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# Clinical Manifestations of Parkinson's Disease and Parkinsonism

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**ABSTRACT:** The most common disorder in a patient presenting to a movement disorder clinic will be parkinsonism. The challenge is to provide the patient with the most accurate diagnosis and prognosis possible. The assumption at the time of initial presentation of the clinical diagnosis of Parkinson's disease is often wrong (20-25%). Waiting to see the pattern of progression, and response to medication provides invaluable additional information. This manuscript summarizes the clinical manifestations of Parkinson's disease and the main akinetic-rigid syndromes (progressive supranuclear palsy, multiple system atrophy, cortical-basal ganglionic degeneration, and dementia with Lewy bodies) that make up the differential diagnosis.

**RÉSUMÉ:** *Sémiologie de la maladie de Parkinson et parkinsonisme.* La majorité des patients d'une clinique des troubles du mouvement présente du parkinsonisme. Le défi est de poser le diagnostic et de déterminer le pronostic avec le plus de précision possible. La présomption d'un diagnostic clinique de maladie de Parkinson au moment de la consultation initiale est souvent erronée (20 à 25% des cas). Des informations supplémentaires précieuses peuvent émaner de l'évolution de la maladie et de la réponse à la médication. Cet article présente un sommaire des manifestations cliniques de la maladie de Parkinson et des principaux syndromes akineto-rigides (paralysie supranucléaire progressive, atrophie multisystémique, dégénérescence cortico-basale et démence à corps de Lewy) faisant partie du diagnostic différentiel.

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The examination of a patient with a disorder of movement starts with the identification of the visual phenomenology. The first breakdown is the separation between too much movement (hyperkinetic disorders), versus too little movement (hypokinetic disorders). Parkinson's disease (PD) would be the most typical example of the latter group of akinetic-rigid syndromes.

The four classic features of PD include tremor, rigidity, akinesia, and postural instability.<sup>1,2,3</sup> One must realize that not all patients with these features are parkinsonian. Physicians can be fooled by the tremor of essential tremor, the stiffness produced by joint (ankylosing spondylitis) or neuromuscular (stiff person syndrome) pathology, the hypokinesia of catatonia, depression, and hypothyroidism, or the postural instability due to a variety of other disorders including normal aging.<sup>4</sup> By acquiring the skills of the clinical exam of parkinsonian patients a neurologist should be able to minimize incorrect conclusions and maximize potential therapeutic success.

## **PARKINSONS DISEASE: THE CLASSIC FEATURES ON EXAMINATION**

### **Tremor**

Tremor is the most common initial manifestation. It may begin intermittently, occurring during stress for years prior to the

diagnosis.<sup>2</sup> The typical tremor is maximal at rest with a frequency of 3.5 - 7 hertz. It is a supination-pronation movement with alternating contraction of agonist and antagonist muscles.<sup>5</sup> Essential tremor is usually flexion-extension in direction, 4 - 12 hertz, with co-contraction of agonists and antagonist muscles during action.<sup>5</sup>

Parkinson's tremor usually begins in one arm. It can initially affect just the fingers, or even the thumb alone. The classic pill rolling or rotational component may be absent. Initially the tremor worsens ipsilaterally. If the leg is to be involved, it will be affected prior to spread (typically within two years) to the opposite side. The chin, jaw, lips and tongue may be affected but not the head.<sup>2</sup> The tremor improves with relaxation and resolves during sleep.

When assessing the patient for rest tremor, observe them sitting with their hands supported on their lap. The tremor, if absent, can be provoked by the nervousness created by mental

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arithmetic or by rapid alternating movements with the opposite extremity. If absent while sitting, the tremor may become evident standing with the arms hanging down. To eliminate an apparent “rest” tremor in essential tremor examine the patient supine.

