

Multiple System Atrophy

A Focus on Motor Symptoms



Elena Call, MD

Movement Disorders Specialist

The Permanente Medical Group- Santa Clara



**Northern California Comprehensive
Movement Disorders Program**

Outline

Overview

Motor Symptoms of Disease

Clinical Diagnosis

Management

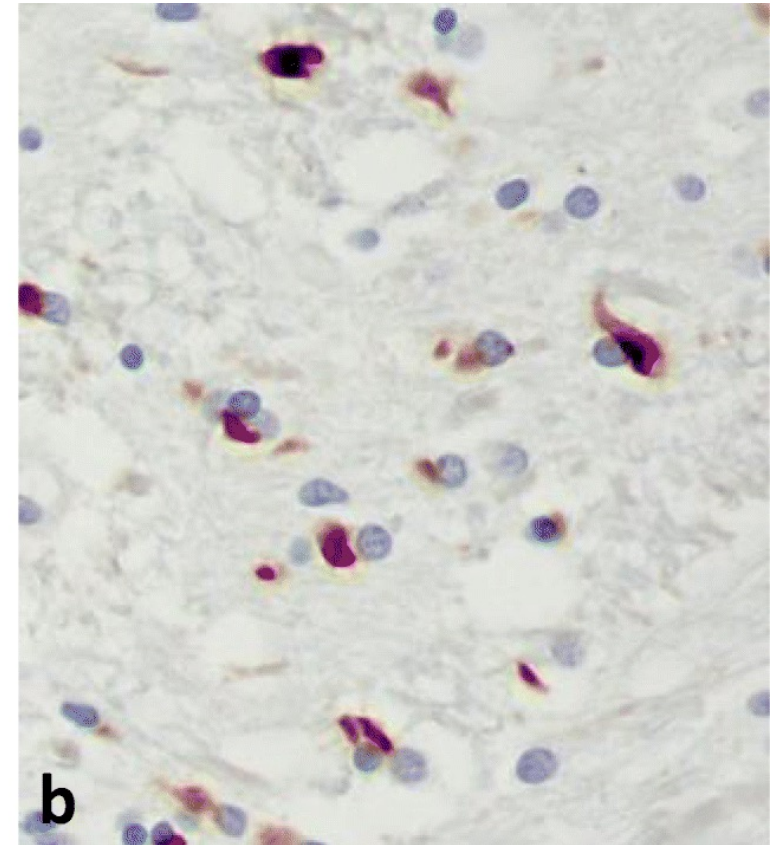
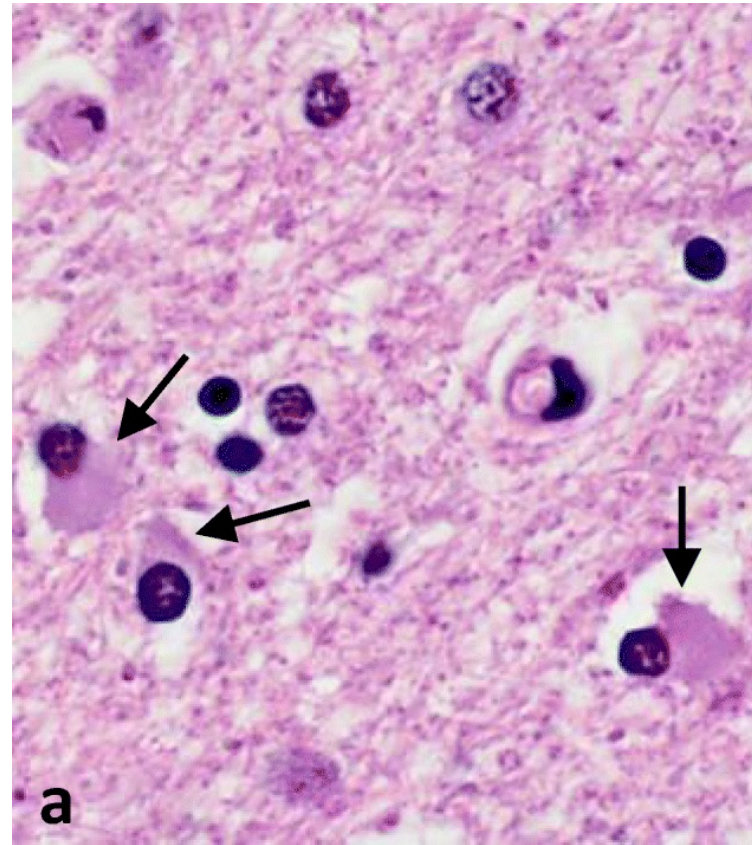
Disease Progression

Future Directions

What is MSA anyway?

