Atypical Parkinsonism

Victor Fung
Acknowledgements

- Movement Disorders Unit
  - Sangamithra Babu
  - Florence Chang
  - Ainhi Ha
  - Mariese Hely (ret)
  - Samuel Kim
  - Ivan Lorentz (Emeritus)
  - Neil Mahant
  - John Morris (Emeritus)
  - Nigel Wolfe
  - Russell Dale
  - Greg DeMoore
  - Shekeeb Mohammad
  - Michael Tchan

- Fellows
  - Alessandro Fois
  - Hugo Morales Briceno
  - 2016
  - Margaret Kit Kwan Ma

- Referring Neurologists
  - Peter Brimage
  - Paul Clouston
  - Paddy Grattan-Smith
  - Mohammed Shaffi
  - Shaun Watson

- Nurses
  - Emma Everingham
  - Donna Galea
  - Jane Griffith
  - David Tsui
Learning Objectives

• At the conclusion of the activity, participants should be able to:

1. Identify a patient with movement disorders
2. Differentiate between Parkinson’s disease and atypical parkinsonism
3. Understand Movement Disorders through case discussions
1. Clinically Established PD: Maximizing specificity, the category is anchored with the goal that the large majority (ie, at least 90%) will have PD. It is presumed that many true PD cases will not meet this certainty level.

2. Clinically Probable PD: Balancing sensitivity and specificity, the category is anchored with the goal that at least 80% of patients diagnosed as probable PD truly have PD, but also that 80% of true PD cases are identified.
TABLE 1. MDS Clinical Diagnostic Criteria for PD—Executive Summary/Completion Form

The first essential criterion is parkinsonism, which is defined as bradykinesia, in combination with at least 1 of rest tremor or rigidity. Examination of all cardinal manifestations should be carried out as described in the MDS-UPDRS parkinsonian Rating Scale. Once parkinsonism has been diagnosed:

Diagnosis of Clinically Established PD requires:
1. Absence of absolute exclusion criteria
2. At least two supportive criteria, and
3. No red flags

Diagnosis of Clinically Probable PD requires:
1. Absence of absolute exclusion criteria
2. Presence of red flags counterbalanced by supportive criteria
   - If 1 red flag is present, there must also be at least 1 supportive criterion
   - If 2 red flags, at least 2 supportive criteria are needed
   - No more than 2 red flags are allowed for this category

Supportive criteria (Check box if criteria met)

1. Clear and dramatic, beneficial response to dopaminergic therapy. During initial treatment, patient returned to normal or near-normal level of function. In the absence of clear documentation of initial response, a dramatic response can be classified as:
   - Marked improvement with dose increases or marked worsening with dose decreases. Mild changes do not qualify. Document this either objectively (≥ 30% in UPDRS III with change in treatment, or subjectively [clearly documented history of marked changes from a reliable patient or caregiver])
   - Unpredictable and marked on-off fluctuations, which must have at some point included predictable end-of-dose wearing off
2. Presence of levodopa-induced dyskinesia
3. Best tremor of a limb, documented on clinical examination (in past, or on current examination)
4. The presence of either olfactory loss or cardiac sympathetic denervation on MIBG scintigraphy
5. Unilateral cerebellar abnormalities, such as cerebellar gait, incomplete ataxia, or cerebellar ocular motor abnormalities (lag, sustained gaze-evoked nystagmus, macro gaze and saccade, ataxic gait)
6. Documented vertical supranuclear gaze palsy, or selective sparing of downward vertical saccades
7. Diagnosis of probable behavioral variant frontotemporal dementia or primary progressive aphasia, defined according to consensus criteria within the first 5 y of disease
8. Parkinsonian features restricted to the lower limbs for more than 3 y
9. Treatment with a dopamine receptor blocker or a dopamine-depleting agent in a dose and time-course consistent with drug-induced parkinsonism
10. Absence of observable response to high-dose levodopa despite at least 6 months of therapy
11. Unpredictable cortical sensory loss (e.g., graphesthesia, amnesia with intact primary sensory modalities), clear limb ideational apraxia, or progressive aphasia
12. Normal functional neuroimaging of the presynaptic dopaminergic system
13. Documentation of an alternative condition known to produce parkinsonism and plausibly connected to the patient’s symptoms, or, the expert evaluating physicians, based on the full diagnostic assessment feels that an alternative syndrome is more likely than PD

