

**Management and Clinical Course
of PSP / CBD / MSA**

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Overview

- Describe the clinical course of PSP, CBD, MSA

- Review management of early and late symptoms

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**Clinical Course
Early**

- PSP, CBD and MSA may look very similar, or resemble other conditions
 - e.g. Parkinson's; dementia; speech/language disorder (PSP, CBD); other cerebellar ataxias (MSA)
- This can lead to misdiagnosis or a period of uncertainty before diagnosis
- Early hallmark signs can help diagnosis
 - e.g. Difficulty looking down (PSP); incontinence, faints, REM sleep disorder (MSA); single rigid limb (CBD)
- Tests may be helpful
 - MRI, PET, neuropsychometry, speech, autonomic

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Clinical Course

- Progressive
 - Usually faster than Parkinson disease
- Natural history is very variable
 - No two patients exactly alike, difficult to predict course
- Affects quality of life; dependence
- Survival is variable

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PSP

- Clinical picture:
 - Richardson's syndrome
 - PSP-parkinsonism
 - Corticobasal syndrome (CBS)
 - Freezing of gait
 - Frontotemporal dementia
- Progression:
 - Imbalance, falls (need walker), vision problems, speech reduced and hard to understand
 - Dependent for self-cares (3-4 years)
- Survival (6-9 years)

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CBD

- Clinical picture
 - Corticobasal syndrome (CBS)
 - PSP
 - Frontotemporal dementia
 - Alzheimer-like dementia
 - Aphasia (language disorder)
- Progression
 - Can start in 1 arm or leg (very rigid, fixed posture, apraxia) and spreads to other limbs, gait change, imbalance, falls, speech difficulty, reduced eye movement, cognitive decline, alien limb
- Survival (5-8 years)

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MSA

- Clinical picture:
 - MSA, parkinsonian type
 - MSA, cerebellar type
- Disease progression over 1-18 years
 - Blood pressure/bladder problems (2.5 years)
 - Walking aid (3 years)
 - Wheelchair (3.5-5 years)
 - Bedridden (5-8 years)
- Survival (6-8 years, can be >15 years)

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Parkinsonism

- Common in PSP, CBD, MSA
- Often occurs early (late in MSA-C)
- =Stiffness (rigidity), slowness (bradykinesia), tremor, imbalance
- Treatment
 - Levodopa is favored medication
 - About 1/3 patients benefit
 - Other Parkinson meds often ineffective
 - PT- stretching program for rigidity

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Postural instability / falls

- Common in PSP, CBD, MSA
- Early or late
- Noticed by patient or family. Neurologist often checks "pull test"
- Risk of injuries or fractures, especially if osteoporosis
- Management:
 - PT- balance exercises, falls prevention, gait aid (cane, walker, wheelchair), weighted walkers, nonstick low heel shoes, aerobic exercise
 - Vitamin D and calcium

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Freezing of gait

- Can occur in PSP, uncommon in CBD, MSA
- Early or late
- “My feet stick to the floor”
 - Starting walking, turns, doorways
- Treatment:
 - Medications not really helpful (levodopa, amantadine, methylphenidate, rasagiline, pramipexole)
 - PT and OT
 - Walkers with lasers, metronome
 - Visual or rhythmic cues
 - Turn in arc

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Myoclonus

- CBD, MSA, CBD
- Early or late
- Brief lightning-like jerky movements of arms / legs / whole body. Can look like tremor, but irregular.
- Management:
 - Often mild, does not require treatment
 - If bothersome, clonazepam (Klonopin) or levetiracetam (Keppra)

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Tremor

- MSA, PSP, CBD
- Early or late
- Rhythmic shaking of limb
- Management:
 - Medications provide modest benefit
 - Levodopa, propranolol, primidone, gabapentin, topiramate
 - OT, weighted utensils, anti-tremor spoons

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Dystonia

- Very stiff and rigid postures of arm / leg (CBD) or neck (MSA, PSP)
- Early or late
- Management
 - If mild / not bothersome – no treatment needed
 - If bothersome
 - PT stretching program
 - OT arm / leg splinting
 - Botulinum toxin injections
 - Medication (levodopa, baclofen, clonazepam)- stop if ineffective (side effects)

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Spasticity

- MSA, CBD, sometimes PSP
- Early or late
- Usually identified by doctor. "Jumpy" reflexes (hyperreflexic) and upgoing toes. Patient may have no symptoms, or report leg/arm stiffness or cramps
- Management:
 - If mild – none
 - PT- stretching program
 - Antispasmodic medications- baclofen
 - Botulinum toxin