Tremor amplitude can vary significantly during periods of observation and may cease spontaneously. It is expected to improve initially with posturing (arms out in front of the patient) but will return with maintenance of posture only to resolve again with action directed movements.<sup>2</sup> A superimposed action tremor will be evident in approximately 50 percent of Parkinson’s patients.<sup>6</sup>

### Akinesia

Dr. James Parkinson reported that “muscles do not react normally to the dictates of the mind”.<sup>1</sup> There is a failure of movement initiation (akinesia), reduced amplitude (hypokinesia), and speed (bradykinesia).<sup>2</sup>

The clinical assessment of akinesia therefore involves observing the slowing of rapid alternating limb movements. These include repetitive thumb and index finger tapping, hand opening and closing, and foot tapping. In each case the patient is reminded to try to maintain full amplitude of movement. Fatigability in the form of slowness, loss of amplitude, irregular rhythm and arrests in movement are watched for. Tachykinesia (faster than normal movement) is a phenomenon seen when the rhythm of rapid alternating movements is synchronized with the tremor frequency. By asking the patient to increase the amplitude of the movement, bradykinesia will become evident.

Akinetic disorders also involve a loss of associated movements or a decrease in “kinetic versatility” when changing from one movement to another.<sup>2</sup> This explains the characteristic shrinkage of writing from the start to the end of a sentence as well as the loss of facial expression, blinking and other associated (e.g. asymmetric arm swing) automatic movements.

Standardized quantitative measurements of speed of movement include the Purdue Peg Board,<sup>7</sup> timed tapping tests and the “get-up-and-go-test” (rising from a chair, walking a standard distance, turning and returning to starting point).<sup>8</sup>

### Rigidity

Unlike spasticity (velocity-dependent increase in tone) rigidity is evident during slow passive movement throughout the full range of joint movement and is equivalent in agonists and antagonists.<sup>2</sup> After asking the patient to relax, passive movement of the limbs and neck is performed in an irregular manner so that the patient is unable to predict the movement.<sup>3</sup> Flexion or extension of the limbs is recommended.<sup>9</sup> The abnormality of tone will be easier to detect when larger joints are examined (e.g. the elbow and knee). Just testing the wrist or ankle is inadequate. Examine the tone of the neck and exclude conditions causing local muscular or skeletal causes of stiffness (stiff person syndrome, arthritis). The abnormality of tone will be evident in patients with mild disease by the “distraction” of rapid alternating movements of the opposite limb or by the patient slowly raising the opposite arm against gravity (“cross-over maneuver” of Noika – Froment).<sup>2</sup> The examiner shouldn’t conclude the tone is normal without using these amplifying maneuvers.

Cogwheeling (a ratchet like sensation) is typically felt when there is an associated tremor. Beware mistaking the combination

of essential tremor and paratonia which creates a similar sensation.

### Gait abnormalities and postural instability

There is gait initiation failure, smaller stride length (*marche à petit pas*), festination, turning “en bloc”, antero and retropulsion. The posture becomes increasingly flexed. There is a loss of anticipatory proprioceptive reflexes. This progressive failure of righting reflexes results in increasing falls<sup>10</sup> and the physical finding of retropulsion (more than two steps backward or loss of balance) on a pull test. The latter is a safer version of the “push-manoeuvre” of Bouttier.<sup>2</sup> In the pull test, the patient stands with eyes open and feet 20 cms apart. They are warned and reassured that if required the examiner will catch them. They are pulled backwards by a brisk force applied to the anterior shoulders. The examiner is prepared, behind them, to prevent a fall. If postural instability is a presenting manifestation then usually the patient does not suffer from PD.<sup>11</sup>

The axial rigidity and akinesia lead to axial immobility and trouble with turning in bed, tangled bedclothes, and slow rising from low chairs.

### Other features on examination

**Speech** is monotone and therefore lacks prosody. Stuttering is not uncommon. Typically the volume trails off over time. Speech may have delayed initiation followed by excessively rapid production (tachyphemia). The latter is typical of young onset disease or postencephalitic Parkinson’s.<sup>3</sup> Excessive hoarseness or dysarthria early on is suggestive of multiple system atrophy (MSA) or Progressive Supranuclear Palsy (PSP).<sup>2</sup> Hypersalivation is uncommon on exam but can be identified historically by asking if the patient’s pillow is wet at night.

**Writing** should be observed. Avoid having the patient sign their name when testing this. Choose some other less automatic phrase. Look for a trailing off in the size (micrographia) and speed of writing during a repetitive written task. A small amplitude tremor is not uncommon with writing.<sup>3</sup> More severe tremor would be in keeping with essential tremor, or secondary parkinsonism.

