

# ATYPICAL PARKINSONIAN DISORDERS

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# PARKINSONISM

An anatomical diagram of a coronal section of the human brain. The cerebral cortex is shown in pink, the white matter in yellow, and the basal ganglia in orange. The nigrostriatal pathway is highlighted with blue lines, showing the substantia nigra in the midbrain and its projection to the striatum in the telencephalon. A smaller cross-section of the midbrain is shown at the bottom, with blue lines indicating the pathway's continuation.

akinetic-rigid  
syndrome

# PARKINSONISM

- Symptoms of Parkinson's disease: akinesia, bradykinesia, rigidity, postural instability, gait impairment, tremor
- A common, age-related syndrome

# ATYPICAL PARKINSONISM

- Parkinson Plus Syndromes
- Secondary Parkinsonism
- Early falling, early dementia, early autonomic dysfunction

# PARKINSON'S DISEASE

## General Considerations

- The second most common progressive neurodegenerative disorder
- The most common neurodegenerative movement disorder
- It is a complex disease with variable symptoms
- Symptoms and neuropathology are well characterized
- Pathogenesis of PD is not clear
- May be multifactorial and heterogeneous in etiology
- Misdiagnosis rate of PD is about 10-25%



# Parkinson's Disease

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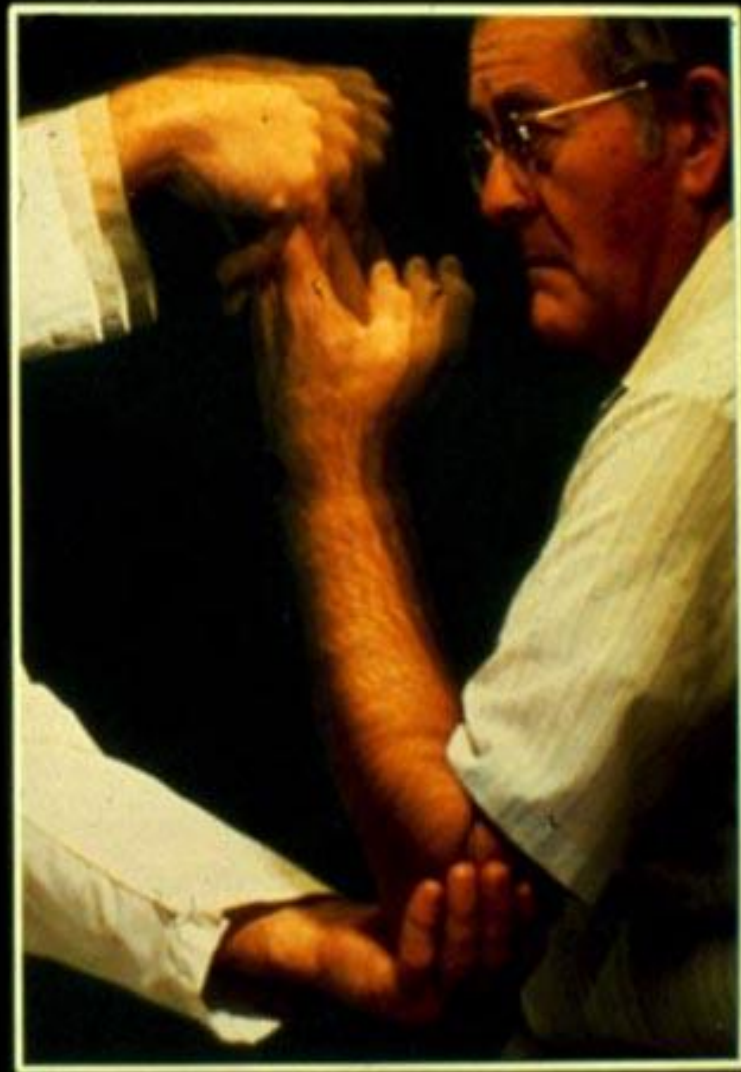
## *Tremor*



# Parkinson's Disease

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## *Rigidity*



# Parkinson's Disease

## *Bradykinesia*





# PARKINSON'S DISEASE

## Classical Clinical Features

- Tremor, resting
- Rigidity, cogwheel
- Akinesia, bradykinesia
- Postural Instability

