

Update on the diagnosis and management of Parkinson's disease

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Disclosure

- None

Parkinson's Disease

- The second most common
- By 2040=> prevalence double
- 60% male and 5% <40 y/o
- SN is the primary but a large number of extranigral and non-dopaminergic brain regions are affected
- Dx: clinical and the core is bradykinesia and resting tremor or rigidity is required to confirm
- 30% no tremor
- Patients with **suspected** PD should be referred quickly and untreated to a specialist in movement disorders for evaluation
- The most common atypical PD: MSA, PSP they are more aggressive

Supportive criteria

- Clear and dramatic response to dopaminergic therapy
- Levodopa-induced dyskinesia
- Limb rest tremor
- Olfactory loss
- Abnormal MIBG SPECT

Exclusion criteria: PD excluded if present

- Cerebellar signs => MSA
- Downward vertical supranuclear gaze palsy or slow downward saccades => PSP
- Behavioural variant FTD or progressive aphasia within 5 years => FTD, PSP
- Lower limb signs only for >3 years => VP, NPH
- Treatment with dopamine receptor antagonists => drug induced PD
- Absence of observable response to high dose levodopa (>600 mg/day) => MSA, PSP, CBD
- Cortical sensory loss, apraxia, progressive aphasia => CBD, AD
- Normal dopaminergic functional imaging (eg dopamine transporter SPECT) => Non-degenerative eg essential tremor, dystonic tremor, drug-induced

Red flags: Possible alternative diagnosis

- Wheelchair use within 5 years of onset => MSA, PSP
- Absent progression over 5 years => Non-degenerative eg essential tremor, dystonic tremor, drug-induced
- Early severe dysphonia, dysarthria, dysphagia => MSA, PSP
- Inspiratory stridor => MSA
- Severe autonomic failure within 5 years
- Recurrent falls within 3 years => PSP
- Disproportionate antecollis (excessive forward neck flexion) or limb contractures within 10 years => MSA
- Absence of any non-motor features after 5 years => Non-degenerative
- Otherwise unexplained pyramidal signs => MSA, VP
- Symmetrical parkinsonism throughout disease course => Atypical parkinsonism

• Putaminal tremor is the main feature:
ET or dystonic tremor => DAT scan
but not for others