**Axial movement** should be observed by watching the patient rising from lying and sitting positions. Standing posture needs to be assessed looking for neck, trunk and arm flexion. Scoliosis can also be seen.<sup>12</sup>

### SECONDARY PARKINSONISM

The examiner needs to have an organized approach to the differential diagnosis (Table 1). The main clues will be found on history. Check the medication record with patient, family and pharmacy as the most frequent cause of parkinsonism is medication. (Table 2). Review the history for toxin exposure, past occupations, infections, or stroke-like history. Any pathologic process affecting the basal ganglia can produce parkinsonism.

On examination, look for signs of a drug-induced disorder including tardive movements, akathisia, tremor that was symmetric from the start or a tremor that persists at rest, posturing and action. The classic triad of dementia, incontinence, ataxia with parkinsonism should lead one to consider normal pressure hydrocephalus.<sup>2</sup> Nystagmus, hyperactive deep tendon

**Table 1:** Differential diagnosis of Parkinsonism

Medication induced (direct or withdrawal)

**Primary neurodegenerative disorders with Parkinsonism:****Inherited:**Parkinson's disease; [types with confirmed gene site and inheritance type<sup>48</sup>]

|                 |            |                     |
|-----------------|------------|---------------------|
| Alpha Synuclein | 4q21-q23   | Autosomal dominant  |
| Parkin          | 6q25.2-q27 | Autosomal recessive |
| UCH-L1          | 4p14-15.1  | Autosomal dominant  |
| ? (PARK3)       | 2p13       | Autosomal dominant  |
| ? (PARK4)       | 4p15       | Autosomal dominant  |
| ? (PARK6)       | 1p35-p36   | Autosomal recessive |
| ? (PARK7)       | 1p35-p36   | Autosomal recessive |

Alzheimer's disease

Huntington's disease

Spinocerebellar atrophies (SCA2, SCA3)

Neuro-acanthocytosis

Dopa responsive dystonia (DRD)

Dentato Rubral Pallidal Luysian atrophy (DRPLA)

Pantothenate kinase-associated neurodegeneration (PKAN) formerly Hallervorden Spatz syndrome<sup>49</sup>

Familial depression, alveolar hypoventilation and parkinsonism

Neuronal intranuclear inclusion disease

**Sporadic:**

Idiopathic Parkinson's disease

Parkinson 'Plus':

Progressive supranuclear palsy

Multiple system atrophy

Cortical basal ganglionic degeneration

Dementia with Lewy bodies

Alzheimer's disease

Pick's disease

ALS-Parkinson-dementia of Guam

Hemiparkinsonism with hemiatrophy

**Secondary disorders with Parkinsonism:****Inherited:**

Wilson's disease

Gauchers disease

GM1 gangliosidosis

Chediak-Higashi syndrome

**Sporadic:**

Toxic (1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine, carbon monoxide, carbon disulfide, cyanide, manganese)

Hepatocerebral degeneration (non-Wilsonian)

Endocrine (hypothyroidism, hypoparathyroidism)

Mass lesions (arteriovenous malformation, neoplasm - primary or metastatic or paraneoplastic syndrome)

Vascular (vasculitis, infarction, lacunar state)

Infection related (viral encephalitis, syphilis, HIV, Cruetzfeldt-Jakob disease)

Trauma

Autoimmune or inflammatory

Lack of substrate (hypoxia, hypoglycemia)

**Others:**

Normal pressure hydrocephalus

reflexes, a Babinski response, sensory abnormalities or ataxia are inconsistent with PD and suggest a multiple system degeneration, or are suggestive of more than one neurologic problem.<sup>2</sup>

Provided the examiner has excluded secondary parkinsonism, and we have at least two of the three criteria for PD (akinesia and rigidity or tremor), we can now entertain the diagnosis of PD. This will be accurate 75% of the time.<sup>13</sup> Hughes attempted to improve the diagnostic accuracy by adding exclusion criteria (Table 3).<sup>13</sup> These criteria improved diagnostic accuracy to a 90% predictive value but the sensitivity dropped to 67%.