Red flags
1. Rapid progression of gait impairment requiring regular use of wheelchair within 5 y of onset
2. A complete absence of progression of rest tremor symptoms or signs over 5 y or more severe disability is related to treatment
3. Early involuntary hypokinesia, severe dysphonia or dysarthria (speech unrecognizable most of the time) or severe dysthymia (requiring soft food, NG tube, or gastrostomy feeding) within 5 y
4. Inspiratory respiratory dysphonia: either diurnal or mocastral inspiratory stridor or frequent inspiratory sighs
5. Severe autonomic failure in the first 5 y of disease. This includes:
   - Orthostatic hypotension—orthostatic decrease in blood pressure within 5 min of standing by at least 20 mm Hg systolic or 10 mm Hg diastolic
   - Severe hyperepigescia or other autonomic diseases that could plausibly explain autonomic dysfunction
   - Severe cardiac arrhythmia or cardiac insufficiency in the first 5 y of disease or severe heart disease (including long-standing or small amount stress insufficiency in women, that is not simply functional insufficiency)
   - Severe autonomic failure must not be attributable to postural disease, and must be associated with autonomic dysfunction
6. Recurrent (<15) falls because of impaired balance within 5 y of onset
7. Disparities in walking or cognitive performance on tests of hand or feet within the first 10 y
8. Absence of any of the common motor features of disease despite 5 y disease duration. These include sleep dysfunction (sleep maintenance insomnia, excessive daytime somnolence, symptoms of REM sleep behavior disorder), autonomic dysfunction (constipation, daytime urinary urgency, sympathetic orthostatic hypotension, hypertension, or psychiatric dysfunction [depression, anxiety, or hallucinations])
9. Otherwise-unexplained pyramidal tract signs, defined as pyramidal weakness or clear pathologic hyperreflexia (excluding mild reflex asymmetry and isolated extensor plantar responses)
10. Bilateral symmetric parkinsonism. The patient or caregiver reports bilateral symptom onset with no side predominance, and no side predominance is observed on objective examination

Criteria Application:
1. Does the patient have parkinsonism, as defined by the MDS criteria?  
   - Yes □ No □
2. Are any absolute exclusion criteria present?  
   - Yes □ No □
3. Number of red flags present □
4. Number of supportive criteria present □
5. Are there at least 2 supportive criteria and no red flags?  
   - Yes □ No □
6. Are there more than 2 red flags?  
   - Yes □ No □
7. Is the number of red flags equal to, or less than, the number of supportive criteria?  
   - Yes □ No □
What is a Parkinson’s disease mimic?

- Any syndrome or disease that resembles (typical) Parkinson’s disease

- Multiple etiologies:
  - Other neurodegenerative diseases (AKA atypical parkinsonian or PD plus syndromes)
  - Structural lesions
  - Drugs and toxins
  - Other (autoimmune, neuromuscular etc)
Aims

- How to diagnose typical Parkinson’s disease?
- How to recognise atypical Parkinsonism
General Neurology vs Movement Disorders

- Careful search for subtle (?imagined) neurological signs
- Where is the lesion?
- Generate a DDx based on:
  - where is the lesion
  - tempo of the disease
- Signs are so obvious they are overwhelming
- The pathology can almost always be assumed to involve the basal ganglia
- The tempo of the disease is almost always slow as neurodegenerative disease is a common cause of movement disorders
Diagnostic approach in movement disorders

- **Phenomenology**
  - What kind(s) of involuntary movements are present?
  - What is the nature of any impairment of movement?