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Cerebellar ataxia

- MSA-C (also reported in PSP)
- Early
- Management:
 - Mild – no treatment
 - Bothersome or severe – speech therapy for speech; OT, PT, gait aid (cane, walker, wheelchair)
 - No specific medications approved for ataxia

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Orthostatic hypotension (lightheaded) + syncope (faints)

- Common in MSA
- PSP often feel lightheaded or dizzy, but blood pressure does not drop on standing
- Can be very bothersome or unsafe (fainting and falls).
- Treatment:
- Fluids (6-8 large glasses water daily), add salt to food
- Compression garments (thigh or waist-high)
- Maneuvers
- Elevate head of bed
- Small meals
- Caffeine or salty drink (V8, gatorade) can boost BP after 15-30 mins for 1 hour
- Medications
 - Midodrine 5-20mg TID (last dose 4 hours before bedtime)
 - Fludrocortisone 0.1mg once or twice daily (before noon)
 - Pyridostigmine 30-60mg QID
 - Droxidopa 100-600mg TID

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Bladder / bowel

- Common in MSA (often early), PSP and CBD later
- Urine frequency/urgency (overactive bladder)
 - No treatment if mild
 - Medications- oxybutynin, tolterodine help but side effects; mirabegron less side effects
- Incomplete bladder emptying
 - Intermittent self catheterization

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Vision / eye problems

- Common in PSP (also CBD), early or late
- Double vision
 - Prisms
- Eye redness, dryness, light-sensitive (photophobia)
 - Dark glasses
 - Artificial tears, autologous serum tears
- Unable to move eyes up or down (gaze palsy)
 - Mirror prisms
- Eyes blink shut (blepharospasm), unable to open (apraxia of eyelid opening)
 - Botulinum toxin injections
 - Eyelid crutches

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Drooling

- Common in MSA and PSP
- Often late
- Management
 - Botulinum toxin injections to parotid glands
 - Nortriptyline/amitriptyline (bedtime dose, also helps sleep and depression)
 - Possible side effects

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Stridor

- May occur in MSA
- Early or late
- Harsh breathing noise in upper airway
- If suspected – sleep medicine evaluation (if happens when sleeping) or ENT (if happens when awake).
- Treatment:
 - CPAP/BIPAP machine (night)
 - If severe/life threatening– consider tracheostomy

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Speech / language / swallow disorders

- Dysarthria
- Dysphasia/Aphasia
- Dysphagia
- Apraxia of speech

- Covered in Speech lecture

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Cognitive impairment / Dementia

- Usually PSP or CBD
- Can be early or late
- Memory usually fine, but other cognitive difficulties
 - “frontal subcortical” – reduced attention + concentration, slowed thinking and retrieval of information, poor organization
 - “parietal”- difficulty with calculation, 3D shapes
- Management:
 - Education patient + caregivers
 - If memory problem – Alzheimer medications (donepezil, rivastigmine, galantamine, memantine)

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Alien limb

- CBD, early or late
- “My arm (leg) has a mind of its own”. “I can’t control it”. “It doesn’t belong to me”
 - May sit on hand or restrain it to stop it moving.
- Management:
 - Mild, non-bothersome- education
 - Bothersome – OT, PT

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Apraxia (arm or leg)

- CBD (rare in PSP, MSA)
- “My hand/arm doesn’t work like it used to”
- Normal strength and sensation, but difficulty performing complex skilled movements with the hand
 - e.g. unable to brush teeth, comb hair, use scissors, copy finger signals (e.g. thumbs up, peace sign)
- Management:
 - Explanation
 - OT

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Sleep problems

- REM sleep disorder
 - MSA (very rare PSP/CBD)
 - Treatment:
 - Bedroom safety
 - Melatonin 3mg bedtime, increase up to 12-15mg
 - 2nd line- clonazepam 0.25-1mg at bedtime
- Daytime sleepiness
 - Common in all
 - Causes: Often inadequate overnight sleep (too little, poor quality), or switch in day/night pattern.
 - Management:
 - Evaluate by doctor. If bothersome, may need sleep medicine evaluation