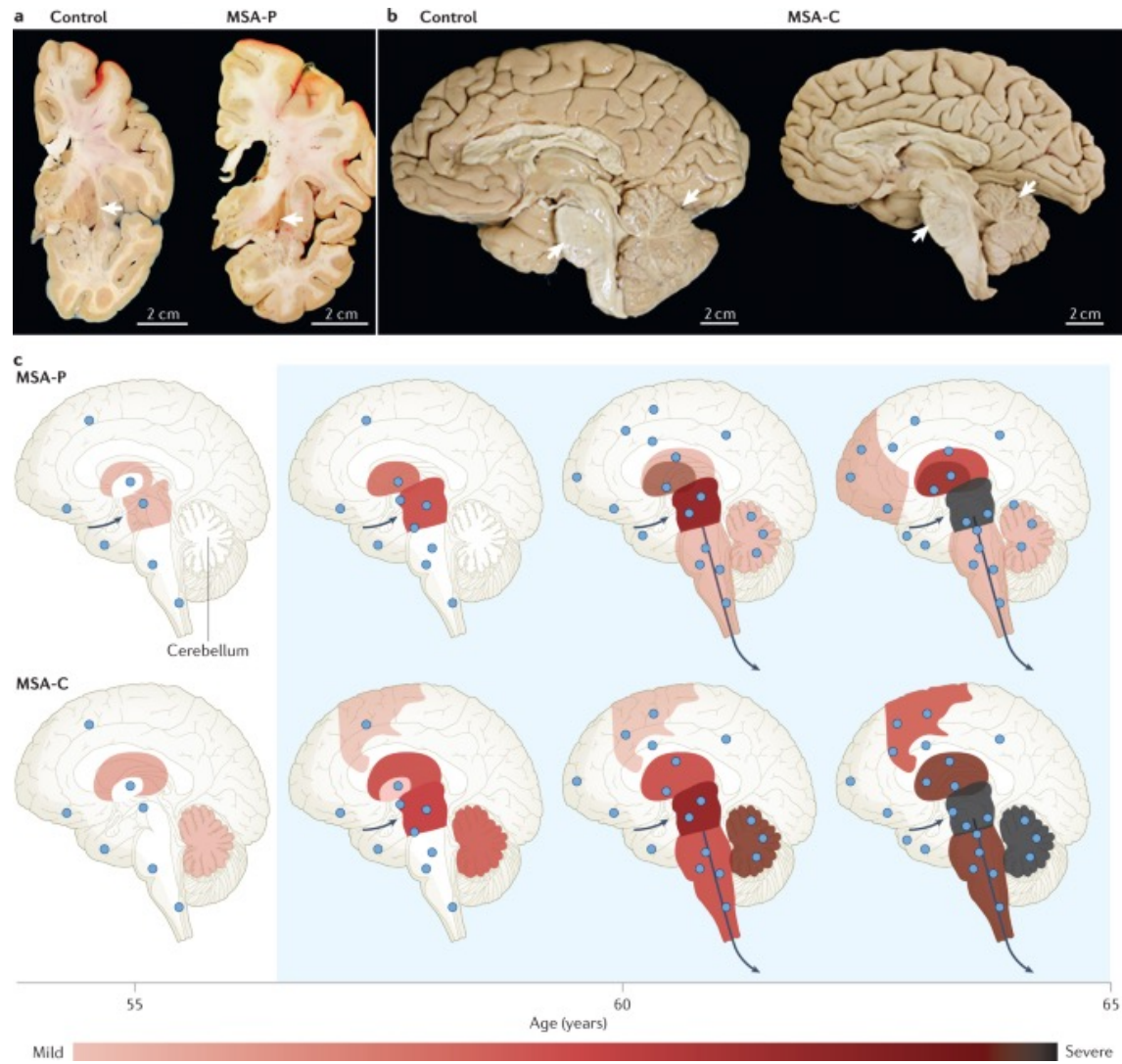
- Progressive neurodegenerative disease
- Causes parkinsonism, ataxia, autonomic and cognitive symptoms
- Pathology shows glial cytoplasmic inclusions of alpha synuclein and striatonigral and olivopontocerebellar neuronal loss
- Affects 15,000-50,000 Americans
- M:F equal
- Prevalence: 1.9-4.9 per 100,000
- Can present as early as 30s, 50s-60s more common
- Progresses on average over 6-10 years

Pathology of MSA



Burns, M. & McFarland, N.
Neurotherapeutics. 6 August 2020.

Pathological Spread in MSA



Motor Symptoms of MSA

Parkinsonism (slowness, rigidity, tremor)