- **Syndromic diagnosis**
  - What mix of phenomenology is present?
  - What other features are present?

- **Aetio-Pathological diagnosis**
  - What are the potential diseases that cause that syndrome?

- **Genetic diagnosis**
Phenomenology: Parkinson’s disease versus atypical Parkinsonism

- Parkinson’s disease
- Atypical Parkinsonism
Phenomenology: Parkinson's disease versus atypical Parkinsonism
55 yo, 8 yr h/o Parkinson’s disease
Note: pill rolling tremor, pause when he outstretches arms with re-emergent tremor, absent armswing with tremor when walking.
55 yo, 8 yr h/o Parkinson’s disease
Note: pill rolling tremor, pause when he outstretches arms with re-emergent tremor, absent armswing with tremor when walking.
55 yo, R UL tremor for about 15 years, onset of head tremor a few years later. No FH or response to EtOH. Note: tremor is supination-pronation, not pill-rolling.
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55 yo, R UL tremor for about 15 years, onset of head tremor a few years later. No FH or response to EtOH. Note: no major change 5 yrs later, and 20 years after tremor onset.
55 yo, R UL tremor for about 15 years, onset of head tremor a few years later. No FH or response to EtOH. Note: no major change 5 yrs later, and 20 years after tremor onset.
Successful Antiparkinsonian Medication Withdrawal in Patients With Parkinsonism and Normal FP-CIT SPECT

Vicky L. Marshall, MRCP,1,* Jim Patterson, PhD,2
Donald M. Hadley, PhD,3
Katherine A. Grosset, MBChB,1 and
Donald G. Grosset, MD1

Movement Disorders, Vol. 21, No. 12, 2006

Patients With Adult-Onset Dystonic Tremor Resembling Parkinsonian Tremor Have Scans Without Evidence of Dopaminergic Deficit (SWEDDs)

Susanne A. Schneider, MD,1 Mark J. Edwards, MD,1 Pablo Mir, MD,1,2 Carla Cordivari, MD,3
Juzar Hooker, MD,1 John Dickson, PhD,4 Niall Quinn, MD,1 and Kailash P. Bhatia, MD1,*
64 yo, 3 yr h/o akinetic rigid syndrome, poorly LD responsive. Note: low amplitude twitches of individual fingers of right hand (polyminimyoclonus) and fixed dystonia of left fingers.
64 yo, 3 yr h/o akinetic rigid syndrome, poorly LD responsive. Note: low amplitude twitches of individual fingers of right hand (polyminimyoclonus) and fixed dystonia of left fingers.
Striatonigral degeneration (MSA-p)
67 yo, 5 yr h/o involuntary jerks, Parkinsonism, dysautonomia. Note: irregular jerky tremor of upper limbs with stimulus-sensitive myoclonus.
67 yo, 5 yr h/o involuntary jerks, Parkinsonism, dysautonomia. Note: irregular jerky tremor of upper limbs with stimulus-sensitive myoclonus.
Akinesia

66 yo, 23 yr h/o typical, levodopas responsive PD. Note: moderate-severe akinesia (smallness and slowness) for finger taps, with preserved fractionated finger movements.
66 yo, 23 yr h/o typical, levodopa responsive PD. Note: moderate-severe akinesia (smallness and slowness) for finger taps, with preserved fractionated finger movements.
58 yo, L internal capsule stroke. Note: normal L hand movements, R hand has impaired alternating finger movements, finger taps, unable to fractionate finger movements but preserved all-finger movements
58 yo, L internal capsule stroke. Note: normal L hand movements, R hand has impaired alternating finger movements, finger taps, unable to fractionate finger movements but preserved all-finger movements
“Limb-kinetic” apraxia from L supplementary motor area & primary motor cortex lesion
“Limb-kinetic” apraxia from L supplementary motor area & primary motor cortex lesion
• 74 yo, walking & balance problems 1-2 yrs. Legs will not do what she tells them to do, drags left leg behind her. Left hand feels clumsy. No speech, memory problems
74 yo, walking & balance problems 1-2 yrs. Legs will not do what she tells them to do, drags left leg behind her. Left hand feels clumsy. No speech, memory problems
Corticobasal degeneration