# PARKINSON'S DISEASE

## Associated Clinical Features

- Micrographia
- Hypophonia
- Hypomimia
- Shuffling gait / festination
- Drooling
- Dysphagia
- Autonomic dysfunction
- Depression
- Dementia

# PARKINSON'S DISEASE

## Features supporting diagnosis

- Unilateral symptom onset
- Characteristic resting tremor
- Narrow-based gait with flexed/  
stooped posture
- Reduced arm swing with  
tremor
- Sustained and significant  
levodopa effect

# DISEASES ASSOCIATED WITH PARKINSONISM

## *Sporadic Disorders*

- Parkinson's disease
- Multiple system atrophy
- Dementia with Lewy bodies
- Progressive supranuclear palsy
- Corticobasal degeneration
- Prion diseases
- Amyotrophic-parkinson-dementia complex of Guam
- Pallidal degeneration
- Hemiatrophy hemiparkinsonism

# DISEASES ASSOCIATED WITH PARKINSONISM

## Hereditary Disorders

- Huntington's disease
- Wilson's disease
- Juvenile onset parkinsonism
- Hallervorden-Spatz disease
- Dentatorubropallidoluysian atrophy (DRPLA)
- Frontotemporal dementia with parkinsonism
- Hereditary prion diseases
- Lubag
- Machado-Joseph disease (SCA 3)
- Neuroacanthocytosis
- Type 3 GM1 gangliosidosis

# DISEASES ASSOCIATED WITH PARKINSONISM

## Acquired Disorders

- Drug-induced parkinsonism
- Vascular parkinsonism
- Toxic parkinsonism
- Post-traumatic parkinsonism
- Post-encephalitic parkinsonism
- Prion diseases
- Extrapontine myelinolysis
- Space occupying lesions
- Hydrocephalus

# PARKINSONISM

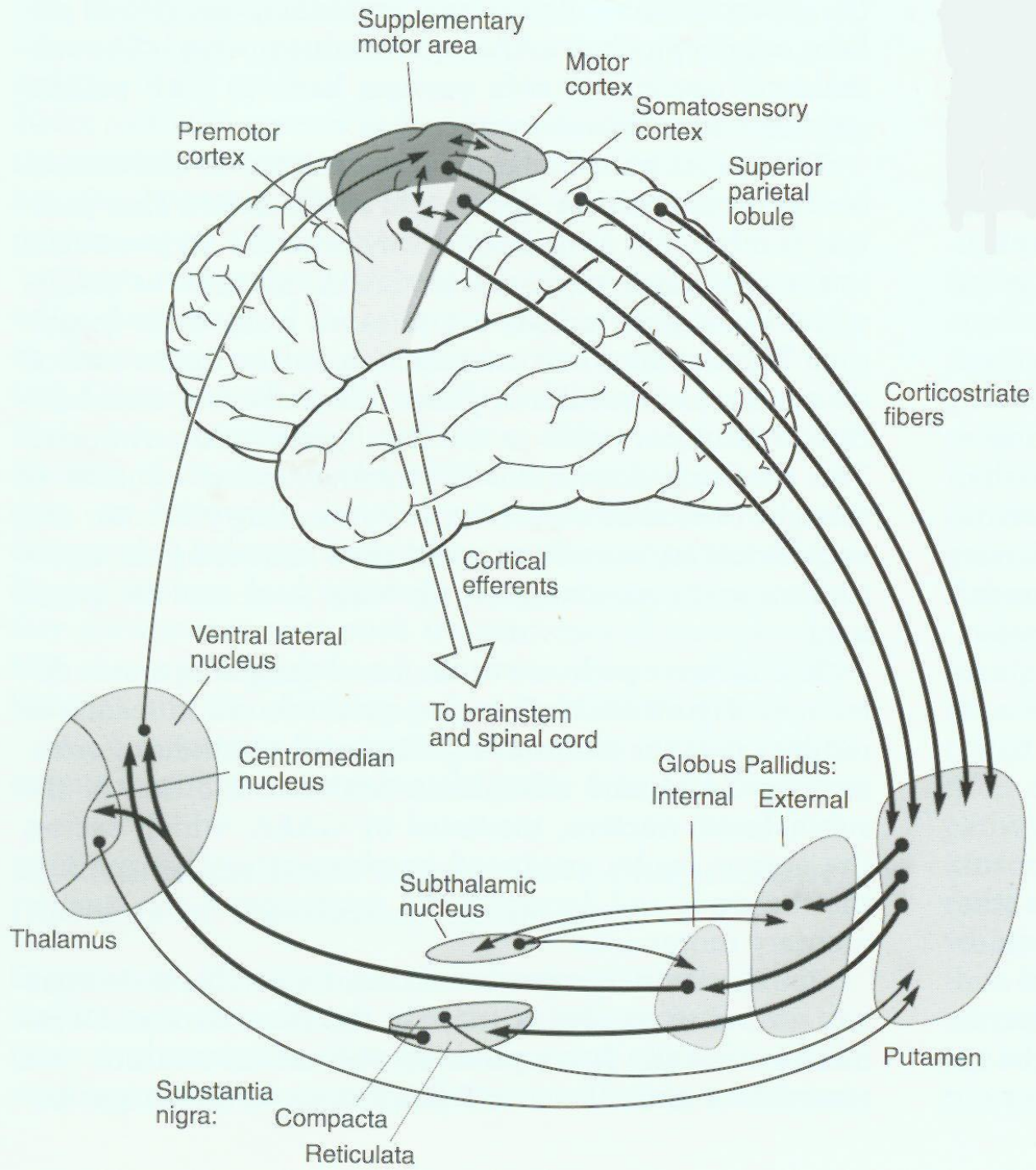
## AAN Practice Parameter Recommendations: Clinical features distinguishing other parkinsonian syndromes from PD