Ataxia

Dystonia

Swallowing problems

Speech changes

Laryngeal stridor

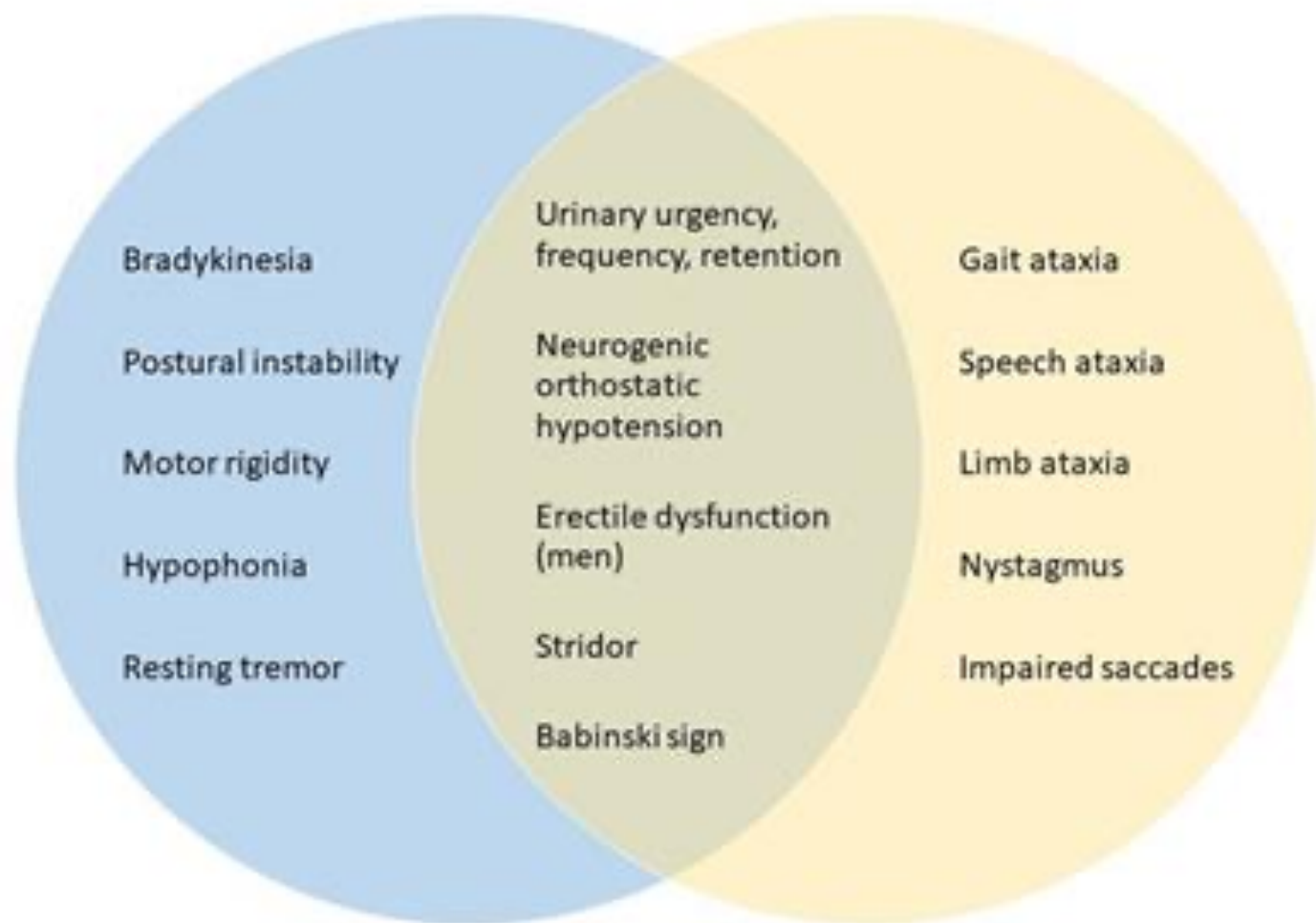
Posture changes

Gait disturbance

Dyskinesias

MSA-P

MSA-C



Parkinsonism

Parkinsonism

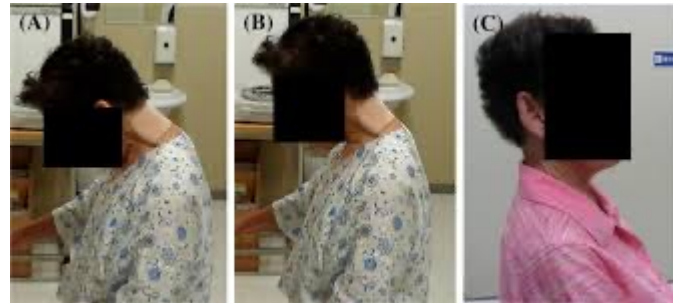


Cerebellar Ataxia

- Incoordination of fine motor movements
- Slurred speech
- Wide-based, unsteady gait
- Intention tremors in the arms
- Nystagmus



Dystonia



Rotational

Retrocollis



Laterocollis

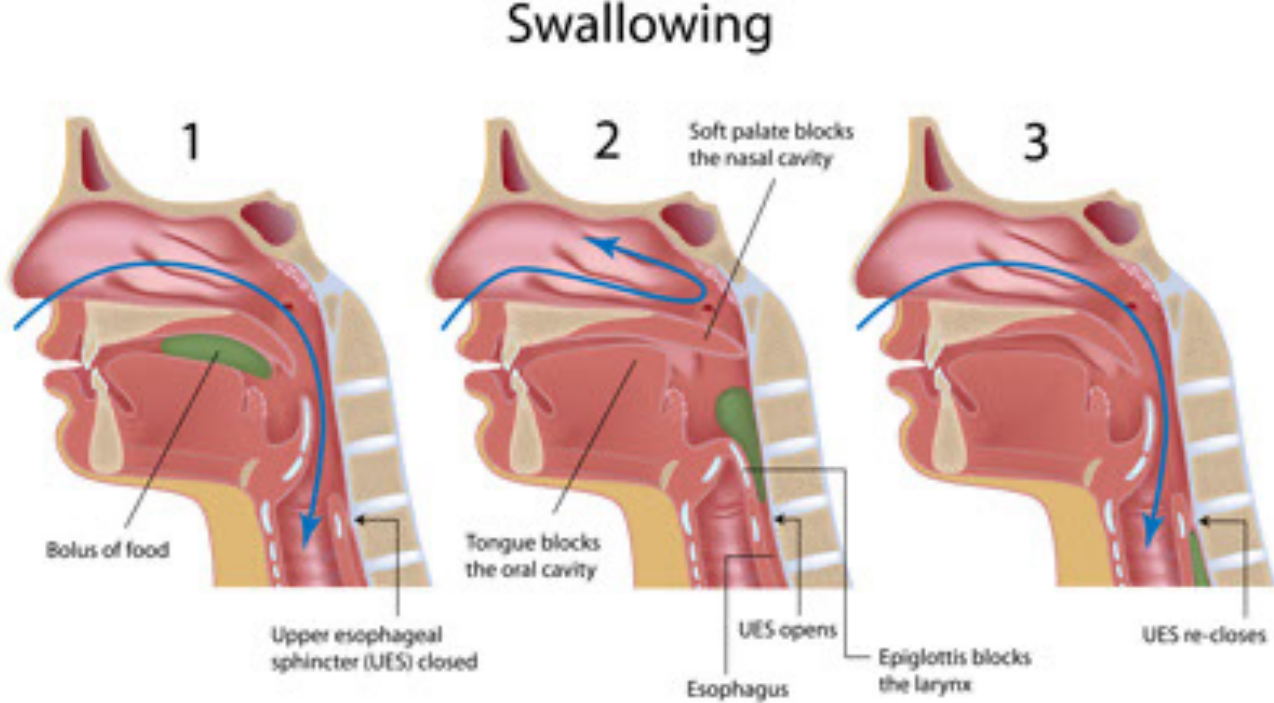
Anterocollis

Dysphagia

Symptoms of Dysphagia

- Choking on food or drink
- Coughing during or after swallowing
- Coughing or vomiting up food
- Having a weak, soft voice
- Aspirating (getting food or liquid into your lungs)
- Excessive saliva or drooling
- Difficulty chewing
- Trouble moving food to the back of your mouth
- Food sticking in your throat