- 74 yo, walking & balance problems 1-2 yrs. Legs will not do what she tells them to do, drags left leg behind her. Left hand feels clumsy. No speech, memory problems
• 71 yo with progressive gait unsteadiness and falls. Note: difficulty getting up from chair, wide based unsteady gait.
• 71 yo with progressive gait unsteadiness and falls. Note: difficulty getting up from chair, wide based unsteady gait.
• 71 yo with progressive gait unsteadiness and falls. 2 years later: he now has L UL akinesia, a more shuffling gait but still with a slightly widened base.
• 71 yo with progressive gait unsteadiness and falls. 2 years later: he now has L UL akinesia, a more shuffling gait but still with a slightly widened base.
Multiple system atrophy

- 71 yo with progressive gait unsteadiness and falls.
  2 years later.
• 79 yo, 2 yr h/o speech disturbance, 6/12 h/o blurred vision, gait unsteadiness and occasional falls. Vertical supranuclear gaze palsy. Note: inability to tandem gait, loss of postural reflexes.
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79 yo, 2 yr h/o speech disturbance, 6/12 h/o blurred vision, gait unsteadiness and occasional falls. Vertical supranuclear gaze palsy. Note: inability to tandem gait, loss of postural reflexes.
Ten steps to identify atypical parkinsonism

W F Abdo, G F Borm, M Munneke, M M Verbeek, R A J Esselink, B R Bloem

Background: Balance impairment is a frequently encountered problem in patients with Parkinson’s disease. A profound balance disorder, however, is an atypical feature. Methods: Tandem gait performance (10 consecutive tandem steps) was judged in 36 consecutive patients with Parkinson’s disease and 49 consecutive patients with atypical parkinsonism. Results: Only 9 (18%) patients with atypical parkinsonism had a fully normal tandem gait (not a single side step) as opposed to 33 (92%) patients with Parkinson’s disease. Analysis for the subgroup of patients with a disease duration of <3 years yielded the same diagnostic accuracy.

parkinsonism. Eighty five consecutive patients referred to the Parkinson Centre Nijmegen, Nijmegen, The Netherlands, were diagnosed by movement disorder specialists (BRB and RAJE) according to established diagnostic criteria. Our cohort included 36 patients with Parkinson’s disease, 24 with the parkinsonian variant of multiple system atrophy, 4 with progressive supranuclear palsy (PSP), 2 with dementia with Lewy bodies, 3 with corticobasal degeneration, 14 with vascular parkinsonism and 2 with clear atypical parkinsonism that did not fulfil any of the established diagnostic criteria. Clinical diagnosis was based on a detailed and standardised protocol that included comprehensive clinical
The phenomenology is determined by the anatomical location of the pathology, not necessarily the nature of the pathology.
What features improve the accuracy of clinical diagnosis in Parkinson’s disease:
A clinicopathologic study

Andrew J. Hughes, FRACP; Yoav Ben-Shlomo, MRCP; Susan E. Daniel, MRCPATH;
and Andrew J. Lees, FRCP

Article abstract—Many authorities have drawn attention to the difficulties in clinically distinguishing Parkinson’s disease (PD) from other parkinsonian syndromes. We assessed the clinical features of 100 patients diagnosed prospectively by a group of consultant neurologists as having idiopathic PD according to their pathologic findings. Seventy-six percent of these cases were confirmed to have PD. By using selected criteria (asymmetrical onset, no atypical features, and no possible etiology for another parkinsonian syndrome) the proportion of true PD cases identified was increased to 93%, but 32% of pathologically confirmed cases were rejected on this basis. These observations suggest that studies based on consultant diagnosis of PD, using standard diagnostic criteria, will include cases other than PD, thus distorting results from clinical trials and epidemiologic studies. The strict use of additional criteria can reduce misdiagnosis but at the cost of excluding genuine PD cases.