#### CAN WE IMPROVE DIAGNOSTIC ACCURACY?

The literature confirms that 100% clinical diagnostic accuracy of PD at the time of initial presentation is not possible. By adding specific parts to the history and physical examination of every parkinsonian patient, an earlier conclusion that the parkinsonism may not be due to PD becomes possible (Table 4). Although some of the features listed in Table 4 may be present in PD, they would be uncommon at the time of initial diagnosis. If present, these features would increase the chance of the “parkinsonism” being due to a multiple system degeneration (Parkinson’s “plus”).

#### PROGRESSIVE SUPRANUCLEAR PALSY (PSP)

The first full description of PSP occurred in 1963.<sup>14</sup> Progressive supranuclear palsy begins during the late 5th to mid 6th decade (earliest reported age 43). Men are slightly more frequently affected than women. Progressive supranuclear palsy accounts for about 7 - 12% of parkinsonian patients in a typical movement disorders center.<sup>15</sup>

**Table 2:** Common medication types that cause Parkinsonism<sup>50</sup>

|   |   |
|---|---|
| Classic neuroleptics                    | (e.g. haloperidol, chlorpromazine, perphenazine)  |
| Novel neuroleptics                      | (e.g. risperidone tartrate, olanzapine)   |
| Dopamine reuptake blockers              | (e.g. reserpine, tetrabenazine)   |
| ‘Gastrointestinal’ dopamine blockers    | (e.g. metoclopramide)   |
| Calcium channel blockers                | (e.g. flunarizine hydrochloride, verapamil, amlodipine)   |
| Selective serotonin reuptake inhibitors | (e.g. fluoxetine hydrochloride)   |
| Tricyclics                              | (e.g. amitriptyline)  |
| Anticonvulsants                         | (e.g. diphenylhydantoin, carbamazepine, valproic acid)  |
| Monoamine oxidase inhibitors            | (e.g. phenelzine)   |
| Benzodiazepines                         | (e.g. diazepam, clonazepam, bromazepam)   |
| Other medications:                      | Trazodone hydrochloride, buspirone, lithium, amphetamines, cocaine, meperidine, amiodarone, H1 and H2 blockers. |

**Table 3:** Hughes Diagnostic Criteria For Parkinson’s Disease

|  |
|--|
| Akinesia and one of:                   |
| 1) Tremor                              |
| 2) Rigidity                            |
| Plus asymmetric onset                  |
| Plus no atypical features:             |
| Early marked autonomic disturbance     |
| Early marked dementia                  |
| Cortical spinal tract dysfunction      |
| Supranuclear gaze palsy                |
| Plus no history of an alternate cause: |
| Neuroleptics                           |
| Cerebrovascular events                 |
| Episode of encephalitis at onset       |

Adapted from Hughes<sup>13</sup>

**Table 4:** Early clues that parkinsonism may not be due to Parkinson’s disease

#### Historical features

Medication history includes drugs from Table 2  
 Past toxic exposure  
 Past encephalitis  
 Positive family history  
 Memory problems  
 Visual complaints  
 Swallowing and speech changes  
 Bladder, bowel, sexual dysfunction  
 Postural dizziness, syncope  
 Falls  
 No response to medication trial

#### Physical features

Abnormal mental status  
 Symmetric signs  
 Blood pressure drops from lying to standing  
 Kayser-Fleischer rings  
 Abnormal eye movements and/or optico-kinetic nystagmus  
 Neck in a marked flexed or hyperextended posture  
 Cortico-spinal signs  
 Postural instability / ataxia  
 Excessive space between ankles on walking  
 Prominent primitive reflexes (e.g. grasp and grope reflexes)  
 Apraxia, alien hand  
 Prominent myoclonus

The typical supranuclear eye movement abnormalities are present within three years after the onset of the other symptoms.<sup>16</sup> These begin as an impairment of down gaze. This can be picked up early by checking vertical optico-kinetic nystagmus and identifying a disorder of downward saccades. Associated ocular findings are horizontal square-wave jerks,

slow and hypometric saccades, lid levator inhibition (apraxia of eyelid opening), failure of suppression of vestibulo-ocular reflexes, blepharospasm or a severely reduced blink rate. The abnormalities lead to a progressive paresis of gaze in all directions.<sup>17</sup>