Dysphagia

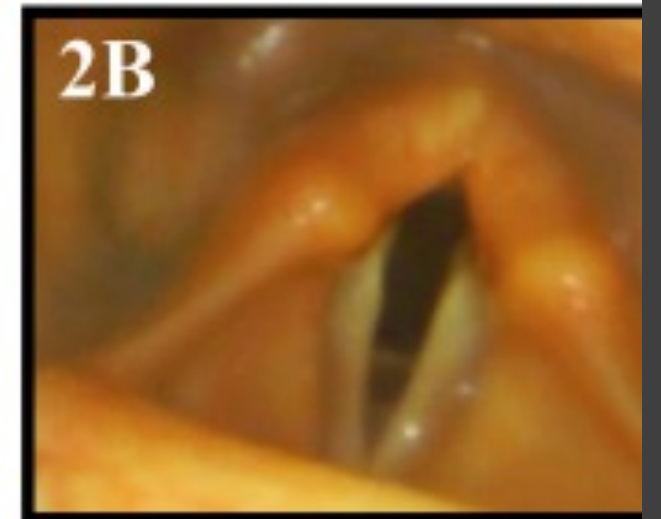
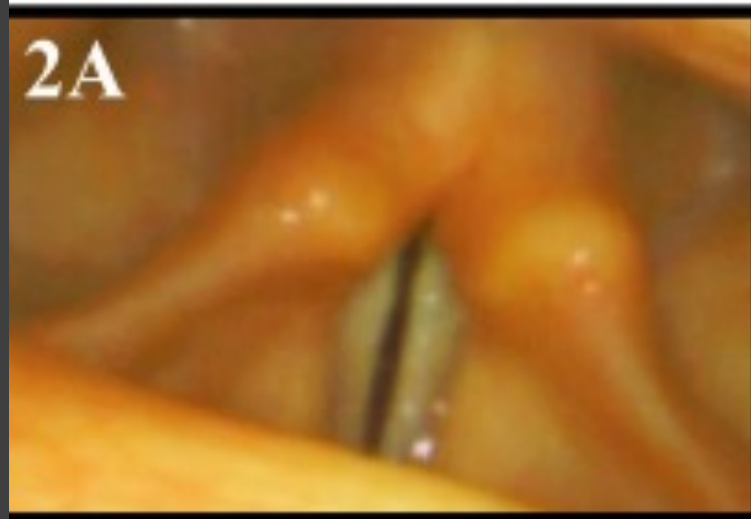
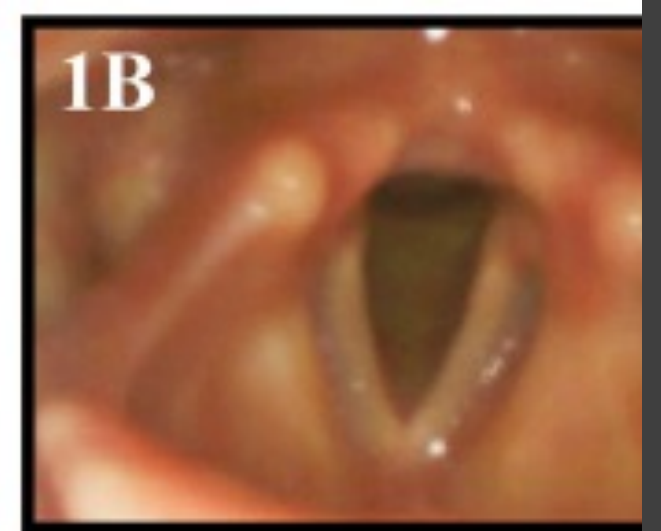


Speech Changes

- Slurring
- Decreased speed of speech
- Decreased volume
- Loss of prosody
- Lower pitch
- Scanning