NEUROLOGY 1992;42:1142-1146
**Early Motor Symptoms**

<table>
<thead>
<tr>
<th>Green Flags (PD)</th>
<th>Red Flags (ataypical Parkinsonism)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Tremor (70%)</td>
<td>• “Tremor”</td>
</tr>
<tr>
<td>- unilateral</td>
<td>- disabling action tremor</td>
</tr>
<tr>
<td>- rest (pill-rolling) tremor</td>
<td>- jerks (myoclonus)</td>
</tr>
<tr>
<td>- UL &gt; LL &gt;&gt; jaw</td>
<td>- rest tremor in 5%</td>
</tr>
<tr>
<td>• Limb akinesia</td>
<td>• “Can’t do…”</td>
</tr>
<tr>
<td>- Difficulty or slowness</td>
<td>- apraxia rather than akinesia</td>
</tr>
<tr>
<td>• Stiffness</td>
<td>• Stiffness</td>
</tr>
<tr>
<td>- unilateral limb</td>
<td>- bilateral legs or neck</td>
</tr>
<tr>
<td>- mild-mod discomfort</td>
<td>- severe pain</td>
</tr>
<tr>
<td>• Gait &amp; balance</td>
<td>• Gait &amp; balance</td>
</tr>
<tr>
<td>- slowness of walking</td>
<td>- gait freezing</td>
</tr>
<tr>
<td>- shuffling gait</td>
<td>- falls</td>
</tr>
<tr>
<td>- poor balance</td>
<td></td>
</tr>
</tbody>
</table>
## Evolution of disease

### Green Flags (PD)
- **Motor progression**
  - slow
  (mild-moderate disability after 3-5 years)
- **Response to levodopa**
  - Very good to excellent
  - Sustained peak benefit
- **Cognition preserved**
  - slowed thinking
  - mild memory retrieval
- **Autonomic symptoms**
  - mild-moderate

### Red Flags (atypical Parkinsonism)
- **Motor progression**
  - fast
  (moderate-severe disability within 3-5 years)
- **Response to levodopa**
  - None or modest
  - Waning peak benefit
- **Impaired cognition**
  - frontal disinhibition
  - language disorder
  - memory encoding
  - prominent visuospatial
- **Prominent autonomic symptoms**
- 79 yo, 2 yr h/o difficulty using left hand, mumbling, oral dysphagia. Independent ADLs. No cognitive decline. Falls x 2. No response to levodopa.
• 79 yo, 2 yr h/o difficulty using left hand, mumbling, oral dysphagia. Independent ADLs. No cognitive decline. Falls x 2. No response to levodopa.
Multiple system atrophy

• 79 yo, 2 yr h/o difficulty using left hand, mumbling, oral dysphagia. Independent ADLs. No cognitive decline. Falls x 2. No response to levodopa.
• 60 yo, “I can’t talk (12 mths), I can’t write (18 mths) and I can’t walk (6 months – freezing through doorways)”. No falls.
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• 60 yo, “I can’t talk (12 mths), I can’t write (18 mths) and I can’t walk (6 months – freezing through doorways)”. No falls. 6 months later.
• 60 yo, “I can’t talk (12 mths), I can’t write (18 mths) and I can’t walk (6 months – freezing through doorways)”. No falls.