Expect an early disorder of gait with falls.<sup>18</sup> Axial rigidity, particularly in the neck, may be associated with hyperextension. Limb tone may be increased only mildly, increasing from distal to proximal. Dystonia of facial muscles create a recognizable pattern of a surprised, wide open eyes look. Tremor is uncommon (12 - 16%) and is evident more often with posturing and action than at rest.<sup>19</sup> Personality and cognitive changes occur frequently and early. These changes include emotional incontinence, irritability, and social withdrawal. Severe dementia is rare.<sup>20</sup>

By five years, 68% of patients have significant speech dysfunction. Some may progress to anarthria. Forty-six percent are affected by dysphagia by five years.<sup>21</sup> Sleep disturbance is common. Autonomic failure is less common than in Parkinson's disease with the exception of incontinence.<sup>21</sup> Forty percent to 50% of patients will have an initial mild, transient response to levodopa.<sup>22</sup> Median survival is under 10 years.

Progressive supranuclear palsy is not a synucleinopathy like PD, dementia with Lewy bodies (DLB) or MSA, but a tauopathy, relating it more with cortical-basal ganglionic degeneration (CBGD).<sup>23</sup> Tau is a microtubular-associated protein normally found in axonal processes, which collects in neuronal cytoplasm in some pathologic states. The number and location of tau staining neurons is used by pathologists to assist in defining different neurodegenerative disorders.

#### Criteria for the clinical diagnosis of PSP

*From the National Institute of Neurological Disorders and Stroke (NINDS) and the Society for PSP.<sup>21,24</sup>*

**Possible PSP:** presence of a gradually progressive neurologic disorder with onset at age of 40 years or older, either vertical supranuclear gaze palsy or both slowing of the vertical saccades and prominent postural instability with falls in the first year of onset and no evidence of other diseases that could explain these features. These criteria are substantially sensitive but less specific.

**Probable PSP:** vertical supranuclear palsy, prominent postural instability, and falls in the first year of onset and other features of possible PSP.

**Definite PSP:** Either of the above plus pathologic evidence of typical PSP.

**Supportive criteria include:** symmetric akinesia or rigidity, proximal greater than distal, abnormal neck posture, especially retrocollis, poor or absent response of parkinsonism to L-dopa therapy, early dysphagia or dysarthria, and early onset of cognitive impairment including at least two of the following: apathy, impairment in abstract thought, decreased verbal fluency, utilization or imitation behavior, or frontal release signs.

**Mandatory exclusion criteria include:** a recent history of encephalitis, alien limb syndrome, cortical sensory loss, focal frontal or temporoparietal atrophy; hallucinations or delusions

unrelated to dopaminergic therapy; cortical dementia of Alzheimer's type; prominent, early cerebellar symptoms or prominent, early unexplained dysautonomia; severe, asymmetric parkinsonian signs; neuroradiologic evidence of relevant structural abnormality; Whipple's disease confirmed by polymerase chain reaction.

#### MULTIPLE SYSTEM ATROPHY

Multiple system atrophy defines a specific syndrome within the larger category of the multiple system degenerations. Multiple system atrophy is the second (half the frequency of PSP) most common of the multiple system degenerations. The features of MSA include: parkinsonism with cerebellar or corticospinal signs. Autonomic symptoms of orthostatic hypotension, impotence, and urinary incontinence or retention usually precede or occur within two years of the onset of the motor symptoms. The previous division into Shy Drager syndrome, striato-nigral degeneration, and olivopontocerebellar atrophy is no longer used. Immunohistochemistry has demonstrated that these three disorders share a common pathology; the presence of glial cytoplasmic inclusions.<sup>25</sup>

Wenning et al<sup>26</sup> determined that the combination of autonomic insufficiency, speech or bulbar dysfunction, absence of dementia, postural instability with falls, poor response to levodopa, and absence of levodopa-induced confusion gave a diagnostic sensitivity and specificity greater than 90%.