- Falls at presentation and early in the disease course
- Poor response to levodopa
- Symmetry at onset
- Rapid progression (to H&Y stage 3 in 3 years)
- Lack of tremor
- Early dysautonomia

# THE BASAL GANGLIA

- Consists of a group of nuclei in the deep part of the cerebrum and upper brain stem: caudate, putamen, globus pallidus, subthalamic nucleus, substantia nigra
- Coordinates muscle actions and voluntary movements
- Controls the higher-order, cognitive aspects of voluntary movement: the planning and execution of complex motor strategies
- Cognitive functions (procedural memory - skills & habits)
- Structural defects and neurotransmitter imbalance cause movement disorders: hypokinesia or hyperkinesia





# ATYPICAL PARKINSONIAN DISORDERS

- Multiple system atrophy
- Dementia with Lewy bodies
- Progressive supranuclear palsy
- Cortical basal degeneration
- Vascular parkinsonism
- Drug-induced parkinsonism
- Normal pressure hydrocephalus

# NEURODEGENERATIVE PARKINSONIAN DISORDERS

## ALPHA-SYNUCLEINOPATHIES

- Parkinson's disease (PD)
- Dementia with Lewy bodies (DLB)
- Multiple system atrophy (MSA)

## TAUOPATHIES

- Progressive supranuclear palsy (PSP)
- Corticobasal degeneration (CBD)

# ACQUIRED PARKINSONIAN DISORDERS

- Vascular parkinsonism
- Normal pressure hydrocephalus
- Drug-induced parkinsonism

# DEMENTIA WITH LEWY BODIES

## Clinical Features

- Second most common form of degenerative dementia in old age
- Early psychotic symptoms: hallucinations/delusions
- Mild extrapyramidal dysfunction
- Fluctuations in attention or level of arousal
- Orthostatic hypotension, syncope
- Depression
- Diurnal variations in behavior
- Neuroleptic sensitivity
- REM sleep behavior disorder

# DEMENTIA WITH LEWY BODIES

(McKeith Criteria, 2005)

- Probable DLB
  - Dementia
  - Two or more: marked fluctuations, typical visual hallucinations, parkinsonism
- Possible DLB
  - Dementia
  - One of the following: marked fluctuations, typical visual hallucinations, parkinsonism
- Specificity is high (>85%), but sensitivity is low