6 months later.
Progressive supranuclear palsy (Pure akinesia with gait freezing)

• 60 yo, “I can’t talk (12 mths), I can’t write (18 mths) and I can’t walk (6 months – freezing through doorways)”. No falls. 6 months later.
- 79 yo, 18/12 h/o of progressive difficulty walking with increasing falls. Unable to give history answering “I don’t know”. A few episodes of urinary incontinence.
• 79 yo, 18/12 h/o of progressive difficulty walking with increasing falls. Unable to give history answering “I don’t know”. A few episodes of urinary incontinence.
Normal pressure hydrocephalus

- 12/12 post V-P shunt
Normal pressure hydrocephalus

- 12/12 post V-P shunt
78 yo. 20/11/2010 when walking started to take smaller and smaller steps and then fell. Since, daily episodes of “dizziness” & a feeling that he will fall forwards with increasing shuffling gait, truncal flexion, painful calves, forced to sit for a few minutes before he recovers. Still walks 1km most days.
78 yo. 20/11/2010 when walking started to take smaller and smaller steps and then fell. Since, daily episodes of “dizziness” & a feeling that he will fall forwards with increasing shuffling gait, truncal flexion, painful calves, forced to sit for a few minutes before he recovers. Still walks 1km most days.
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Normal pressure hydrocephalus

- Gait variable
- Similarities to Parkinsonian gait:
  - Reduced velocity
  - Reduced stride length
  - Reduced step height
  - Relatively preserved cadence
- Differences to Parkinsonian gait
  - Widened base
  - Relatively preserved armswing
- Single tap test has good positive predictive value but low sensitivity (25-60%)
- Diagnosis is clinical and radiological
- Look for early festination leading to falls
66 yo. 20 yr h/o falls which became daily, speech slurred 10 yrs, impaired hand function 5 yrs. V-P shunt for hydrocephalus 2012 with mild improvement. Still having daily falls due to FOG, even with levodopa 400mg 3x/day.
66 yo. 20 yr h/o falls which became daily, speech slurred 10 yrs, impaired hand function 5 yrs. V-P shunt for hydrocephalus 2012 with mild improvement. Still having daily falls due to FOG, even with levodopa 400mg 3x/day.
66 yo. 20 yr h/o falls which became daily, speech slurred 10 yrs, impaired hand function 5 yrs. V-P shunt for hydrocephalus 2012 with mild improvement. Still having daily falls due to FOG, even with levodopa 400mg 3x/day.
On levodopa 300mg 3x/day + amantadine 100mg 3x/day
2015 Oct

On levodopa 300mg 3x/day + amantadine 100mg 3x/day
• 71 yo, 9/12 h/o stiffness and weakness of left leg causing gait disturbance, left leg spasms with noise or touch, better with diazepam
• 71 yo, 9/12 h/o stiffness and weakness of left leg causing gait disturbance, left leg spasms with noise or touch, better with diazepam
Stimulate median nerve single shocks, 100mA for 1ms, 9 trials
Stiff-man syndrome

- 71 yo, 9/12 h/o stiffness and weakness of left leg causing gait disturbance, left leg spasms with noise or touch, better with diazepam
61 yo. 2013 L hand cramping when using fork, difficulty opposing thumb to other fingers. Since Mar 2014, difficulty walking, esp. during dual tasking, “freezing of gait”, L leg dragging with trips causing falls. MRI brain and spine normal.
61 yo. 2013 L hand cramping when using fork, difficulty opposing thumb to other fingers. Since Mar 2014, difficulty walking, esp. during dual tasking, “freezing of gait”, L leg dragging with trips causing falls. MRI brain and spine normal.
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61 yo. 2013 L hand cramping when using fork, difficulty opposing thumb to other fingers. Since Mar 2014, difficulty walking, esp. during dual tasking, “freezing of gait”, L leg dragging with trips causing falls. MRI brain and spine normal.
C9ORF72 expansions, parkinsonism, and Parkinson disease
A clinicopathologic study

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ABSTRACT

Objective: To determine the histopathologic bases for the observed incidence of parkinsonism in families with C9ORF72 expansions, which typically cause amyotrophic lateral sclerosis (ALS) and/or frontotemporal dementia.