• MSA and PSP: MRI

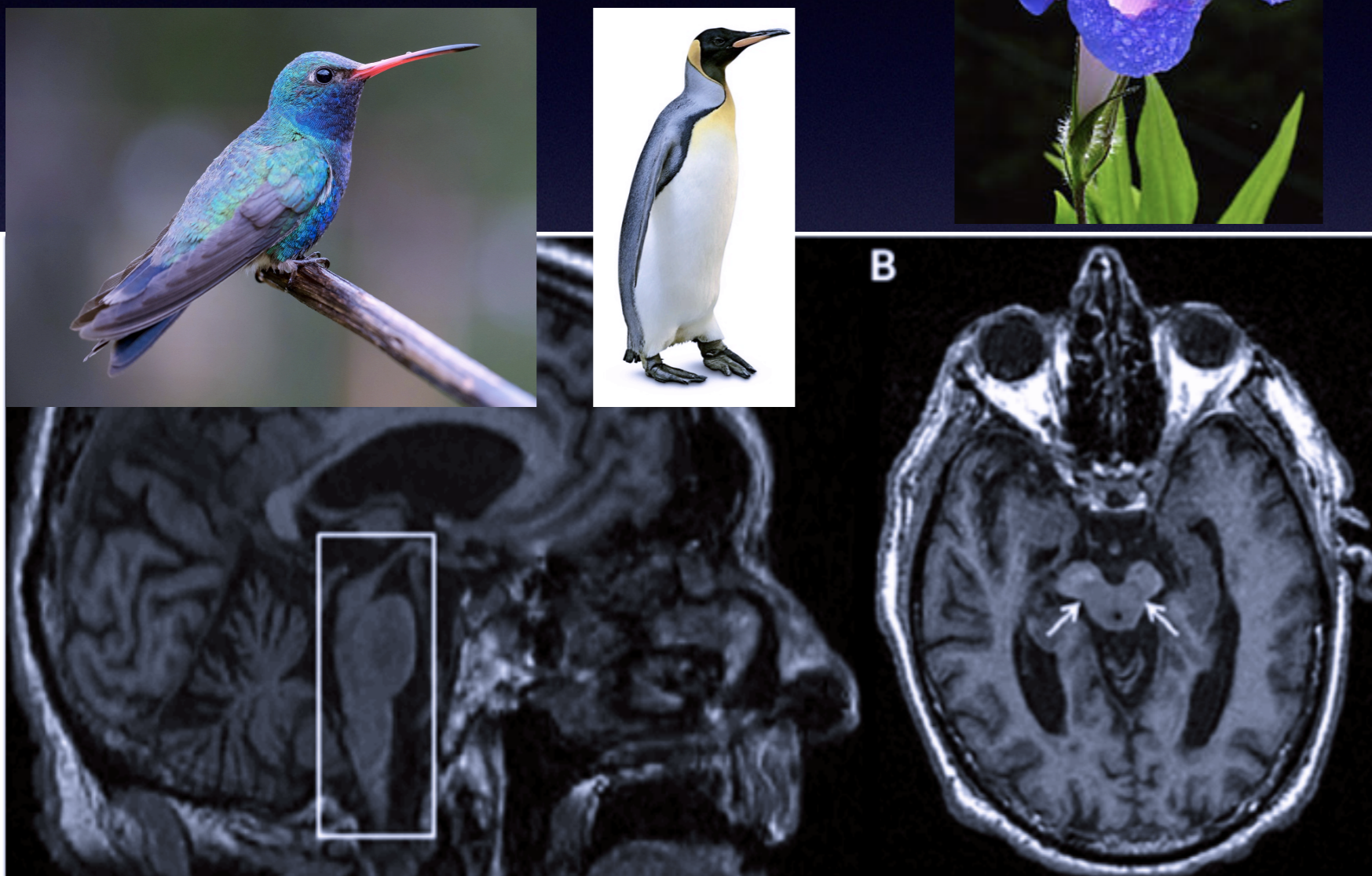


FIGURE 2-1
Hummingbird sign and morning glory sign. T1-weighted images of the brain in a patient with clinically diagnosed progressive supranuclear palsy. A, Hummingbird sign is shown (box). B, Arrows indicate morning glory sign.

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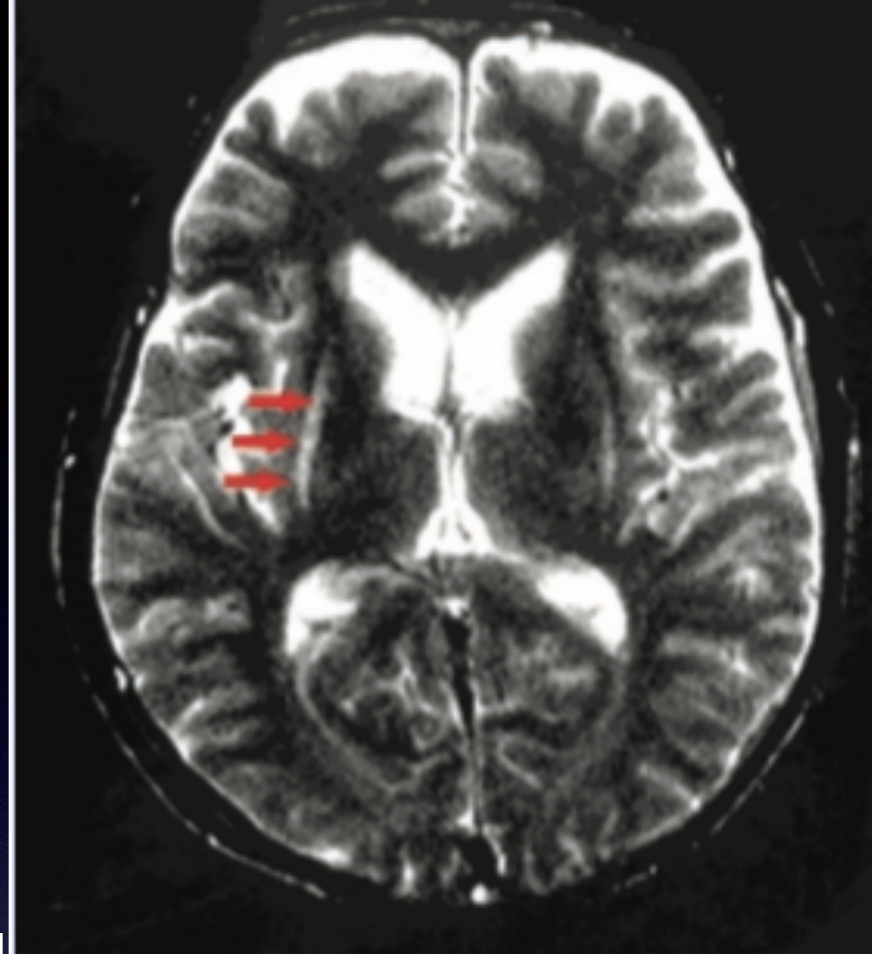
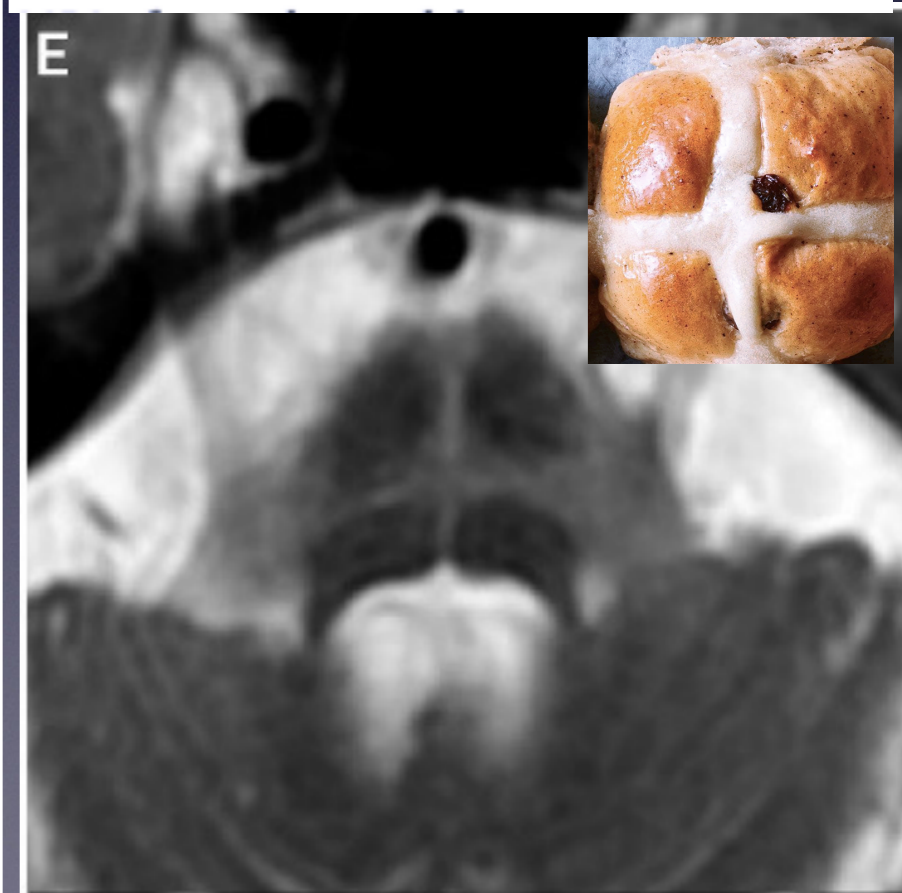