Laryngeal Stridor

Warnecke, et al. (2019).
Frontiers in Neurology

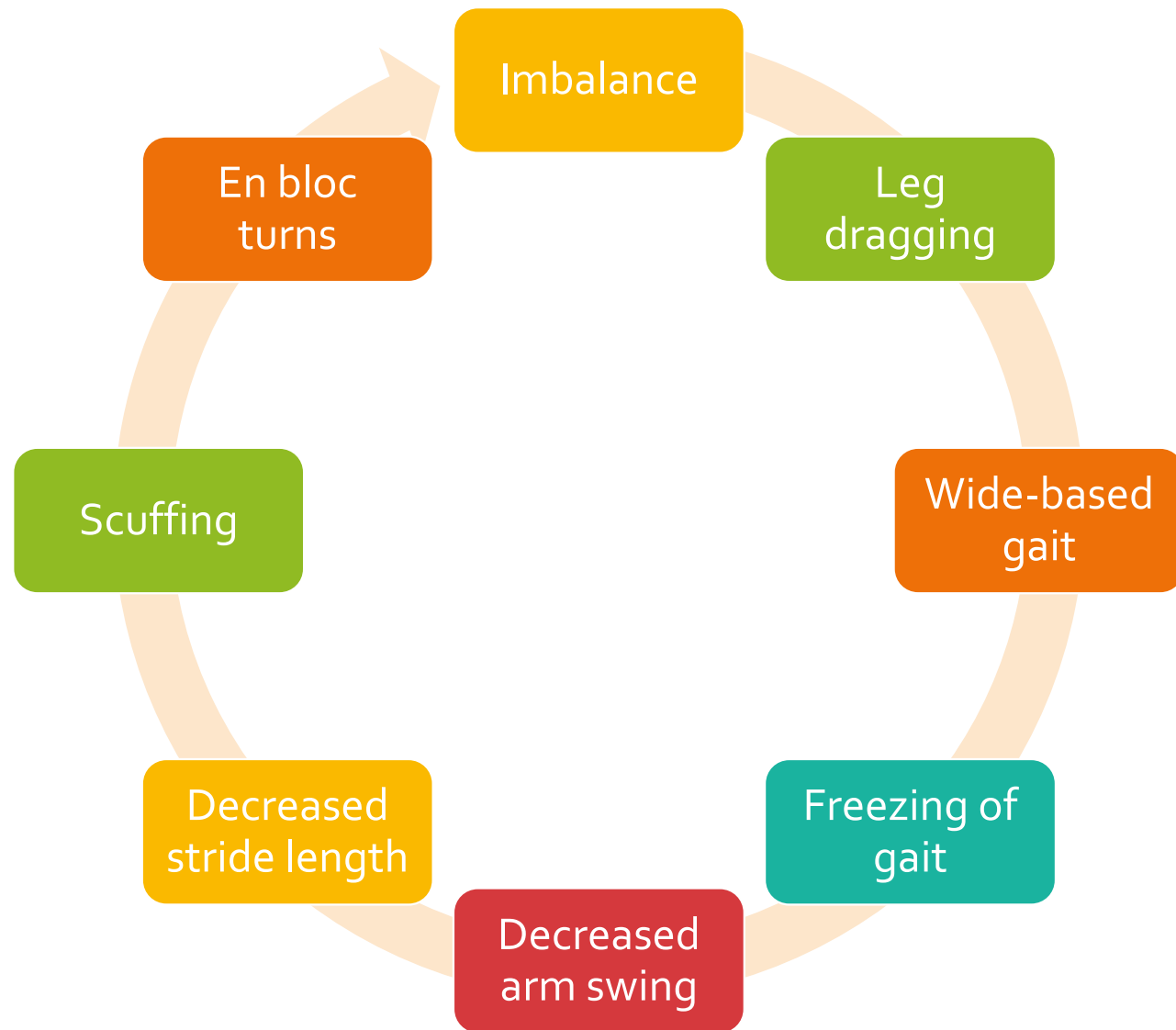


Posture Changes



*National Parkinson's
Foundation website*

Gait Disturbance



Dyskinesias

- Involuntary dance-like movements, often seen in an ON medication state
- Can occur in any part of the body
- Orofacial are common

- Sporadic disease, onset >30
- Autonomic failure
 - Urinary retention or urgency incontinence
 - Orthostatic hypotension
- Parkinsonism that is levodopa unresponsive or has cerebellar syndrome
- 2+ supportive clinical markers
- 1+ MRI markers
- No exclusion criteria

Clinical Diagnosis of MSA

*MDS Criteria
2022*

Supportive Clinical Features

Motor

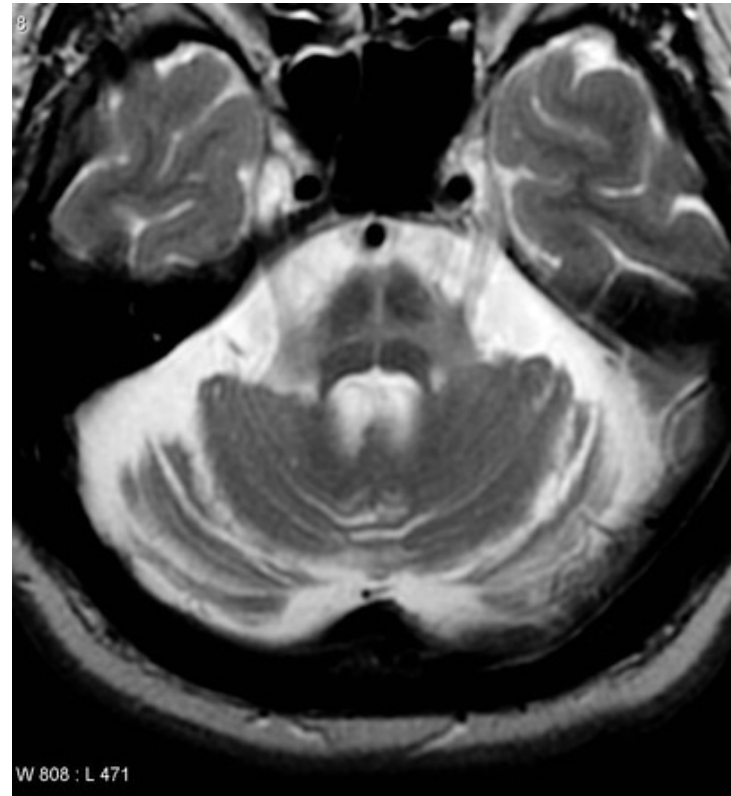
- Rapid motor progression
- Early balance issues, postural instability
- Severe speech impairment and swallowing problems within 3 years of onset
- Dystonia of the head or neck without dyskinesia in the limbs
- Babinski sign
- Myoclonus
- Jerky tremors

Non-Motor

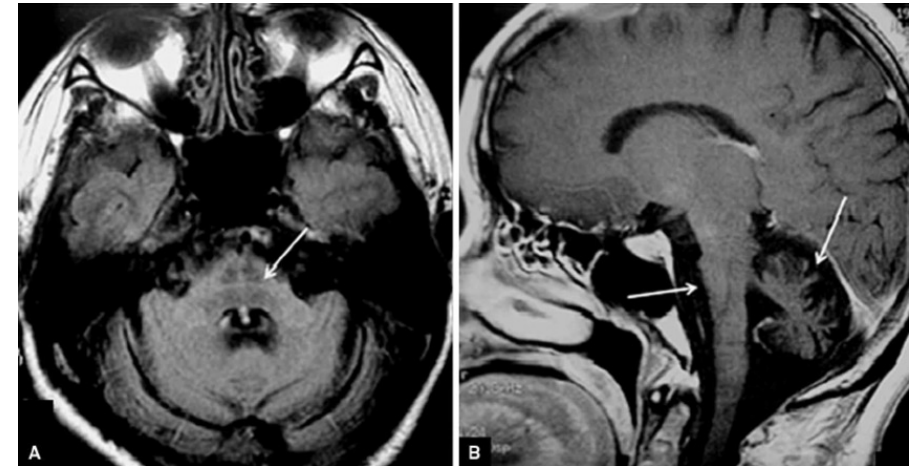
- Stridor
- Inspiratory sighs
- Cold discolored hands and feet
- Erectile dysfunction
- Emotional incontinence