Median age of onset of MSAs is about age 55 years (range of 33 to 76).<sup>27</sup> Men are more frequently affected than women (1.3 - 1 ratio).<sup>27</sup> Approximately 50% are disabled or wheelchair bound within five years.<sup>28</sup> Mean survival is six to seven years.<sup>29</sup> Eighty percent of MSA patients develop predominant parkinsonism (MSA-P) and 20% develop predominant cerebellar signs (MSA-C).<sup>27</sup> There is considerable overlap with cerebellar findings in over 40% of patients with MSA-P type, and parkinsonism in 50% of MSA-C type patients. Classic rest tremor is uncommon (9 - 29%).<sup>27,28</sup> Symptoms of cerebellar dysfunction (not seen in PD) include gait ataxia (49%), limb ataxia (47%), intention tremor (24%) and nystagmus (23%).<sup>27</sup>

Autonomic failure is present in both MSA-C and MSA-P. The separate entity of Shy Drager syndrome given the degree of overlap is not beneficial. Autonomic symptoms were an initial feature in 41% of patients, but ultimately 97% develop some degree of autonomic dysfunction.<sup>26</sup> In a review of 203 cases autonomic problems included urinary incontinence (55%), postural hypotension (51%), impotence (47%), recurrent syncope (18%), and fecal incontinence (12%).<sup>26</sup> The most frequent autonomic symptom was impotence in men and urinary incontinence in women.

Upper motor neuron signs occur in 49 - 61% but rarely contributed significantly to functional difficulty.<sup>26,28</sup> In one series, 31% of cases had finger myoclonus (often stimulus sensitive).<sup>26</sup> Anterior horn cell loss may occur but is uncommon. Anal sphincter EMG (90% have an abnormality) is a sensitive and specific diagnostic test for MSA.<sup>30</sup> A mild sensory neuropathy is infrequently seen. Severe dementia is uncommon enough (0.5%) that some consider it an exclusion criterion.<sup>26</sup>

Respiratory stridor (which ultimately occurs in one third of cases) in combination with parkinsonism is highly suggestive of MSA; although it rarely can occur in PD.<sup>26</sup>

Initial response to medication occurs more frequently than commonly thought; 30 - 65% of MSA patients will respond to medication at some stage; 13 - 30% will maintain some response through the course of the illness;<sup>29,31</sup> 25% to 50% of those treated with levodopa experience dyskinesias (often orofacial) and dystonia. These involuntary drug-induced movements may occur without an improvement in motor state.<sup>29</sup>

### Criteria for the clinical diagnosis of MSA<sup>26</sup>

#### *MSA; Olivo-ponto-cerebellar Type (MSA-C) (predominantly cerebellar)*

*Possible:* A sporadic adult-onset disorder (age > 30 years) with features of parkinsonism and a cerebellar syndrome.

*Probable:* A sporadic adult-onset cerebellar syndrome (age > 30 years) (with or without parkinsonism or pyramidal signs) plus severe symptomatic autonomic failure (postural syncope or presyncope and/or urinary incontinence or retention not due to other causes) or pathological sphincter EMG.

*Definite:* Postmortem confirmed.

#### *MSA; Striato-nigral degeneration Type (MSA-P) (predominant parkinsonism)*

*Possible:* A sporadic adult-onset disorder (age > 30 years) with features of parkinsonism which is non or poorly levodopa-responsive (moderate or good, but often waning, response to levodopa may occur, in which case multiple atypical features need to be present).

*Probable:* Above, plus severe symptomatic autonomic failure (postural syncope or presyncope and/or urinary incontinence or retention not due to other causes), cerebellar signs, pyramidal signs or pathological sphincter EMG.

*Definite:* Postmortem confirmed.

#### **Mandatory exclusion criteria**

Include age < 30, a positive family history (one other case of typical clinical idiopathic PD among 1st or 2nd degree relatives allowable), presence of hallucinations, generalized tendon areflexia, DSM III dementia, vertical (downgaze) supranuclear gaze palsy, or other identifiable cause.

### CORTICAL-BASAL GANGLIONIC DEGENERATION

There are no universally accepted criteria for the diagnosis of CBDG.<sup>32</sup> The full clinical picture continues to develop as more cases are confirmed pathologically.

This condition usually begins from 50 - 70 years of age. Mean survival is about eight years. Typical features are an asymmetric levodopa-resistant akinetic-rigid syndrome associated with cortical features including apraxia, cortical sensory loss, and alien limb phenomenon.<sup>33</sup> General cognitive function had been thought to be preserved. This "classical" description emphasizing a parietal/perceptual-motor presentation started to change with the report of pathologically confirmed cases presenting to a dementia clinic.<sup>34</sup> In a recent review by Grimes et al,<sup>32</sup> only four of 13 pathologically proven patients had a prior clinical diagnosis of CBDG. Dementia may be the most common feature.

