangles indicate disease duration, commencing with the timepoint of first symptoms. The vertical lines denote time of clinical diagnosis of a parkinsonian or a cerebellar syndrome (Dx) and time of documentation of milestones of disease advancement. Reproduced from O'Sullivan and colleagues,[21] with permission from Oxford University Press. C=cognitive disability. D=dysarthria or dysphagia. Dx=clinical diagnosis. F=frequent falls. MSA=multiple system atrophy. PD=Parkinson's disease. PSP=progressive supranuclear palsy. R=residential care. U=urinary catheter. W=wheelchair dependent.

1. Stefanova N *et al. Lancet Neurol* 2009;8:1172-78.
2. O'Sullivan SS *et al. Brain* 2008;131:1362-1372,

Hints to improve diagnostic accuracy

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- Be alert for red flag features
  - Not just at initial presentation!
- MR brain imaging can help identify MSA/PSP
  - Low sensitivity so can “rule in” not “rule out”
- Regional atypical parkinsonism service at Salford
  - help with difficult diagnostic cases, management, involvement in research

Case 5

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- 70 year old female
- Parkinson's diagnosed 12 years ago
- Bilateral STN deep brain stimulator inserted 5y previously, doing well
- Fell and fractured right hip
- Call from anaesthetics/surgery – "what do we do about this DBS device?"

DON'T PANIC!

DBS for Parkinson's

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- Used for refractory motor fluctuations, dyskinesia, tremor
- STN most common target
- Other indications – essential tremor, dystonia
- Expanding DBS service at Salford
  - Around 20 PD implants/year

https://www.aans.org/en/Patients/Neurosurgical-Conditions-and-Treatments/Deep-Brain-Stimulation

Surgery in DBS patients

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DBS should be switched off before surgery

Monopolar diathermy is contraindicated (risk of electrical damage)

Good communication and planning is critical

MR imaging only in neuroscience centre and needs proper discussion/planning

DBS: common problems

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Battery failure – worsening rigidity/tremor	• Most patients have programmer which can check battery life • Rechargeable DBS – may need charging
Lead fracture – worsening unilateral symptoms	• Would need to be checked at DBS centre • Skull x ray may help to confirm
Suspected infected battery/system	• Urgent discussion with Salford Neurosurgery

If in doubt – phone your local neurology/DBS centre

Five things about Parkinson's

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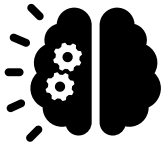
- PD medication management is critical, caution with rotigotine patches in NBM patients
- Psychosis and delirium common and associated with poor outcomes
- Watch out for impulse control disorders
- Keep an open mind on diagnosis (red flags for atypical parkinsonism)
- Don't panic on management of DBS patients, some important perioperative rules


Some useful resources

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www.pdmedcalc.co.uk

MSA Trust

www.msatrust.org.uk

PSPA

www.pspassociation.org.uk