Brain MRI Markers

Hot Cross Bun Sign

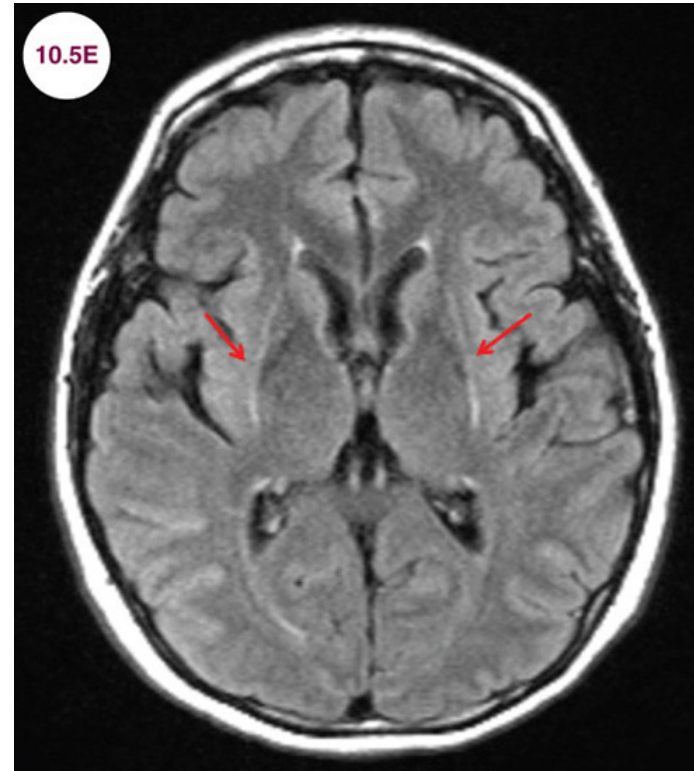


Cerebellar/Pontine Atrophy



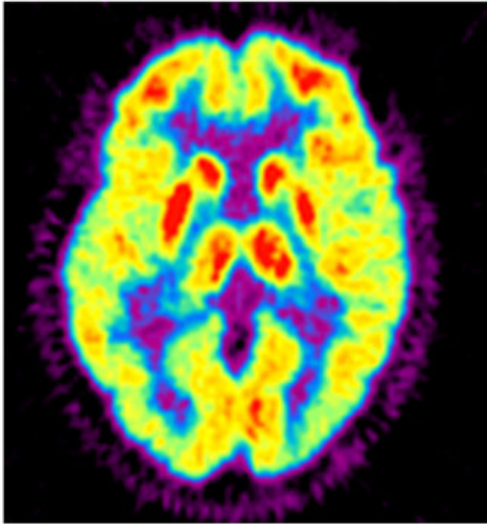
Brain MRI Markers

Putaminal Rim Sign

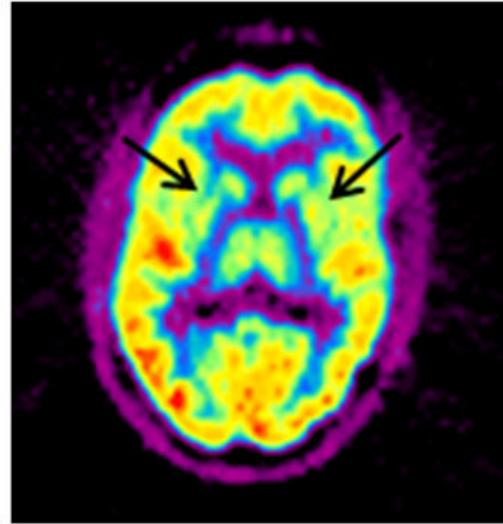


PET Scan

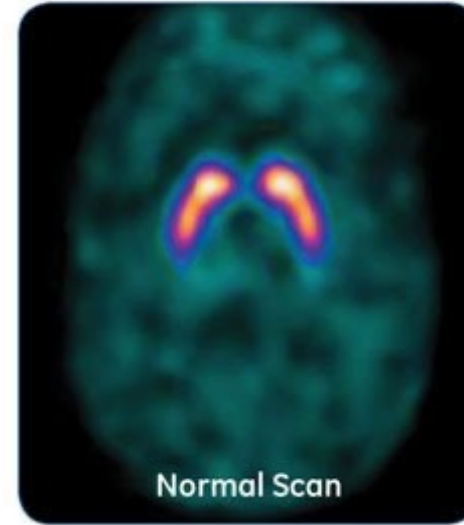
PD



MSA

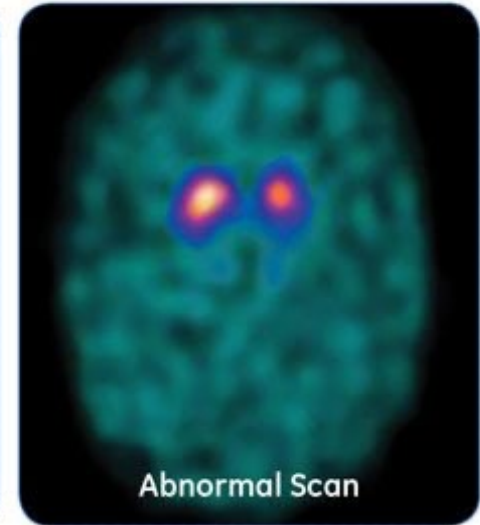


DaT Scan



Normal Scan

"Comma"-shaped
Possible essential tremor

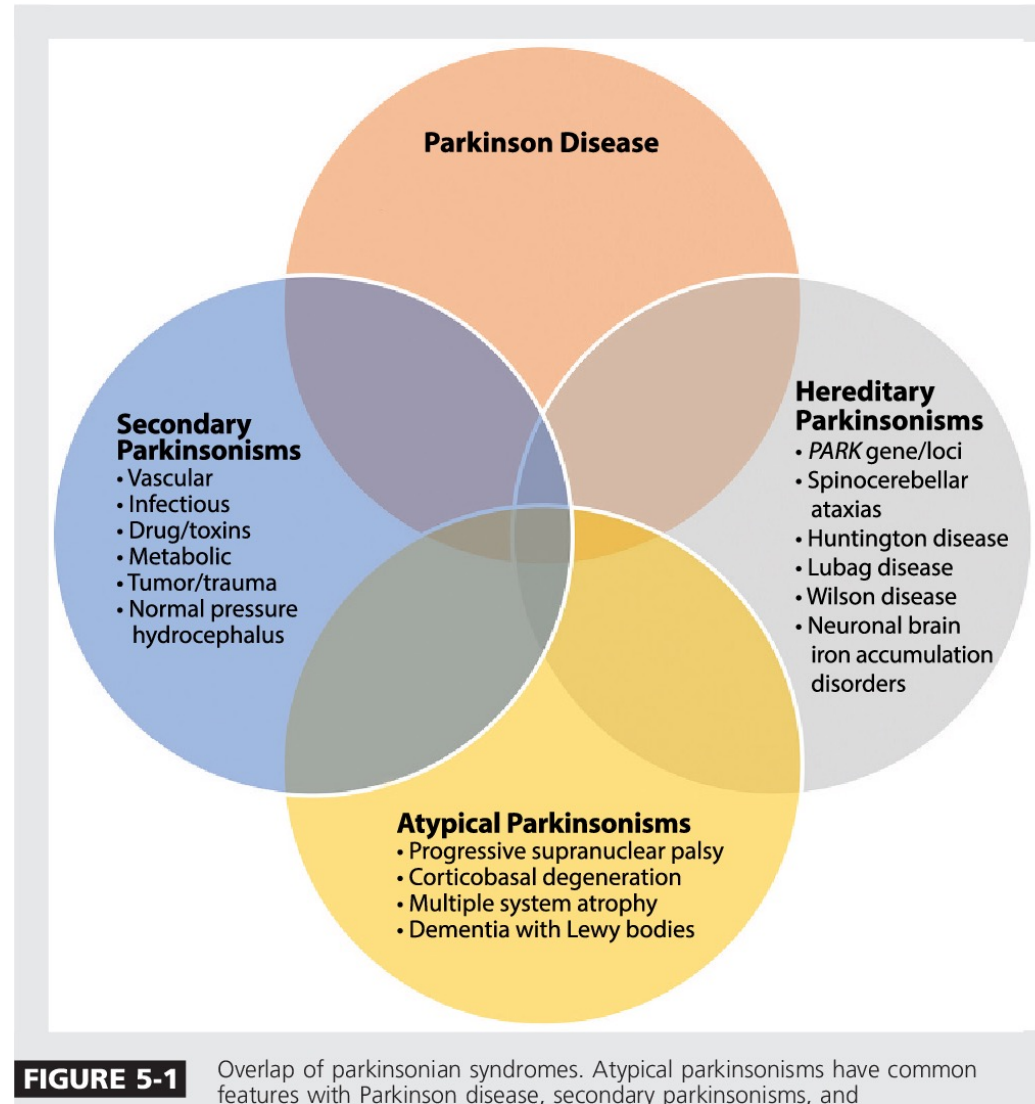


Abnormal Scan

"Period"-shaped
Possible parkinsonian syndrome

Other Diagnostics..

There can be some overlap....



McFarland, N.
(2016). *Continuum*

Management of Motor Symptoms

Aerobic Exercise