Parkinsonian signs including unilateral limb rigidity (79%), bradykinesia (71%), postural instability (45%) and apraxia are found in almost all patients.<sup>29</sup> Dystonic posturing of the arm and

hand is common (43%). Tremor, when present, is typically an action tremor that improves at rest. It frequently has a myoclonic (jerky) component which is often stimulus sensitive.<sup>32</sup> The rigidity may be extreme and associated pain is common.

Aphasia can be seen in over 50% of patients.<sup>35</sup> Depression is common. Apathy, social withdrawal, bizarre behavior, hypersexuality, irritability, and anarthria have been described.<sup>36</sup>

Alien limb phenomena develop in 50% of cases. It may be as simple as levitation of a limb. "Magnetic apraxia" (an approach behavior with groping and manipulation) is a sign of CBDG.<sup>37</sup> Described eye movement abnormalities include saccadic pursuit, difficulty initiating saccades and, rarely, supranuclear palsy.<sup>38</sup>

Cortical-basal ganglionic degeneration, like PSP, is a disorder of the tau protein (a tauopathy). It seems to have significant pathologic and clinical overlap with frontotemporal dementias, parkinsonism associated with chromosome 17, primary progressive aphasia, Pick's disease and PSP.<sup>39</sup>

### Criteria for the clinical diagnosis of CBDG<sup>34</sup>

- I. Chronic progressive course
- II. Asymmetric at onset (includes speech dyspraxia, dysphasia)
- III. Presence of both:
  1. Higher cortical dysfunction (apraxia, or cortical sensory loss or alien limb)
  2. Movement disorders (rigid akinetic syndrome resistant to levodopa, and dystonic limb posturing at rest, with spontaneous and reflex focal myoclonus spreading beyond the fingers when provoked).

#### **Exclusion criteria**

Include presence of down gaze palsy or global dementia while patient is still ambulatory, typical parkinsonian rest tremor, or severe autonomic disturbances.

### DEMENTIA WITH LEWY BODIES

Diffuse Lewy body disease was first described in the late 1970s. The three core features are fluctuating cognitive performance, visual hallucinations and parkinsonism.<sup>40</sup> Once thought to be rare, it is now assumed that this condition accounts for 15-25% of elderly demented patients. The age of onset range from 60 to 85 years is higher than PD.<sup>41</sup> The average length of survival after diagnosis is shorter than Parkinson's disease and Alzheimer's disease.<sup>42</sup>

Patients with DLB have deficits in memory, attention, language, executive functions, with visuospatial and visuoconstructional difficulty.<sup>43</sup> Visual hallucinations are reported (usually complex, colorful and nonthreatening) in 40% to 75% of patients with DLB.<sup>44</sup> They will occur without medication but will be provoked easily by antiparkinsonian medication.

Resting tremor is less common and myoclonus is more common in DLB than in PD.<sup>45</sup> Rapid eye movement sleep behavior disorder occurs frequently. Supranuclear gaze palsies, although uncommon, have also been reported.<sup>46</sup>

Clinical criteria for DLB were established in 1995.<sup>47</sup> Parkinsonism preceding dementia by an arbitrary interval of one year or more was termed PD-D, and dementia that precedes or accompanies the onset of parkinsonism was labeled DLB.

**Criteria for the clinical diagnosis of DLB**<sup>47</sup>**Central feature required for a diagnosis of DLB**

A progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational function. Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression. Deficits on tests of attention and of frontal-subcortical skills and visuospatial ability may be especially prominent.

**Core features for DLB**

1. Fluctuating cognition with pronounced variations in attention and alertness.
  2. Recurrent visual hallucinations that are typically well-formed and detailed.
  3. Spontaneous motor features of parkinsonism.
- Possible DLB* requires one of the three core features.  
*Probable DLB* requires two of the three core features.  
*Definite DLB* requires pathologic confirmation.

**Supportive features**

Include repeated falls, syncope, transient loss of consciousness, neuroleptic sensitivity, systematized delusions, and hallucinations in other modalities.

**Exclude if:**

Evidence on physical or investigation of another brain disorder sufficient to account for the clinical picture.

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