# DEMENTIA WITH LEWY BODIES

## Pharmacological Management

- Cholinesterase inhibitors: rivastigmine, donepezil
  - Multicenter, controlled, 20-week study of rivastigmine (6-12 mg/d)
    - No worsening of motor function
    - Improvement of total Neuropsychiatric Inventory (NPI) score
    - Improvement of 4-item (delusion, hallucination, apathy, depression) subscore
  - Open-label study of donepezil
- Antipsychotic agents:
  - Neuroleptic sensitivity to typical antipsychotics
  - Low dose atypical antipsychotics are tolerated. Consider quetiapine
- Dopaminergic therapy:
  - Carbidopa/levodopa

# MULTIPLE SYSTEM ATROPHY

## Clinical Features

- Prevalence of 2-4 per 100,000 population (may be underestimated)
- Median age of onset is 55 years (range 33-76)
- Men : women = 1.3 : 1
- Mean survival 6-9 years; half of pts disabled or WC bound within 5 years of onset of motor symptoms
- Autonomic dysfunction, cerebellar signs, parkinsonism, poorly or transiently responsive to levodopa therapy, sleep apnea or RBD, stimulus sensitive myoclonus
- Dysarthria, laryngeal stridor, anterocollis
- Not compatible with MSA: asymmetric sx, rest tremor, early dementia, prominent ophthalmoplegia, apraxia, cortical sensory loss
- Subtypes: Shy-Drager syndrome (MSA-A), striatonigral degeneration (MSA-P), olivopontocerebellar atrophy (MSA-C)



# MULTIPLE SYSTEM ATROPHY

## Symptomatic Treatments

- Levodopa for parkinsonian features
- Sodium, fluid intake, pressure stockings, midodrine, fludrocortisone for orthostatic hypotension
- Oxybutinin or tolterodine for urinary frequency or incontinence
- Sildenafil for impotence
- Selective serotonin reuptake inhibitors for depression
- No good treatment of ataxia or dementia

# PROGRESSIVE SUPRANUCLEAR PALSY

## Clinical Features

- Prevalence of about 6 per 100,000 population
- Median age of onset is mid-60s, gradual sx onset
- Mean survival 5-9 years; half of pts disabled or WC bound within 3-4 years of onset of motor symptoms
- Parkinsonism, early instability with falls, poorly or transiently responsive to levodopa therapy, marked slowing of vertical gaze (esp. downward), eyelid apraxia, axial rigidity, retrocollis, motor perseveration
- Dysarthria, dysphagia, stuttering/palilalia early, laryngeal stridor
- Not compatible with PSP: asymmetric sx, rest tremor, early dementia, cortical sensory loss

# PROGRESSIVE SUPRANUCLEAR PALSY (NINDS-SPSP CRITERIA)

- PROBABLE PSP

- a) Presence of a gradually progressive disorder
- b) Onset at age 40 or older
- c) Supranuclear limitation of vertical gaze AND a hx of prominent postural instability and falls in the first year of onset
- d) No evidence of other diseases that can explain the above features

- POSSIBLE PSP

- a), b), and d) as above
- c) Supranuclear limitation of vertical gaze OR a hx of prominent postural instability and falls in the first year of onset

# CORTICAL BASAL DEGENERATION

## Clinical Features

- Prevalence of about 5-7 / 100,000 population
- Median age of onset is 60s-70s
- Mean survival about 7 years
- Insidious onset and progression of asymmetric cortical and basal ganglionic features
- Akinetic, rigid syndrome; hyperkinetic movement disorder (e.g. tremor, dystonia, myoclonus); alien limb phenomenon; speech impairment; gait disorder with postural instability; eye movement abn (slow horizontal saccades)
- Cortical dysfunction including dementia, apraxia, cortical sensory disturbance
- Not compatible with CBD - prominent ocular impairment, axial rigidity or dystonia out of proportion to limb involvement, rest tremor, autonomic failure, aphasia

# PSP and CBD

## Clinical Features

### SIMILARITIES:

- Relatively rapid disease progression
- Speech and gait disturbance
- Poorly or transiently responsive to levodopa therapy

### DIFFERENCES:

- PSP - symmetric parkinsonism, vertical supranuclear gaze palsy, postural instability at onset and early falls, axial rigidity, wide-based/slow/unsteady gait
- CBD - asymmetric parkinsonism, asymmetric cortical signs, dystonic posturing of unilateral limb, alien limb syndrome