Physical Therapy

Occupational Therapy

Speech Therapy

Sinemet trial

Amantadine

Muscle relaxants

Botox injections

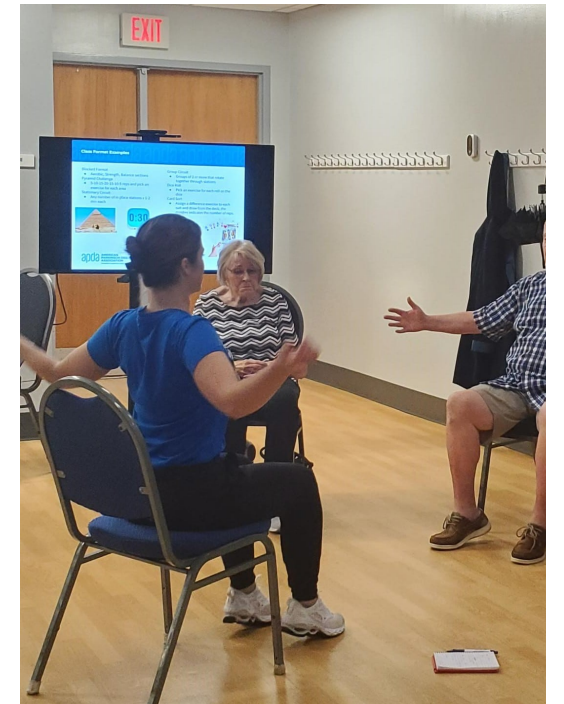
Exercise is Medicine



- Consistency: GOAL is 30 minutes per day
- Variety
- Intensity: GOAL is 80% max heart rate
- Frequency
- Social Engagement

What does a Physical Therapist do?

- Gait and balance training
- Posture exercises
- Establish home exercise program
- Suggest appropriate assistive device and train with it
- Freezing of gait techniques
- Transfer training and safety
- Fall prevention



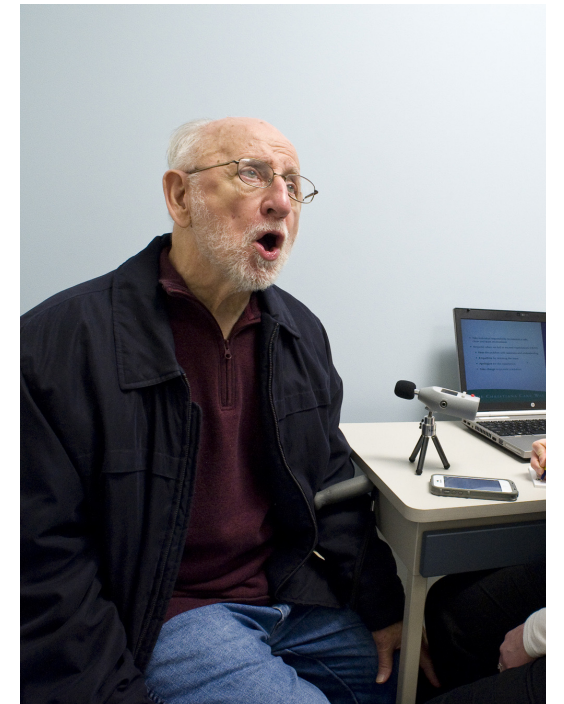
What does an Occupational Therapist do?