FIGURE 2-2
Putaminal slit sign. Axial T2-weighted



Progression of Parkinson's disease

- Prodromal phase: important to recognize, anosmia, constipation and REM sleep behavior disorder
- Axial symptoms such as dysphagia, gait disturbance and fall=> levodopa? How to help?
- Dementia: 80%
- PD course can be more rapid in older age and more severe motor impairment at onset

Pharmacological treatment of Parkinson's disease

- No proven DM or neuroprotective therapy
- Base on NICE, and the international Parkinson and MDS
- Initial: levodopa, MAO-I, DA
- Anticholinergic

Starting treatment in early Parkinson's disease

- The optimal time to start
- In an open-label study of 198 patients with untreated PD, quality of life (QoL) as measured by the Parkinson's Disease Questionnaire-39 (PDQ-39) worsened in those left untreated, but was stable or improved in patients receiving dopaminergic treatment
- Observational study in Ghana early vs. delayed for motor fluctuations and dyskinesia => duration of disease
- The recent delayed-start LEAP study: DM effect of levodopa <2y, PDQ-39
- The PD-MED study randomised 1,620 patients with early PD to either levodopa or 'levodopa-sparing' therapy median F/W of 3 y => **1-** PDQ-39 and overall QoL **2-** stopped treatment 28%, 23% vs. 2% **3-** dyskinesia vs. motor fluctuations => NICE
- ICD: pathological gambling, hypersexuality, and compulsive shopping and eating 14% and 2-3 times in DA

Adjunctive therapies in Parkinson's disease

- To treat motor complications
- The most common: wearing-off and delayed on periods
- Levodopa-induced dyskinesia: worst at the peak dose
- The addition of dopamine agonists, MAOB-I or catechol-O-methyltransferase (COMT) inhibitors to a levodopa-based regimen have all been shown to reduce off-time and improve on-time, although all may result in more dyskinesia
- Amantadin: main oral treatment for dyskinesia
- Once daily COMT: opicapone
- Safinamide: a combined MAOB-I and glutamate release inhibitor

Advanced therapies for Parkinson's disease

- Indication: when significant off-time or dyskinesia persists despite optimized oral treatment
- Apomorphine: the least invasive and most straightforward of these
- The recent double-blind TOLEDO study
- DBS: motor fluctuations or refractory tremor or dyskinesia
- For patients without significant axial or neuropsychiatric problems
- The benefits up to 10 years
- DUPA: levodopa-carbidopa intestinal gel via jejunostomy

Non-pharmacological management

- Exercise: A recent randomised controlled trial in 130 patients with early PD showed a significant improvement in off-state motor severity following 6m home based aerobic exercise
- Specialist physiotherapy, speech and language therapy, and occupational therapy

Inpatient management of Parkinson's disease

- Many hospitals have an alert system to inform members of the PD team of admission to allow proactive in-reach consultations
- Dopamin Blockers
- NGT if not possible patch
- Pimavananserin, Nuplazid: 34mg PO daily
- For strong CYP3A4 inhibitor coadministration
- For renal failure, liver failure
- QT
- For psychosis with dementia