# PSP and CBD

## Pharmacological Treatments

- Levodopa for parkinsonian features
- Clonazepam for action tremor, myoclonus, and RBD
- Baclofen and tizanidine for rigidity, muscle spasms
- Botulinum toxin injection for limb dystonia and blepharospasm
- SSRI for depression, anxiety, pseudobulbar palsy
- Six-week, placebo-controlled, double-blind study of donepezil for PSP: modest improvement in memory test scores were offset by deterioration in functional mobility

# CLINICAL DIFFERENTIATING OF PARKINSONIAN DISORDERS

	PD	MSA	PSP	CBD
Symmetry of deficits	+	+++	+++	--
Axial rigidity	++	++	+++	++
Limb dystonia	+	+	+	+++
Postural instability	++	++	+++	+
<b>Vertical gaze restriction</b>	+	++	+++	++
Frontal behavior	+	+	+++	++
Dysautonomia	+	++	--	--
L-dopa response early	+++	+	+	--
L-dopa response late	++	+	--	--
Asym cortical atrophy on MRI	--	--	--	++

# VASCULAR PARKINSONISM

## Clinical Features

- Acute or subacute onset with stepwise evolution of akinesia and rigidity
- Presence of risk factors for cerebrovascular disease
- Two or more basal ganglia infarcts OR more widespread subcortical white matter lesions evident on neuroimaging
- No rest tremor
- Prominent postural instability and gait disorder
- Unresponsive to levodopa treatment



# VASCULAR PARKINSONISM

## Symptomatic Treatments

- Control stroke risk factors
- Keep active, stretching exercises
- Physical therapy for leg strengthening and gait training
- Assistive devices
- Safety-proof living environment

# NORMAL PRESSURE HYDROCEPHALUS

- Syndrome of gait disturbance, urinary incontinence, and a dementing process
- CT/MRI: ventricular enlargement disproportionate to cortical atrophy and small-vessel ischemic changes
- Confirmed by beneficial response to large-volume cerebrospinal fluid drainage (30-50 ml)

# NORMAL PRESSURE HYDROCEPHALUS

- Surgical treatment by CSF shunting procedure
- Good prognosis is associated with presence of full triad, short duration of symptoms, mild dementia, lack of cerebral atrophy in combination with enlarged ventricles and intermittent CSF pressure elevations
- Complications of shunt procedures include shunt malfunction, subdural hematoma, infection, seizure
- Proper selection of patients and use of appropriate techniques are important for successful treatment

# DRUG-INDUCED PARKINSONISM

- Bradykinesia, rigidity, mild tremor, rabbit syndrome
- Caused by exposure to a dopamine-receptor blocking agent within 6 months of the onset of symptoms
- Offending drugs include: antipsychotics, anti-emetics, metoclopramide
- Mild cases can frequently remit after cessation of the offending drug
- Usually unresponsive to dopaminergic therapy
- Elderly patients are most susceptible
- Treatment may include: tetrabenazine, reserpine, vitamin E, benzodiazepines

# ATYPICAL PARKINSONIAN DISORDERS

The differential diagnosis of atypical parkinsonian disorders is difficult because there are abundant overlapping features of the many disorders. Clinicians should be familiar with the less common but distinctive features of these disorders and have a high index of suspicion in order to tackle the diagnostic challenge, particularly in the early stages of disease. There is no reliable diagnostic markers available for the majority of the disorders.

# RESOURCE INFORMATION

- **We Move** (204 West 84th Street, New York, NY 10024; [www.wemove.org](http://www.wemove.org))  
Provides worldwide education & information about all movement disorders.
- **Lewy Body Dementia Association** ([www.lbda.org](http://www.lbda.org)) A place for LBD caregivers to meet and share through forum & educational materials
- **Shy-Drager Syndrome/Multiple System Atrophy Support Group** (1-866-737-4999; [www.shy-drager-syndrome.org](http://www.shy-drager-syndrome.org))
- **Cure PSP** ([www.psp.org](http://www.psp.org)) A progressive supranuclear palsy support group
- **Movement Disorder Society** ([www.movementdisorders.org](http://www.movementdisorders.org)) An international professional society of clinicians, scientists, and other healthcare professionals, who are interested in PD and related neurodegenerative and neurodevelopmental disorders

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