- Assist with maintaining functional independence of ADLs
- Fine motor skills
- Maintain hobbies that are important to you
- Driver safety assessment
- Focus on strengths
- Change your environment
- Adapt the activity



What does a Speech Therapist do?

- Helps design vocal exercises to assist with dysarthria and hypophonia
- Swallowing evaluation
- Cognitive changes
- Assistive technologies/Speech generation devices
- Alternative forms of communication



Dopaminergic Therapy Trial

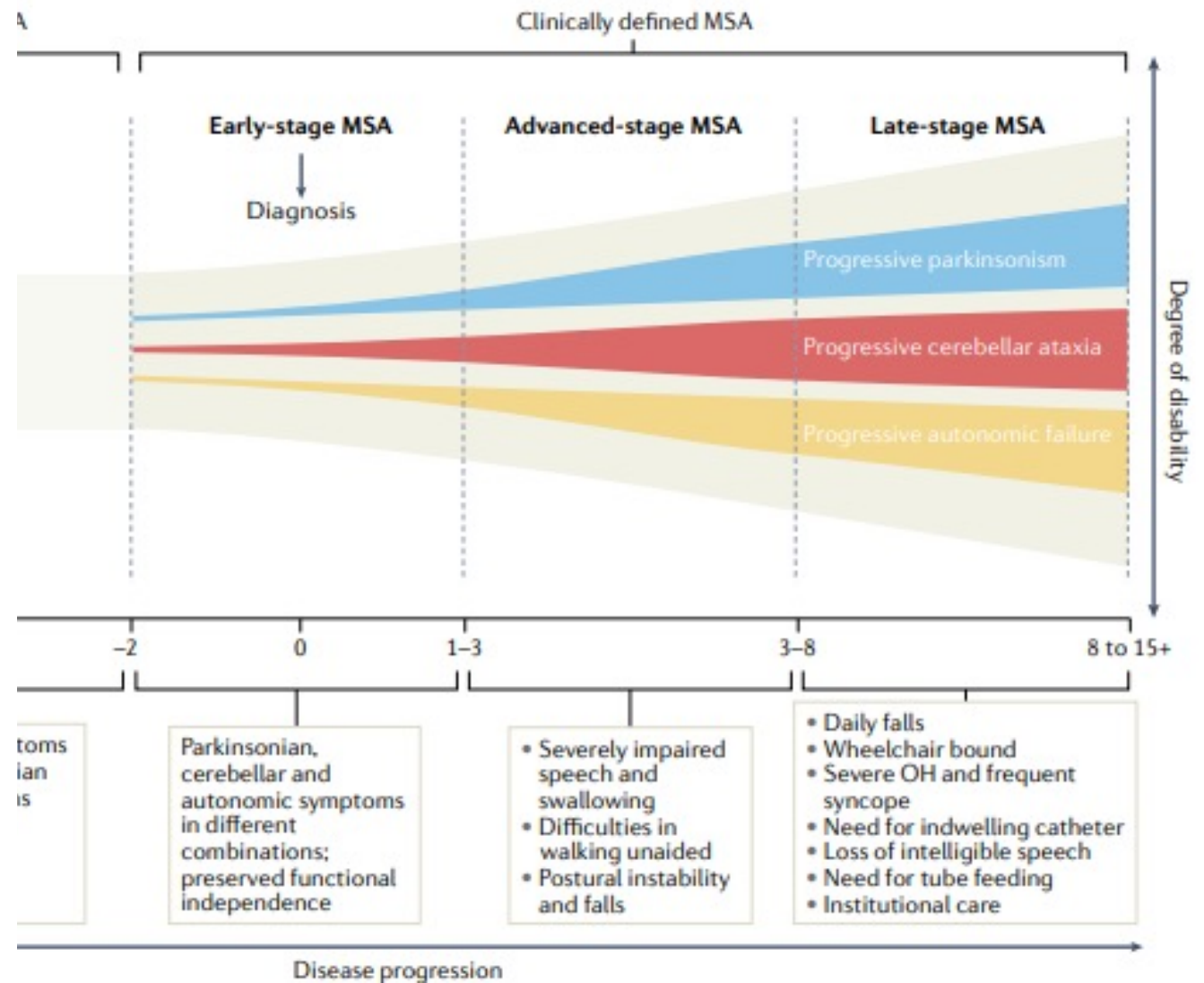
- Can be with either Sinemet IR or CR
- Slow titration up to see if clinical benefit
- 20-70% patients can see partial clinical benefit
- Side effects can include
 - Lightheadedness
 - Fatigue
 - Confusion
 - Hallucinations
 - Nausea, stomach upset
- Generally more helpful in MSA-P
- Can cause dyskinesias and motor fluctuations
- Benefit tends to wear off move time

Other Medications

- Consider amantadine for dyskinesias
- Botox injections for anterocollis or other cervical dystonia
- No strong evidence for medications for ataxia
- Muscle relaxants

Disease Progression

Poewe, et al. (2022). *Nature Reviews*.



Future Directions

- **Disease modifying therapies**
 - Stem cells
 - Ubiquinol (form of CoQ10) (small phase 3 trial completed)
 - Immunotherapy
 - Monoclonal alpha synuclein antibody- LuAF82422 (phase II)
 - Antisense oligonucleotides (ASOs) (phase 1)
 - Small molecules interfering with alpha-synuclein folding
 - Anle138b, NPT200-11A, ATH434 (all phase 1)
 - Microglial inhibitors (animal models)
- **Diagnosis and enrollment of preclinical and prodromal MSA patients in clinical trials**
- **Use of biomarkers for increased diagnostic accuracy**
 - Skin assays of alpha-synuclein
 - CSF/blood alpha-synuclein seed amplification assays