Methods: DNA was extracted from 377 brains with the histopathologic diagnosis of idiopathic Parkinson disease or related disorders and analyzed for C9ORF72 expansions. α-Synuclein and p62 immunohistochemistry of the substantia nigra (SN) was undertaken in brains of 17 ALS cases with (C9ORF72+) and 51 without (C9ORF72−) the C9ORF72 expansion.

Results: Only 1 of 338 cases with pathologically confirmed idiopathic Parkinson disease had a C9ORF72 expansion. Similarly, only 1 of 17 C9ORF72+ brains displayed features suggestive of α-synucleinopathy. In contrast, p62-positive, TDP-43-negative neuronal cytoplasmic inclusions within the SN were considerably more frequent in C9ORF72+ brain tissue than in the C9ORF72− brains (p = 0.005). Furthermore, there was a more marked loss of dopaminergic neurons in the SN of C9ORF72+ ALS brains than C9ORF72− ALS brains (p = 0.029).

Conclusions: SN involvement is common in C9ORF72+ ALS but can be clearly distinguished from Parkinson disease-related mechanisms by the presence of p62-positive inclusions and the absence of α-synuclein-positive Lewy bodies or Lewy neurites. Neurology® 2013;81:808-811
• 72 yo, 3 yr h/o sporadic PD on levodopa/carbidopa 600mg/day, increasing gait disturbance and falls
• 72 yo, 3 yr h/o sporadic PD on levodopa/carbidopa 600mg/day, increasing gait disturbance and falls
Inclusion body myositis

• 72 yo, 3 yr h/o sporadic PD on levodopa/carbidopa 600mg/day, increasing gait disturbance and falls
• 55 yo, 18/12 h/o pain in left buttock, worsening of previous mild low back pain and shoulder pain, increasingly disabling.
  Mild tremor L UL.
• 55 yo, 18/12 h/o pain in left buttock, worsening of previous mild low back pain and shoulder pain, increasingly disabling. Mild tremor L UL.
• On treatment with levodopa 600 mg/day & benzhexol 6mg/day
On treatment with levodopa 600 mg/day & benzhexol 6mg/day
Sporadic PD presenting with dystonic gait

- On treatment with levodopa 600 mg/day & benzhexol 6mg/day
Typical Parkinson’s disease presenting atypically

• “Uncommon presentations of common diseases are more common than common presentations of uncommon diseases”

• Unusual motor findings
  – Hemidystonia mimicking hemiparetic gait
  – Asymmetrical reflexes due to asymmetrical rigidity
  – Superimposed musculoskeletal pathology e.g. frozen shoulder

• Seemingly dopa-unresponsive
  – Inadequate dose or duration (600mg x 6 months)
  – Anxiety or depression masking levodopa response
  – Adverse response due to dopa-induced dystonia
Parkinson’s disease mimics

- Atypical parkinsonian / PD plus diseases
  - Multiple system atrophy
  - Progressive supranuclear palsy
  - Corticobasal degeneration
  - Motor neuron disease
- Structural lesions
  - Normal pressure hydrocephalus
  - Lesion of motor cortex
- Drugs and toxins
- Other (autoimmune, neuromuscular etc)
  - Dystonic tremor / SWEDDs
  - Stiff-man syndrome
  - Inclusion body myositis
- Atypical “typical” PD
AN

ESSAY

ON THE

SHAKING PALSY.

BY

JAMES PARKINSON,
MEMBER OF THE ROYAL COLLEGE OF SURGEONS.

LONDON:
PRINTED BY WHITTINGHAM AND ROWLAND,
Gough Street,
FOR SHERWOOD, NEELY, AND JONES,
Paternoster Row.
1817.
• Clinico-pathologically defined
  – Clinical syndrome of Parkinsonism
  – Neuronal loss in the substantia nigra with α-synuclein present in the degenerating cells
  – Sporadic or Familial

• Clinico-genetically defined
  – Clinical syndrome of Parkinsonism
  – Proven disease-causing gene
  – May or may not have α-synuclein pathology
  – Family history may be negative

D Berg et al., Mov Disord 2014