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Behavioral change

- PSP, CBD (less in MSA)
- Early or late
 - Depression (common)
 - Compulsive behaviors
 - Agitation
 - Irritability
 - Social withdrawal
 - Apathy
- Management:
 - Treat depression- psychology counselling, medication
 - Counselling, strategies to minimize

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Caregiver strain

- Common to all
- Early and late
- Spouse/caregiver feels burdened
 - Poor sleep, limited time for self care
 - Can lead to stress, depression, anxiety, burnout, guilt
- Management:
 - Recognize it is ok to feel this way
 - Ask for help
 - Family, social circle
 - Professional resources- foundations, counselling

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Study ID	Study Title	Conditions	Interventions	Locations
1	Recruiting: Testing Therapies of Insecticides (Pirfenidone, Dithiazine, PLS, Eserinil) in Cerebral Degeneration (CSD), Multiple System Atrophy (MSA), and Parkinson's Disease	• Essential Tremor • Multiple System Atrophy • Cerebellar Degeneration		• University of Colorado Denver, MSU, IUPUI, Indiana University, IUPUI, Washington State University
2	Recruiting: Systemic Cannabinoids (THC and CBD) in Parkinson's Disease	• Parkinson's Disease • Dementia with Lewy Bodies • Multiple System Atrophy	• Behavioral Plasma Test Program • Behavioral Urinal Cannabinoid Screen	• Rush University Medical Center • Chicago, Illinois, United States
3	Recruiting: Long-term Assessment of Disease Progression, Neuroprotection, and Motor Response	• Parkinson's Disease • Alzheimer's Disease • Multiple System Atrophy		• UCSF Department of Neurology • Los Angeles, California, United States
4	Recruiting: Subcutaneous Neuroleptic Therapy	• Parkinson's Disease • Atypical Antipsychotics • Atypical Antipsychotic Medication	• Drug, Subcutaneous • Medication	• Ohio State University • Columbus, Ohio, United States
5	Recruiting: Genetic Characterization of Inherited Disorders and Genotypes	• Parkinson's Disease • Parkinson's Disease • Parkinson's Disease	• Genetic Testing • Genetic Testing • Genetic Testing	• National Institute of Aging, Clinical Research Branch • Baltimore, Maryland, United States

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Study ID	Study Title	Conditions	Interventions	Locations
1	Recruiting: PET Imaging Study of Neurotransmitter and Adenosine Receptors in Multiple System Atrophy (MSA)	• Multiple System Atrophy • Parkinson's Disease (MSA) • Multiple System Atrophy, Genetic		• University of Michigan - Department of Neurology • Ann Arbor, Michigan, United States
2	Recruiting: Neuroprotective Therapies (Resveratrol, Resveratrol, Fisetin)	• Multiple System Atrophy (MSA) • Parkinson's Disease	• Drug, Resveratrol • Drug, Fisetin	• New York University School of Medicine • New York, New York, United States
3	Recruiting: Testing Therapies of Insecticides (Pirfenidone, Dithiazine, PLS, Eserinil) in Cerebral Degeneration (CSD), Multiple System Atrophy (MSA), and Parkinson's Disease	• Essential Tremor • Multiple System Atrophy • Cerebellar Degeneration		• University of Colorado Denver, MSU, IUPUI, Indiana University, IUPUI, Washington State University
4	Recruiting: The Neurobiology of Cerebellar Degeneration	• Frontotemporal Degeneration • Progressive Supranuclear Palsy • Multiple System Atrophy	• Other, None (Observation Only)	• University of Pennsylvania • Philadelphia, Pennsylvania, United States
5	Recruiting: Relation of Neurotrophic Capacity to Disease Progression in Parkinson's Disease	• Multiple System Atrophy • Cerebellar Degeneration • Parkinson's Disease	• Drug, Transcranial • Drug, Placebo	• Washington University School of Medicine • St. Louis, Missouri, United States
6	Not yet recruiting: Safety and Efficacy of Cannabinoids in Parkinson's Disease	• Parkinson's Disease • Multiple System Atrophy • Progressive Supranuclear Palsy	• Drug, Cannabinoids • Drug, Placebo (Oral Tablet)	• Johns Hopkins University, Parkland Institute • Dallas, Texas, United States

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Resources




- CurePSP (USA) www.psp.org
- The PSP Association (Europe) www.pspassociation.org.uk
- MSA Coalition www.multipleystematrophy.org
- National Ataxia Foundation www.ataxia.org
- National Parkinson Foundation www.parkinson.org





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Questions & Discussion
